BREAST CANCER

review articles

Impact of COVID-19 Disease in Early Breast Cancer Management: A Summary of the Current Evidence

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abstract

PURPOSE An expert panel on breast cancer and COVID-19 disease was convened to address the impact of the COVID-19 pandemic for early breast cancer (eBC) management.

METHODS To ensure that the most clinically relevant information was addressed, essential information was drawn from several of the latest national and international guidelines and another technical document. The expert panel met in five virtual closed sessions from November 2020 to May 2021 to consult on the relevant data from evidence-based results. The data gathered were discussed on an online platform.

RESULTS This article reports the expert panel's highlights of these meetings' discussions. In addition, it provides practical recommendations covering topics regarding diagnosis, treatment, and management of patients with eBC in clinical settings routinely encountered by health care professionals amid the COVID-19 pandemic.

CONCLUSION This article provided guidance on several topics regarding eBC management amid the COVID-19 pandemics to inform safer care practices.

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INTRODUCTION

In 2020, the predicted number of new breast cancer (BC) cases was 2.3 million worldwide, with an estimated age-standardized rate incidence of 47.8 per 100,000 person-years and an age-standardized rate mortality of 13.6 per 100,000 person-year with 684,996 deaths predicted.[1] The COVID-19 pandemic has challenged the medical community on many fronts, significantly affecting access to cancer diagnosis and treatment.[2] The fear of becoming infected while using health care facilities, fueled by the rising number of infected individuals seeking medical care, is one of the main factors delaying cancer diagnosis and treatment.[3-5] A significant decrease in cancer diagnoses has been observed during the COVID-19 pandemic, with the most marked decline seen in BC care (51.8%).[6]

Surgery remains the primary curative treatment for BC.[7] However, because of the COVID-19 pandemic, BC teams have been forced to review triage for surgical procedures to optimize clinical resource usage. This move has entailed assessing risks and deciding which surgery cases should be postponed,[8] such as elective surgeries[9] and taking preventive measures for potentially infected nondeferrable surgery candidates.[10,11] Brazil has registered more than 600,000 deaths, with more than 4,000 daily obits during the worst moments of the pandemic.[12] The purpose of this review is to provide an evidence-based update on the management of early BC (eBC) during the COVID-19 outbreak, with a particular emphasis on avoiding risks to both patients and health care professionals (HCPs).

METHODS

With the aim of pooling information on the host of clinical scenarios in which patients with eBC may present during the COVID-19 pandemic, a group of specialists in Brazil was invited to join an expert panel. To ensure that the most clinically relevant information was addressed, essential information was drawn from several of the latest national and international guidelines and other technical documents.[4,9,10,13-31] The data gathered were discussed on an online platform (Within3), covering topics regarding diagnosis, treatment, and management of patients with BC in clinical settings routinely encountered by HCPs amid the COVID-19 pandemic.

Thirteen recognized experts joined an online expert panel and worked collaboratively in five virtual closed sessions from November 18 to May 25, 2021, in five virtual closed sessions. A three-step process was conducted: (1) prework, in which all relevant material

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CONTEXT

Key Objective

To discuss relevant evidence-based data on the management of early breast cancer (eBC) during the COVID-19 pandemic.

Knowledge Generated

We provided expert panel recommendations regarding the best practices on eBC management during the COVID-19 pandemic, concerning both patient and health care professionals' health and safety.

Relevance

Our results contribute with evidence-based information that supports the development of protocols and algorithms to adapt the management of eBC during the COVID-19 pandemic or during times of higher restrictions.

was shared and notes on crucial aspects were acknowledged; (2) steering committee meeting, where participants discussed and shared clinical expertise, drafting recommendations; and (3) meeting convening all experts, in which a comprehensive review of all evidence provided was performed online and resultant recommendations were discussed and refined.

