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Strategies for Breast Cancer Surgery During & After COVID-19 Pandemic

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ABSTRACT

Background: In December 2019, a severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), also named "COVID-19", has produced a global pandemic and has seriously affected many health systems around the world. Since the World Health Organization (WHO) declared the novel COVID-19 outbreak as a global pandemic, many international societies and groups of experts have published clinical guidelines and recommendations for surgical management of breast cancer patients in this time of crisis and issued COVID guidelines to prioritize surgery where time is critical and it cannot be deferred.

Methods: In this study, we review current recommendations for breast cancer surgery during the COVID-19 pandemic and propose a plan for future waves of the current pandemic while minimizing the risk of the contagious disease and oversaturating the health systems regarding the burden of accumulating untreated disease.

Results: We create a critical and constructive vision from learnt lessons for similar future situations and propose a moving forward plan during and after the COVID-19 pandemic.

Conclusion: Although in many parts of world, it would appear that now we are past the peak of the COVID-19 pandemic, we still face as uncertainty as to the future course of the pandemic and the challenges of the second wave. It is important to reappraise continuously the guidance and to emphasize the need for new protocols under new norms to continue to deliver breast cancer surgery safely.

INTRODUCTION

In December 2019, a severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) was described in Wuhan, China. This novel disease, also named "COVID-19", has produced a global pandemic and has seriously affected many health systems around the world, especially in countries where preventive measures were taken after the virus had already spread remarkably.[1,2] As of November 1st, 2021, the John Hopkins Coronavirus Research Center has reported more than 247 million cases of COVID-19 and more than 5.0 million deaths related to COVID-19 infection worldwide (http://coronavirus.jhu.edu).[3]

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Because the disease is contagious, hospitals had to reduce access to elective patients to avoid the spread of infectious disease among health care workers and non-COVID hospitalized patients. Furthermore, with a high percentage of patients requiring admission to intensive care units (ICU) for mechanical ventilation, many health systems have been overwhelmed.

Breast cancer is the commonest malignancy in women worldwide. Over 80% of breast cancer patients undergo primary surgery, the main curative modality in early breast cancer.[4] Moreover, since the World Health Organization (WHO) declared the novel COVID-19 outbreak as a global pandemic, many international societies and groups of experts have published clinical guidelines and recommendations for surgical management of breast cancer patients in this time of crisis and issued COVID guidelines to prioritize surgery for whom time is critical and cannot be deferred.[4-10,12]

The measures implemented as a result of the published recommendations have led to a drastic reduction in the number of patients who had access to screening and second level radiological examinations to finalize the diagnosis of breast cancer, significantly decreasing breast surgery outpatient clinical activity to more than 80% compared with that from the same period in 2019 at the European Institute of Oncology.[13]

In this study, we analyze expert recommendations and guidelines from leading specialty groups and societies in breast cancer surgery during the first COVID-19 pandemic wave. Moreover, we create a critical and constructive vision from learned lessons for similar future situations and propose a moving forward plan during and after the COVID-19 pandemic.

METHODS

This research was carried out using the following electronic database: MEDLINE, ISI Current Contents database, Cochrane Library database, Google scholar and PubMed from November 1, 2019 to January, 2021. Keywords used were Coronavirus, COVID-19, Breast Cancer, Corona Crisis, Breast Surgery, Breast Cancer Screening and Breast Cancer Guidelines. Relevance of publications was evaluated from titles at the beginning, then from abstracts. Concerning inclusion criteria, studies were included if they fulfilled specific eligibility criteria such as the combination of keywords to focus on the subject of COVID-19 and breast surgery. We included all the relevant scientific publications written in English. Non-scientific commentary, reports, and newspaper articles were excluded from the analysis.