RESULTS

Clinical Presentation of BC

BC is a heterogeneous disease with different subtypes. Most patients with BC are asymptomatic (findings from screening mammography), whereas others may present with a palpable lump at diagnosis. eBC (stages I and II) represents more than 75% of cases in most parts of the world.[32] The management of eBC is well-defined according to international protocols.[13,14,33] Human epidermal growth factor receptor 2 (HER2)–positive and triple-negative (TN) BC are biologically more aggressive tumors, whereas luminal cancers (which express hormone receptors) are more indolent.[34] On the basis of the Ki-67 proliferation index, the St Gallen Consensus defines two luminal subtypes: luminal A (better prognosis) and luminal B (more aggressive disease).[34] Surgery is the mainstay treatment for eBC, and the procedure may be performed upfront or after neoadjuvant therapy (chemotherapy or endocrine therapy). As a rule, HER2-positive, luminal B, and TN patients are priority categories for urgent BC therapy.[33]

Pathophysiology

Patients with cancer have dysregulated immunity with depleted immune cells, such as CD8+ T cells, CD4+ T cells, natural killer cells, and others.[35] COVID-19 disease in patients with cancer significantly increases inflammatory factors and cytokines (high-sensitivity C-reactive protein, procalcitonin, interleukin [IL]-2, IL-6, and IL-8), possibly explaining the poorer prognosis in individuals with cancer relative to those without cancer.[36] SARS-CoV-2 infection can enter the cell by mediating spike proteins using the angiotensin-converting enzyme 2 receptor via plasma membrane fusion or endosomes.[37] SARS-CoV-2 infection stimulates the innate immune system and antigen-specific responses of B and T cells through a mechanism similar to that seen for the influenza virus.[38] The development of virus-neutralizing antibodies is essential for protection against viral infections, and clinical studies of SARS-CoV-2 vaccines have been pursuing this therapeutic target.[39]

Management

Assessment and diagnosis. In the context of the COVID-19 pandemic, the management of patients with eBC has become more complex, as SARS-CoV-2 infection can be symptomatic or asymptomatic.[40] A summary of the recommendations discussed in the sections below is presented in Table 1.

The diagnosis of SARS-CoV-2 infection can be established on the basis of the reverse transcription-polymerase chain reaction (RT-PCR) test for symptomatic or asymptomatic patients exposed within 5-10 days to SARS-CoV-2–infected individuals.[49,50] An RT-PCR should be performed, when available, 24-48 hours before the surgery and 14 days after self-isolation.[15] Considering that RT-PCR has a false-negative rate of 20%-30%,[51] $<$ 10% of COVID-19–infected patients will inadvertently undergo surgery during the incubation period with this approach.[16]

Serologic tests can be used for screening symptomatic patients after day 10 of symptoms as an alternative method to RT-PCR for COVID-19 diagnosis (gold standard).[50] However, serologic tests alone are not recommended because they are less sensitive before 10 days of symptom onset and given the possibility of false positives.[22]

Another practical approach is to assess eBC management in those cases with SARS-CoV-2 test results available (positive or negative) and a more controversial clinical scenario (Table 2). The risk of overall postoperative mortality is increased up to 6 weeks after SARS-CoV-2 infection.[52] However, longer delays could negatively affect disease progression and patient outcome.[53] This delay should be considered when deciding whether to postpone elective and nonurgent eBC surgeries in patients with preoperative positive SARS-CoV-2 diagnosis.

In addition, the decision to defer a surgical operation because of COVID-19 disease should be based on positive RT-PCR results (or antigen point-of-care [POC] tests when RT-PCR is unavailable) and clinical symptoms. Serologic

TABLE 1. Summary of Specialist Panel Recommendations

Topic	Recommendation
Assessment and diagnostic	RT-PCR is the gold standard for COVID-19 diagnosis. An RT-PCR should be performed, when available, 24-48 hours before the surgery and 14 days after self-isolation.
	Serologic tests can be used for screening symptomatic patients after day 10 of symptoms as an alternative method to RT-PCR for COVID-19 disease.
	The POC antigen test is a viable approach when RT-PCR is unavailable.[18] There was no consensus regarding the utility of POC antibody tests.
Neoadjuvant therapy	Neoadjuvant therapy is used to allow the delay of surgery. NET and NCT appear to be safe choices to postpone nonurgent surgeries,[41] and G-CSF can be used to diminish neutropenia. Chemotherapy schedules may be modified to minimize hospital visits[42]
	The panel recommends that the management of the axilla after neoadjuvant therapy with positive SLN should be discussed on a case-by-case basis to assess the possibility of omitting AD, especially after NET. AD is not recommended if the SLN is negative at the time of surgery[43]
Radiotherapy	Hypofractionated schemes are used to minimize the number of visits to radiotherapy centers. Radiotherapy could be omitted after surgery in > 65-year-old patients with < 2 cm HER2-positive tumors and negative axilla.[44,45]
Breast surgery	The risk of contamination for less invasive surgeries, such as BCS, is low. Whenever possible, more conservative surgeries should be indicated. The panel suggests caution in recommending major surgery (such as mastectomies) during the pandemic.
	Contralateral prophylactic mastectomy is not recommended during the pandemic period. BCS, or even unilateral mastectomy, should be considered as a replacement. Immediate breast reconstruction should be evaluated on a case-by-case basis, considering local sanitary conditions.
COVID-19 vaccines and eBC	Patients with eBC should take the COVID-19 vaccine as soon as it is available and complete the vaccination scheme. If mammography is planned at the time of vaccination, it should be performed before vaccination, because of reports of RNA vaccine–related axillary adenopathy 2-4 days after vaccination.[46-48]

Abbreviations: AD, axillary dissection; BCS, breast conservative surgery; eBC, early breast cancer; G-CSF, granulocyte colony-stimulating factor; HER2, human epidermal growth factor receptor 2; NCT, neoadjuvant chemotherapy; NET, neoadjuvant endocrine therapy; POC, point-of-care; RT-PCR, reverse transcriptase polymerase chain reaction; SLN, sentinel lymph node.

testing results should not guide decision making, considering increased seroconversion of the population as vaccination progresses and other issues related to antibody tests discussed below.

Considerations on POC antigen and antibody testing as a replacement for RT-PCR. Antigen detection for the diagnosis of SARS-CoV-2 infection using POC tests provides a workable solution that could enable patients to self-isolate earlier and reduce the spread of infection,[17] representing an option accessible to most outbreak areas compared with standard nucleic acid amplification tests, such as RT-PCR assays.[18] However, the trade-off is a loss of sensitivity compared with nucleic acid amplification tests, particularly among asymptomatic patients.[54] Trained professionals should carry out these tests.

The POC antigen test is a viable approach when RT-PCR is unavailable in the following scenarios[18]:

- Patients presenting with 5- to 7-day onset of symptoms;
- Positive results need confirmation by RT-PCR assays (ideally);
- Outbreak areas and remote settings, where POC testing constitutes an alternative to RT-PCR.

On the other hand, serology tests have limited application diagnosis-wise, particularly in the acute phase,[55] as most patients will develop an antibody response within 1-3 weeks after infection.[19] Crucial windows of opportunity for clinical intervention and isolation measures might have already been missed.[19]

There is also a possibility of cross-reaction with other pathogens, such as other human coronaviruses, increasing the odds for false positives.[55] There was no consensus among the experts regarding the clinical utility of POC antibody tests. Some authors agreed that this technology could be considered in some situations, despite its limitations in[19]

- determining the extent of infection in patients not diagnosed using RT-PCR,
- determining infection fatality rate, and
- supporting the development of vaccines.