RESULTS

Surgical breast cancer guidelines and recommendations from leading specialty societies around the world were reviewed from March 2020 to January 2021: the Association of Breast Surgery (ABS), the Association of Cancer Surgery (BASO), the European Society of Medical Oncology (ESMO), the COVID 19 Pandemic Breast Cancer Consortium (PBCC), the Cancer Care Ontario (CCO), the Society of Surgical Oncology (SSO), the Japanese Breast Cancer Society (JBCS), and the Breast Surgeons of Australian and New Zealand (BSAnz).[5–12] An special communication from the Editorial Board of The Breast (experts from Europe) on triage, prioritization and treatment of breast cancer during the COVID-19 pandemic was also reviewed. [6–8,10,12,14–17] Many developed countries with the best healthcare systems in the world have been hit hard by the pandemic and have proposed recommendations limiting both medical and surgical activity not related to coronavirus disease. We summarized the 8 articles included in Table 1.

Guidelines and Recommendation

In the UK, on March 15, 2020, the Association of Breasts surgery (ABS) suggested that UK breast units develop a plan to be implemented as the pandemic worsens. Given the potential of medical staff shortage and theatres, measures were to be adapted in order to prioritize which breast cancer patients receive surgical treatment.[5] All UK breast units have managed to operate with various numbers and levels of prioritization depending on their location, capacity and availability of resources.

Clinic referrals were triaged and only those with the highest index of suspicion were seen, and clips were put in all cancers when biopsy was performed, especially those candidates for neoadjuvant therapy. At the beginning, theatre space was limited, so surgical priority was given to estrogen receptor (*ER*) negative patients first, then human epidermal growth factor 2 (*HER2*) positive patients, and then pre-menopausal *ER+* patients. Post-menopausal *ER+* patients were commenced on primary endocrine until further notice. Neoadjuvant chemotherapy was prescribed only for inoperable disease, with no aims to downstage from mastectomy to breast conserving surgery (BCS) or to perform axillary conservation. No immediate breast reconstruction was performed. Mastectomy and delayed reconstruction were offered at a later date.[5,6]

All cases were discussed in the breast MDT which has continued with the new COVID-19 measures including some virtual participations, where the risk/benefit ratio was considered and tailored care was offered to some individualized cases, such as considerations for the use of genomic testing OncotypeDx performed on the core biopsy to identify patients most likely to benefit from chemotherapy.[18]

Table 1. Highlighted recommendations for breast cancer care during COVID-19 pandemic published by recognized international societies

Recommandations	ABS	BASO	ESMO	PBCC	CCO	SSO	JBCS	BSAnz
Breast cancer care (surgery, systemic therapy or radiation therapy) prioritisations according to categories depending on patients' clinical conditions or clinical needs or resources.	R		R	R	R		R	R
Deliver a one stop service for patients referred with a high suspicion of cancer.	R							R
Breast cancer imaging prioritization, e.g., ultrasound, short interval mammogram follow-up, MRI.		R	R	R	R		R	
All patients to be discussed in an MDT. The risk/benefit ratio needs to be then discussed with the patient at an individual level.	R				R			
Judicious use of neoadjuvant chemotherapy in appropriate patients.	R	R	R	R		R	R	R
Prioritizing who is offered surgery based on risk of disease, e.g., when surgical capacity is compromised, primary systemic therapy for ER positive or HER2 positive cases, with surgery reserved only for triple negative cases.	R	R	R	R	R	R	R	R
In radiation therapy, the use of hypofractionation where clinically appropriate is recommended to reduce visits.			R	R	R		R	
Women with DCIS may omit radiation therapy, especially those with ER positive lesions taking adjuvant endocrine therapy, or low risk disease.			R	R			R	
The use of neoadjuvant endocrine therapy to enable deferral of surgery in early clinical stage, ER positive, lobular, or with cancers with low genomic scores.	R		R	R		R	R	R