Treatment

Neoadjuvant therapy to allow the delay of surgery. The clinical management guidelines for BC were recently updated in the COVID-19 era. Clinical cases eligible for neoadjuvant treatment are[9,24] as follows:

- TNBC, HER2-positive, and luminal B tumors ≥ 2 cm and/or with positive axilla (≥ N1).
- Luminal A tumors stage T1-T2 and N0-N1 (neoadjuvant endocrine therapy [NET] may be recommended, especially in postmenopausal patients).
- Inflammatory and locally advanced BC (NET or neoadjuvant chemotherapy [NCT]).

TABLE 2. SARS-CoV-2 Test Results in Specific eBC Clinical Scenarios

SARS-CoV-2 test	Clinical Scenario	Notes
Positive RT-PCR	eBC surgery planned	Defer elective eBC surgeries. There is no clinical recommendation to perform primary surgery in patients with eBC who test positive on RT-PCR for COVID-19 disease. The expert panel recommended deferring elective surgery for at least 30 days in asymptomatic patients.[52]
RT-PCR results pending	Patient with BC symptomatic for COVID-19 disease and positive epidemiology history for COVID-19 disease exposure	
Negative RT-PCR and positive serologic test	Patient with BC symptomatic for COVID-19 disease	As vaccination progresses, situations where the patient has already received the full vaccination schedule will be common. Serologic tests may be positive for this patient profile (vaccine immunity), detecting vaccine antigenic targets or even a previous COVID-19 disease (natural immunity). This clinical scenario involving a symptomatic patient and negative RT-PCR will likely reflect diagnosis of an acute infectious disease diagnosis other than COVID-19 disease. Any patient with respiratory tract infections should have elective surgery postponed until symptom resolution.[41]
Negative RT-PCR	Patient with BC symptomatic for COVID-19 disease and urgent surgery indication	Patients with urgent indications (eg, revision of an ischemic mastectomy flap and surgical evacuation of breast hematoma)[9] should be submitted to surgery regardless of COVID-19 status, proceeding with all recommended precautions regarding PPE and patient logistics.[10,24]
Negative RT-PCR	Patient with BC symptomatic for COVID-19 disease	RT-PCR test confirmation is crucial; therefore, the expert panel recommends postponing nonurgent hospital procedures for 10-14 days after symptom onset and 20 days for persistent symptoms. After that, the test is repeated. Patients with respiratory tract infections should have elective surgery postponed until symptom resolution.[41]
Negative serologic test	Patient with BC symptomatic for COVID-19 disease	Serologic testing should not be used to establish the presence or absence of COVID-19 disease or COVID-19 reinfection.[23] Symptomatic patients should be diagnostically confirmed by RT-PCR.[23] Patients with respiratory tract infections should have elective surgery postponed until symptom resolution.[41]

Abbreviations: BC, breast cancer; eBC, early breast cancer; PPE, personal protective equipment; RT-PCR, reverse transcription polymerase chain reaction.

- Any type—to complete NCT that has already been initiated.

Specifically, for estrogen receptor–positive and HER2-negative patients, both the European Society for Medical Oncology and the American Cancer Society have stated that NET is an option to enable deferral of surgery by 6-12 months in clinical stage I or II BCs according to menopausal status.[23,24] In addition, the Johns Hopkins Women's Malignancies Program has developed a guideline for BC management during the COVID-19 pandemic on the basis of tumor biology and stage.[56]

Although constraints are often present in terms of resources, workforce, and hospital bed availability in the COVID-19 pandemic, causing a delay in procedures, both NET and NCT appear to be safe choices to postpone surgery in nonurgent indications of estrogen receptor–positive early-stage BC, also potentially contributing to a reduction in outpatient visits.[41]

When NCT is proposed, there is a suggestion for using granulocyte colony-stimulating factor as support to diminish neutropenia.[42] Regarding choices of chemotherapy regimens for early-stage BC, especially for TN, luminal B, and HER2-positive BCs, the recommendation is to follow the usual guidelines for these biologic subtypes. Chemotherapy schedules may be modified from weekly to every 3-week schedule, for example, to minimize hospital visits.[42]

Managing axilla after neoadjuvant systemic therapy. As sentinel lymph node biopsy (SLNB) techniques become more widely practiced, invasive surgical methods for nodal staging such as axillary dissection (AD) are progressively de-escalated and restricted to specific scenarios.[57] Surgeries have been a concern because of the risk of patient infection and human and resource restrictions during the COVID-19 pandemic. A multicenter retrospective study demonstrated that perioperative COVID-19–positive patients who underwent hip fracture surgeries had significantly higher postoperative morbidity and mortality.[58]

According to the panel, AD is not recommended if SLNB is negative at surgery, even in the previously positive axilla. However, if the sentinel lymph node (SLN) is positive, the course of action should be discussed on a case-by-case basis, especially after NET.[43]

Studies of adjuvant therapy in residual disease cases after NCT[59-61] have demonstrated the importance of minimizing SLNB false-negative rates (FNRs).[61] Failure in identifying residual disease in the axilla may alter clinical outcomes, as these patients would not be selected for additional treatment with trastuzumab emtansine, capecitabine, or olaparib. On the other hand, using chemotherapy regimens with lower odds of immunosuppression during the pandemic could decrease the complete pathologic response rate (pathologic complete response [pCR]) in these patients. An option to minimize the negative impact of modified chemotherapy regimens over pCR in axilla-positive patients during the pandemic is to clip the lymph node before NCT. This approach reduces the FNR from 2% to 8%.[62,63] Another alternative would be to perform SLNB with dual tracer. A meta-analysis of 1,921 patients showed an 11% FNR with dual tracer and 4% when three or more lymph nodes were harvested for biopsy.[64] It is worth highlighting that assessing the breast sample is crucial to identify residual disease, as it is uncommon to simultaneously observe breast pCR and residual disease in the axilla.[65]

With the increasing interest in omitting AD after NCT in the past few years, even in patients with residual disease on SLNB, a recent American study demonstrated that the use of isolated positive SLN after NCT has an upward trend after publication results of ACOSOG Z0011.[66,67] The Z0011 study demonstrated excellent local and locoregional control with isolated sentinel lymph node biopsy but excluded patients who underwent neoadjuvant systemic treatment (NCT or NET).[67] In women undergoing NCT, the residual axillary disease can be associated with resistance, and there are no data on cancer safety when omitting AD at this time.

A retrospective review evaluated residual disease burden in positive SLN after NCT. It demonstrated an additional high disease burden, whether micrometastasis (59%) or macrometastasis (63%), possibly an indication for AD.[68] Another analysis showed that the likelihood of non–SLN-centered metastasis at axillary lymph node dissection was high across all tumor subtypes.[69] The core point is whether AD would play a role in residual lymph node disease cases or whether axillary radiation therapy could replace surgery in such cases. For instance, a retrospective study using data from the National Cancer Database (NCDB), with 1,617 women with N1 disease after NCT, compared patients who received AD associated with nodal radiotherapy with those who received only SLNB and radiotherapy, similar to the design of an ongoing randomized study of the ALLIANCE group (A11202)[70] showing increased survival in women undergoing AD.[71] However, in an exploratory analysis, the authors found that SLN was comparable with AD in luminal tumors with single metastases. The panel recommends caution in omitting AD in such cases.

On the other hand, after NET, pCR is generally not expected after systemic treatment.[72] The question is whether these patients match the ACOSOG Z0011 study profile or otherwise. The data in this scenario are limited. A study using the NCDB and Dana-Farber/Brigham and Women's Cancer Center database evaluated tumor burden after NET and the type of axillary surgery performed (SLNB or AD): more than 90% of patients who had cN0 axilla at initial presentation, in both cohorts, they had < 3 positive lymph nodes in the final pathology, with no difference in overall survival regardless of the type of axillary surgery.[43] In another study, using the NCDB for stages 2 and 3, SLNB use after NET was similar to that for upfront surgery and, among those with pathological node-positive disease, the NET patients were less likely to undergo AD.[73] In this scenario, the panel recommended a case-by-case assessment, with the possibility of omitting AD, especially in the initially clinically negative axilla. As NET and NCT become more common approaches during the COVID-19 pandemic, understanding nodal staging in these scenarios is even more relevant.