Recommandations	ABS	BASO	ESMO	PBCC	CCO	SSO	JBCS	BSAnz
Benefits of the recommended treatment and risks associated with Covid-19 should be discussed with patients including those undergoing IBR.	R							
Immediate reconstruction with implant or expander can be considered in selected patients, subject to local theatre capacity and low complication rate. Prolonged autologous reconstruction should not be offered or can be deferred.		R		R				
Deferring risk reducing surgery and delayed reconstruction.	R	R	R			R	R	R
Outpatient remote consultations when appropriate.	R	R	R	R		R	R	R
The use of appropriate personal protective equipment.	R				R			R
When available and recruitment restarts, appropriate clinical trials should be considered.	R							

Abbreviations: ABS (Association of Breast Surgery), BASO (The British Association of Surgical Oncology), ESMO (European Society of Medical Oncology), PBCC (Covid-19 Pandemic Breast Cancer Consortium: representatives from the American Society of Breast Surgeons, the National Accreditation Program for Breast Centers, the National Comprehensive Care Network, the Commission on Cancer and the American College of Radiology, (CCO) Cancer care Ontario, SSO (Society of Surgical Oncology), JBCS (Japanese Breast Cancer Society), BSAnz (Breast Surgeons from Australia and New Zealand), R (Recommends), MRI (Magnetic Resonance Imaging), MDT (multidisciplinary team meeting), ER (estrogen receptor), HER (Human Epidermal Receptor), DCIS (Ductal Carcinoma In Situ), IBR (Immediate breast reconstruction)

Also, adjuvant radiotherapy guidelines have been deployed based on evidence such as the reduction in the number of fractions to 5, as per the FAST and FAST forward trials, to decrease the time spent and travel to radiation therapy.[19] Across the UK, a partnership has been established between the private hospitals to provide ongoing, COVID free sites for breast surgery in some regions. Surgery was performed as day case and followed up and all regions managed to operate, although the number and level of urgency of the cases varied regionally.[5] Several strategies have been implemented, where surgery was initially put on hold for benign disease, risk reduction surgery, immediate reconstructions and oncoplastic procedures. At the start, patients were offered the standard surgical procedures of mastectomy, wide local excision, sentinel node biopsy and axillary clearance. Waiting lists were created for patients with surgical delays: such as those on primary endocrine therapy, ductal carcinoma in situ (DCIS) tumors, candidates of immediate and delayed reconstruction and prophylactics surgery.

On March 23, 2020, the Society of Oncological Surgery (SOS) published their recommendations based on the opinion of experts for the surgical treatment of patients with breast cancer within the conditions of the pandemic. In general, they considered that surgery could be deferred in most of newly breast cancer cases except clinical stage IA triple negative/*HER2*+ tumors and those with progressive disease on systemic therapy, angiosarcoma and malignant phyllodes tumors. If patients were candidates for neoadjuvant hormonal or chemotherapy, this would be the first treatment of choice, and neoadjuvant therapy was given to large size tumors,

for stage IB or by the decision of the breast multidisciplinary team (MDT).[10]

The European Society for Medical Oncology (ESMO) proposed delaying surgery using a stratification system based on the priority of the surgery and divided patients into four groups: urgent, high, intermediate and low priority. They proposed delaying breast surgery after 8 weeks in patients with low priority, including patients with DCIS tumors and post-menopausal patients with luminal A-like cancer.[7]

At the same time, an expert opinion panel from USA and Canada published their recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic.[8,9] Similar to ESMO, the authors proposed stratifying patients into three groups of priority for breast cancer surgery: A, B and C, from the highest to lowest priority. For those in priority C category, breast surgery can be indefinitely delayed until the pandemic has resolved. The priority C group includes, among others, most patients with DCIS tumors, and cT1 N0 *ER+/HER2-* breast cancer.[15,20]

Following the same surgical recommendations as the American and European colleagues, the group of Breast Surgeons from Australia & New Zealand and the Japan Breast Cancer Society published their guidelines for the management of breast cancer patients during the COVID pandemic. Both groups established priority groups for breast surgery and for the management of patients with neoadjuvant therapy.[11,12]