Radiotherapy. COVID-19 is a highly transmissible disease. Potential outbreaks within health care facilities such as radiotherapy services have been a concern since the pandemic, as inpatients and outpatients outside of COVID-19–restricted areas can get ill or further bring the virus to their communities. Thus, the panel recommended using hypofractionated schemes to minimize the number of visits to radiotherapy centers. Five-fraction schemes once a week for 5 weeks (FAST trial)[74] or daily fractions for one week (FAST forward trial)[75] would be viable options for breast conservative surgery (BCS) in patients with negative axilla. A controversial topic is hypofractionation in chest wall after breast reconstruction. The panel believes that hypofractionation would be acceptable (eg, 15 fractions for three weeks)[44] in this pandemic context. Elderly patients (> 65 years old) with < 2 cm HER2-negative tumors and negative axilla could have radiotherapy omitted after conservative surgery.[45]

Management of breast cancer surgeries in hospital restriction scenarios. The COVID-19 pandemic has demanded hospitals reallocate health care resources, with a sudden reorganization of all clinical activities, including oncologic units.[76] The restrictions differ depending on the regional level of acuity of the pandemic and resources availability.

BCS and risk of infection by COVID-19 disease. BCS is associated with lower rates of hospital stay and visits after surgery and hospitalization than mastectomy[77]: a study with patients undergoing nipple-sparing mastectomy had total complication rates of 47% and reoperations around 9%.[78] Regarding the use of oncoplastic surgery, complication rates also tend to be higher than in BCS. In a study using the American College of Surgeons National Surgical Quality Improvement Program database, complications within 30 days were more significant in patients undergoing oncoplastic surgery than BCS

(3.8% *v* 2.6%; $P < .001$).[79] Another prospective cohort (TeaM Study) identified a reoperation rate of 2.8%.[80] In a survey conducted during the pandemic among mastologists from the Brazilian Society of Mastology, 75% of surgeons would recommend partial reconstruction after BCS; however, 54% of those would contraindicate mammoplasty techniques during the pandemic.[81] The panel recommends caution in recommending major surgery during the pandemic.

Although there are still limited data on this subject, it is possible to infer that the risk of contamination for less invasive surgeries, such as BCS, is low because of risks of procedure complications and lower surgery time. In addition, all precautions mentioned previously should also be taken for this surgical procedure.

Elective surgeries that cannot be delayed. Elective surgeries, by definition, can be postponed for up to 8 weeks. A few elective situations are considered essential and require planned or immediate medical assistance surgery-wise. Emergency or urgent surgeries might compromise patient survivorship if not performed. Examples of this type of surgery are a revision of an ischemic mastectomy flap, surgical evacuation of breast hematoma, drainage of breast abscess, and revascularization of an autologous tissue flap.[9]

Bilateral mastectomy. Regarding patients with contralateral prophylactic mastectomy in unilateral BC indication, although there are still limited data on this subject, historically, these cases have a more extended hospital stay than to breast-conserving surgery or unilateral mastectomy and have more postsurgery visits and higher rates of hospitalization.[77] This potential increase in patient exposure could lead to a greater risk of infection by COVID-19 disease.[25] The expert panel suggested that a contralateral prophylactic mastectomy is not recommended during this period, and conservative breast surgery or even unilateral mastectomy should be carried out instead. The panel recommended that immediate breast reconstruction is evaluated on a case-by-case basis, according to the local conditions or resource availability because of the pandemics.