Regarding patients needing prophylactic mastectomies, risk reduction mastectomies and benign pathology, they were deferred for a minimum of 3 months. Regarding reconstructive breast surgery, delayed two-stage reconstruction was recommended to be deferred to a minimum of three months and immediate reconstructions was to be avoided, where patients were offered standard mastectomy with delayed reconstruction.[14,21]

Proposed Plan for Future Pandemic

As we move forward, and the considerations to be taken to 'catch up' with cases postponed during the peak of COVID-19 pandemic, we suggest the following strategy to be implemented to resume and to keep providing breast cancer surgery:

- Provide a one stop service for patients referred with a high suspicion of cancer in the triple assessment clinic.

- All treatment decisions should be undertaken with the agreement of the MDT, balancing risk and benefits of treatment in the context of the specific pandemic level, together with a case by case discussion for Oncoplastic Surgery.

- Single pre-op consultation visit with diagnosis and management planning, in order to decrease unnecessary hospital travel during these visits; surgical consent, tag insertion for localization for impalpable lesions, routine pre-op lab test, medical photography and instructions for isolation and pre-op COVID testing are recommended

- When feasible, offer routine wider margin excision to reduce rates of re-excision and theatre exposure.

- Perform Breast surgery under day case setup whenever possible, where specialized pain control pathways are recommended, such as the local anesthesia and regional blocks to facilitate pain relief and early discharge.

- Oncoplastic and reconstructive breast surgery can be delivered during the pandemic by careful patient selection.

- With regard to post-operative care, patients should be offered single post follow up visit whenever possible using a treatment plan including oncological therapy, which can be followed by routine phone or teleconsultation as needed, provided that all patients have open access to further follow ups and wound checks, if necessary.

- A strategy for a regular locoregional guidelines review to accommodate increased patients' volume without jeopardizing the safety of patients and the staff or the operating capacity.

- During the course of a prolonged pandemic where operating room resources are reduced for prolonged periods, prioritizing patients would be escalated or deescalated according to the level of pandemic with regular revision of pooled waiting lists of surgery.

- Continuous update of COVID surgical precautions and hospital planning (Table 2).

DISCUSSION

In these unprecedented times of COVID-19, in line with other medical and surgical specialties all over the globe, breast surgeons are being forced to triage and prioritize breast surgery cases, in order to comply with the potential shortage of hospital beds, intensive care unit (ICU) beds, and ventilators to minimize patients' unnecessary contact with the hospital and to reduce the risk of contracting the virus in vulnerable groups at risk. Many international scientific societies have provided their recommendations for managing care in oncological specialties, including breast cancer surgery, assuming at least a 3- to 6-month delay in care.[25]

Table 2. Ideal model of COVID-19 free breast cancer center (M: mandatory; O: optional but highly recommended)

Hospital Facilities and Resources	
- Enable a front desk with the followings tasks: temperature check, provide masks and gloves for both staff and patients (M) - Establish a standardized clinical pathway for breast cancer patients at each unit (M) - Re-organize outpatient clinic activity (M) - Promote the use of telemedicine (M) - Establish a strict schedule appointment (encouraging patients and staff to comply with it) (M) - Guarantee appropriate use of personal protection equipment - Prepare a well-stablished protocol for equipment and rooms disinfection adhered to universal protection principles (M) - Offer patients free telephone psychological support both before and after admission (O)	
Staff recommandations	**Patients and visitors recommandations**
- Renew surgical mask daily (M) - Temperature check daily before and after work (M) - Work in two groups (O): o 2 weeks active working at hospital o 2 weeks working remotely at home by telemedicine - COVID-19 PCR Test weekly - Quarantine for symptomatic or positive for COVID-19 PCR test - Follow considerations for optimum surgeon protection before, during, and after operation *	- Surgical mask inside the hospital (M) - Temperature check before entering hospital or admission (M) - Negative COVID test day before admission (M) (Well-organized transfer circuit to COVID centers if positive or suspected by diagnostic tests)

*available at https://www.facs.org/covid-19/clinical-guidance/surgeon-protection

One of the challenges of delaying breast cancer surgery until the pandemic has resolved is the uncertainty regarding the time the pandemic ends. The required timing for returning surgical activity in breast cancer services to its usual activity level is still unknown. Recent studies have showed that delaying breast surgery beyond 12 weeks are associated with increased risk of mortality compared with surgery at 1-4 weeks after diagnosis.[26]

More importantly, the long-term effect of cessation activities of breast screening programs is still unknown, which can cause a drastic increase in the overflow of those who need the service once it opens up.[27] Screening services in many countries around the world have been stopped due to the COVID-19 crisis. The effect of this stoppage on screening programs is still unknown. In Canada, in the pre-pandemic era, approximately 300 screen-detected cancers per month were observed. These cancers would not be detected during the pandemic, because routine screening (including high-risk screening) is on hold according to a joint statement released by the Canadian Society of Breast Imaging and the Canadian Association of Radiologists. Fortunately, some experts in the field of breast imaging have proposed safety guidelines to carry out the same activity as in non-COVID times with minor restrictions.[22,23]

Also, in Ontario cancer surgeries declined by 40% between 15 March and 12 April 2020 compared with the same period in 2019. If fewer patients than 30% of those newly diagnosed during the pandemic are assumed to receive surgery, it could be expected that when operative resources become available, approximately 350 new cancer cases will be accumulated per month.[22] In addition, 1000 new cases each month (plus perhaps more, if imaging or diagnostic capacity is temporarily increased) will be diagnosed in the future. Furthermore, patients diagnosed with cancer in the weeks preceding the pandemic and a number of patients with DCIS or atypical lesions, and some awaiting additional breast procedures would not be captured by the foregoing numbers.[22]

A study from UK estimated that changes in health-seeking behaviors and the lack of access to essential diagnostic services resulting from national pandemic measures will result in a large number of additional deaths from breast cancer in the medium (1 year) and longer term (5 years).[24]

So far, no data is available about the number of patients who have not sought medical advice or refused treatment due to contact with the virus. The consequences of the current pandemic and the effects of future waves are still not yet clear, but figures are extremely worrisome. During the COVID-19 lock-

down, referrals via the 2-week-wait urgent pathway for suspected cancer in England are reported to have decreased by up to 84% over a 3-month lockdown period (with an average presentational delay of 2 months per patient), resulting in an estimated 181 additional lives and 3316 life-years lost as a result of a backlog of referrals of 25%, 361 additional lives and 6632 life-years lost for a 50% backlog of referrals, and 542 additional lives and 9948 life-years lost for a 75% backlog in referrals. If more lockdown is imposed, additional estimated lives to be lost.[28]

On the other hand, the effects of delaying both diagnosis and treatment on women's mental health are unknown. Psychological support is an important aspect in newly diagnosed breast cancer patients, since breast cancer is a potentially life-threatening disease associated with an increased prevalence of depressive symptoms and major depression compared to population-based patients.[29] We agree with Finley *et al.* from Canada that cancer surgery must remain essential and less-overwhelmed institutions should be the first line strategy in this crisis.[21] We go further and believe it is necessary to establish COVID-free referral centers for future waves or for global crises that would allow treating cancer patients safely and according to the standard treatment guidelines. Although Spain is one of the countries most affected by the COVID-19 pandemic, the Spanish Breast Cancer Group GEICAM has published clinical guidelines to minimize the deleterious effect of the pandemic.[30] In this paper, we propose a series of measures to avoid cancellation of breast cancer surgeries given the low probability of admission to intensive care units. In accordance with our proposals, having a negative COVID-19 PCR, reducing doctor-patient contact to the minimum and avoiding long surgeries (i.e., autologous reconstruction) would allow surgical activity to continue in breast cancer patients.[30]