COVID-19 vaccines and breast cancer. According to the panel, patients with BC should receive the COVID-19 vaccine as soon as it becomes available since benefits are likely to outweigh the risks of adverse effects from SARS-CoV-2 vaccination.[82] The National Comprehensive Cancer Network and the European Society for Medical Oncology recently reinforced this position.[26,27] It is essential to point out that limited clinical data support COVID-19 vaccination in patients with cancer.[83] A multicenter, observational, prospective study has shown that SARS-CoV-2–specific immunoglobulin G antibody response after natural infection does not differ in patients with cancer and healthy control patients.[84] Two prospective observational studies have demonstrated that oncologic patients develop poor SARS-CoV-2 spike protein seroconversion after one dose of the BNT162b2 (Pfizer–BioNTech, Mainz, Germany) vaccine, but remarkably increased after the second dose, highlighting the importance of completing the vaccination scheme.[85,86] However, it is uncertain whether long-term protection can be achieved in the oncologic population, as these studies rely on immunogenicity data alone, and real-world data on the long-term protection of vaccinated cancer patients against COVID-19 disease are limited.[83] In the same vein, data from influenza vaccinations indicate the development of a protective immune response in patients with cancer, and, although potentially not the same level as the general population, it is generally safe.[28,87-89] Again, there are long-term uncertainties, and the protection may vary depending on antineoplastic therapies, administration timing, disease stage, and comorbidities.[90]

It is important to note that patients who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment should defer vaccination for at least 90 days as stated by the Centers for Disease Control and prevention recommendations.[29] After the final dose is received, an individual is considered fully vaccinated after a minimum of 2 weeks.[30] If the patient is asymptomatic and has not been in close contact with someone with SARS-CoV-2 infection in the past 14 days, the panel deemed it safe to conduct a surgical procedure. Patients with cancer and surgical patients, especially those undergoing chemotherapy or with chemotherapy planned within 8 weeks, are confirmed to be particularly at risk of infection and might have a negative outcome.[91] A prospective cohort demonstrated that 30-day adjusted mortality was higher in patients with preoperative SARS-CoV-2 infection who had surgery 0-2 weeks, 3-4 weeks, and 5-6 weeks after the diagnosis of the infection (odds ratio [95% CI], 4.1 [3.3 to 4.8]; 3.9 [2.6 to 5.1], and 3.6 [2.0 to 5.2], respectively) compared with the mortality rate in patients without preoperative SARS-CoV-2 infection of 1.5% (95% CI, 1.4 to 1.5).[52]

Vaccination reduces the odds of SARS-CoV-2 infection and negative outcomes of COVID-19 disease. The expert panel recommends that patients with eBC take the COVID-19 vaccine as soon as it is available to them and complete the vaccination scheme. Indeed, they are considered a priority group in national vaccination strategies.[92] Although vaccinated individuals have a lower risk, the panel states that patients with eBC should keep social distancing, masks, and other protective measures. Table 3 summarizes the main vaccines approved worldwide on January 17, 2022.

Recently, an unexpectedly high incidence of axillary adenopathy findings after Moderna and Pfizer-BioNTech COVID-19 vaccines occurred.[46] A solicited adverse event for patients receiving the Moderna vaccine was reported in 11.6% versus 5.0% for placebo after dose 1 and 16.0% versus 4.3% for placebo after dose 2.[47] Adenopathy occurred in the arm and neck 2-4 days after vaccination with a median duration of 1-2 days.[46] For those receiving the

TABLE 3. COVID-19 Vaccine Candidates Approved[a]