There are strong arguments to support providing surgery in breast cancer services during the pandemic under optimal safety measures:

a. It is a simple and rapid surgery in experienced hands.
b. A small number of patients will require admission to ICU; therefore, breast surgery does not interfere with the availability of beds for intensive care.
c. A significant percentage of patients requiring breast surgery are suitable for a day-case procedure, so unnecessary admissions can be avoided in order to reduce patient's exposure to hospital environment.[31]
d. Breast cancer is a disease that generally does not cause pain or serious symptoms, factors which can cause delay seeking advice.[22]

As this was an exceptional and unprecedented situation, many patients have suffered a delay in both diagnosis and treatment. To avoid this happening again, in undesirable future pandemics or possible recurrences of the current pandemic, strategies should be immediately mobilized to minimize the interruption of breast cancer treatment. Governments should provide the population COVID-19 free centers for the management of breast cancer in line with standardized safety protocols. COVID-19 pandemic had a tremendous impact on all facets of the society. It has caused enormous shifts in treatment paradigms for patients with breast cancer. There are also substantial increases in the number of avoidable cancer deaths to be expected as a result of diagnostic delays, making urgent policy interventions necessary.[24]

In the UK after the peak of the pandemic, *Moving Forward Recommendations* were issued from the ABS to ensure that breast surgery can be delivered safely in their individualized units, and as more theatre space became available, patients were prioritized in accordance with clinical need in the following order:[32]

- *ER*- patients
- *HER2*+ patients
- Pre-menopausal patients & high-risk *ER*+ post-menopausal patients
- Large areas of high-grade DCIS
- Post-menopausal *ER*+ lower risk patients
- Remaining DCIS patients.

Although previous studies documented the elevated risk of COVID-19 in the perioperative period with relatively poorer outcomes for patients undergoing surgery, limitations exist regarding the extent to which findings can be used to guide surgical practice.[33,34]

A UK study on high-risk group cancer patients showed that the risk of COVID-19 following elective cancer surgery appears to be minimal, and that patients who required a post-operative inpatient admission did not show increased rates of COVID-19.[35] Another multi-center observational study during the peak of the COVID-19 pandemic showed no patients presented post-operatively with COVID-19 symptoms and at 30 days, there had not been any identified COVID-19 cases. There were also no unexpected critical care admissions or deaths.[36] This is an important finding, which supports increasing the current operative capacity for elective cancer surgery, reassuring patients awaiting surgery and reducing some of the massive psychological stress caused by having a cancer diagnosis in the era of COVID-19. However, precautions are still important to reduce the risk of transmission of COVID-19 and providing treatment in COVID free areas.

As reopening of resources is indispensable, given the impact of further delays on screening, and given the

estimated burden of breast cancer cases requiring surgery, strategic planning is of paramount importance.

COVID-19 may live with us for many months and perhaps years, and there is also a considerable concern over the potentially severe impact of COVID-19 on cancer patients which occur alongside with the psychological effects that worsen patients' well-being. It is important to consider the needs of cancer patients at the same level as those receiving care for COVID-19 and other illnesses. Knowing that the individual is at higher risk of serious complication if infected by COVID-19, loneliness and isolation as a result of social distancing, and the underlying constant fear of the cancer, and the stigma of being left with a deformity after breast cancer surgery without reconstruction, patients' feelings of uncertainty associated with their prognosis and emotional distress have negative effects on clinical outcomes in cancer patients.[37,38]

CONCLUSION

Although in many parts of the world, it would appear that now we are past the peak of the COVID-19 pandemic, we still face the uncertainty as to the future course of the pandemic and the challenges of the second wave. It is important to reappraise continuously the guidance and to emphasize the need for new protocols under new norms to continue to deliver breast cancer surgery safely.

To conclude, a reflection from an American poet named Archibald MacLeish that should make us all think "The only thing that is normally more painful than learning from experience is not learning from it".

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CONFLICT OF INTEREST

Authors declare no conflicts of interest to disclose.

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