Manufacturer	Vaccine	Mechanism of Action	Patients With Cancer Enrolled?
AstraZeneca/University of Oxford	AZD-1222	Viral vector	Only if malignancy with low potential risk for recurrence after curative treatment or metastasis (eg, indolent prostate cancer) at investigator discretion
Sinovac Biotech	CoronaVac	Inactivated virus	No
Pfizer/BioNTech	BNT162b2	Lipid nanoparticle–encapsulated mRNA	No
Moderna/NIAID	mRNA-1273	Lipid nanoparticle–encapsulated mRNA	No
Gamaleya Research Institute	Sputnik V	Viral vector	No
Novavax	NVX-CoV2373	Recombinant protein	Only if basal cell carcinoma of the skin and cervical carcinoma in situ, at investigator discretion
Center for Genetic Engineering and Biotechnology of Cuba	Abdala	Recombinant protein	No
Instituto Finlay de Vacunas	Soberana 2	Recombinant protein	Only with stabilized disease and not undergoing chemotherapy/radiotherapy in the past 3 months
Beth Israel Deaconess Medical Center and Janssen	Ad26.COV2.S/JNJ-78436735	Inactivated virus	Only if squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix or other malignancies with minimal risk of recurrence
CanSino Biologics	Convidecia/A d5-nCoV	Viral vector	Only if basal cell carcinoma of the skin and cervical carcinoma in situ
Anhui Zhifei Longcom	ZF2001/RBD-Dimer	Recombinant protein	Only if basal cell carcinoma
Beijing Institute of Biological Products (Sinopharm)	BBIBP-CorV (Vero Cells)	Inactivated virus	No
Wuhan Institute of Biological Products (Sinopharm)	BBIBP-CorV (Vero Cells)	Inactivated virus	No
Bharat Biotech	Covaxin/BBV152A, B, C	Inactivated virus	No
Chumakov Center	KoviVac/CoviVac	Inactivated virus	Only if nonmelanoma skin cancer or cervical carcinoma in situ

[a]Data updated on January 17, 2022.

Pfizer-BioNTech vaccine, resultant lymphadenopathy lasted for a mean of 10 days. However, in the Pfizer-BioNTech study, adenopathy was only reported as an unsolicited adverse event.[46] A single-institution report found similar findings, and the authors are considering magnetic resonance imaging–detected isolated unilateral lymphadenopathy ipsilateral to the vaccination arm to be most likely COVID-19 vaccine–related if within 4 weeks of either dose.[48]

Five cases of COVID-19 vaccine–related axillary lymphadenopathy that mimicked metastasis in a vulnerable oncologic patient group have been described.[93] Because of widescale vaccination, axillary lymphadenopathy because of COVID-19 vaccination is likely to be encountered in screening or diagnostic mammography. A recent retrospective study reported a vaccine axillary adenopathy incidence rate of 3% among women who underwent mammography after at least one vaccine dose. This study included data from 750 women, and most women with lymph nodes had received two vaccine doses (18 out 23 patients).[94] Despite these findings, experts do not recommend postponing either vaccination or mammography but ideally performing mammography before vaccination.[95]

Few recommendations have been made to obtain supplementary information specific to the COVID-19 vaccine on the patient anamnesis, such as vaccination status date(s) of vaccination(s), type of vaccine, injection site (left or right arm), and any history of palpable axillary adenopathy. Radiologists and oncologists should be aware of this secondary effect of vaccination to avoid false-positive results and unnecessary changes in management, patient emotional stress, or biopsy.[96,97]

What Is the Role of Postvaccine Antibody Quantification Tests in Patients With eBC?

The current evidence supports that seroconversion rates among patients with cancer are similar to those without

the disease, particularly in solid tumors like BC.[98] Vaccine-wise, serologic tests can often be misinterpreted as they might not distinguish between past infection and postvaccination immunologic response.[23] Furthermore, serologic testing does not evaluate cellular immune response. When performed against nucleocapsid protein, these tests will not detect immune responses resulting from vaccination and are unsuitable for vaccine decision making.[29] Most experts do not see a clinical application for these tests.

DISCUSSION

In conclusion, we have provided guidance on several topics regarding eBC management amid the COVID-19 pandemic to inform safer care practices for both patients and HCPs.

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