

RECOMMENDATIONS FOR BREAST SURGICAL CARE DURING COVID-19 OUTBREAK IN IRAN: SETTING PRIORITIES OF MANAGEMENT

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Abstract – Objective: During the recent pandemic of COVID-19, apposite planning is necessary to maintain health system resources. Cancer patients are susceptible to COVID-19, but accurate cancer management should be carried out. As breast cancer is the most common female cancer in Iran, and surgery is the main treatment, we carried out this study to provide the best recommendations for breast surgery and care during the outbreak of COVID-19 in Iran.

Materials and Methods: As cancer and breast surgeons at Cancer Institute of Iran, based on our personal and institutional experience and recently released guidelines, we defined the main headings about breast surgery issues during the outbreak. We investigated the present literature and then discussed each issue.

Results: The best agreed recommendations were delineated. Briefly, telemedicine should be prioritized over in-hospital presence of patients. Visits should be postponed except for cancer workups and treatments, or cases suspicious for cancer. Appropriate protective, preventive, and instructive measures related to COVID-19 should be observed in the outpatient and inpatient departments for patients, companions, and health care providers. Staging procedures should be minimized. Surgery for non-malignant lesions, reconstructive and cosmetic surgery should be postponed. When breast cancer surgery can be substituted by non-operative treatments without impairing prognosis or quality of life, it should be deferred. Surgeries with lower complication rates and length of stay are favored.

Conclusions: At the time of COVID-19 epidemic, surgery should be performed for breast cancer only if this modality is more advantageous than other therapies in terms of disease outcome and is worth the increased risk of transmission of COVID-19. Otherwise, it should be deferred until control of the epidemic.

KEYWORDS: Breast cancer, Breast Surgery, COVID-19, Coronavirus, Epidemic, Iran, Neoadjuvant, Pandemic, Telemedicine.

INTRODUCTION

COVID-19 has been declared a pandemic by the World Health Organization (WHO) since March 11, 2020¹, and as of April 16, 2020, globally confirmed cases and death have mounted to 2,183,581 and 146,855, respectively. In Iran, the first cases were officially reported on February 19, 2020. On April 16,

the total number of cases and deaths in Iran amounts to 77,995 and 4,869, respectively².

The outbreak has affected many aspects of health care in the world; the availability of enough health-related resources including human workforce, equipment and medical facility are the primary concerns. These issues had already been perfectly designated as staff, stuff and space in 2014³ for previous global infectious



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outbreaks. Cancer management is specifically affected in this context. Patients with malignant disease were previously recognized as susceptible to infections^{4,5} due to a relative immunosuppressive state caused by cancer itself, and its related treatments namely chemotherapy, radiation, immunotherapy, and endocrine therapy. In the COVID-19 era, some studies have investigated the subject from the point of view of infection rate, disease severity and prognosis in oncology patients. Liang et al⁶ have shown a higher rate of transmission of the 2019-Novel coronavirus in patients with active or previous cancer; however, the vulnerability of cancer survivors has been debated by Wang et al⁷. Nevertheless, the severity of the viral disease and its outcomes were shown to be more serious in the population affected by cancer in the cohort of Liang et al⁶. Ganatra et al⁸ have reported a COVID-19 mortality of 7.6% in patients affected by malignancy, vs. 3.8% in the normal population. Wu et al⁹ have cited mortality figures of 5.6% and 2.3 % for cancer-bearing and general population, respectively.

Surgery is an essential part of cancer management for many solid tumors. However, it has at least three main undesirable fallouts at the time of this epidemic. First, it greatly increases the use of medical resources. Second, it warrants staying at the hospital for a significant time, which intensifies the potential for transmission of the viral disease. Third, it increases infection susceptibility as a complication of the operation. Lei et al¹⁰ have investigated the outcomes of patients who had undergone surgery during the incubation period of COVID-19 among 34 cases. They found a 44% rate of ICU admission, and a mortality of around 20%.

Nonetheless, the higher susceptibility of cancer patients to COVID-19, the risks induced by surgery, and the necessity to preserve medical resources should be considered against the obligation to approach cancer treatment in the short-term for appropriate disease control.

Breast cancer is the most common female cancer in Iran¹¹, and surgery is a chief measure among various therapeutic modalities in non-metastatic breast cancer¹². Also, considering the benign face of the subject, one of the most common complaints among women attending surgical clinics in normal situations is breast-related condition¹³. Therefore, we carried out a study to delineate a rational approach to breast surgery and breast care during the COVID-19 outbreak. Our objective was to define the best management option regarding disease outcomes while minimizing patient exposure to medical surroundings and preserving health-related resources as much as possible.

MATERIALS AND METHODS

Initially, main questions and considerations regarding breast surgery concerns during COVID-19 pandemic

were proposed in a meeting held virtually among surgery and cancer sub-specialists in the Cancer Institute of Iran (affiliated with Tehran University of Medical Sciences) in a web-based social media. These were further refined by investigating the present literature for pertinent headings used in recently released guidelines and protocols or similar material which consisted of: the American College of Surgeons (ACS) COVID-19-Elective Case Triage Guidelines for Surgical Care¹⁴, The American Society of Breast Surgeons (ASBrS) Recommendations for Prioritization, Treatment and Triage of Breast Cancer Patients During the COVID-19 Pandemic¹⁵, The Society of surgical Oncology (SSO) Resource for Management Options of Breast Cancer during COVID-19¹⁶, the American Society of Oncology (ASCO) COVID-19 Patient Care Information¹⁷, NHS Clinical Guide for the Management of Cancer Patients During the Coronavirus Pandemic 2020¹⁸, European Society for Medical Oncology (ESMO) COVID-19: Supporting Oncology Professionals¹⁹, the National Comprehensive Cancer Network (NCCN)- Managing Cancer Care During the COVID-19 Pandemic: Agility and Collaboration Toward a Common Goal²⁰, COVID-19 Prevention and Care Guidelines for Cancer Patients and their Family, Directors and Personnel of Health Care Centers²¹ and Guidelines to Encounter COVID-19 in Cancer Patients and Bone Marrow Recipients Issued by the Ministry of Health and Medical Education of Iran²², COVID-19 Prevention and Care; A Cancer Specific Guideline²³, Cancer Guidelines During the COVID-19 Pandemic²⁴, and Modifications in Breast Cancer Guidelines in COVID-19 Pandemic, an Iranian Consensus²⁵. Headings that needed to be approached were again discussed and finally determined throughout a virtually held group encounter.

In the next stage, each heading and sub-heading was put to debate and comments were released through e-mails and in a WhatsApp group among cancer and breast surgeons. In this step, a thorough search for the recent literature about cancer, breast neoplasm, breast cancer, guidelines and COVID-19 was performed in above-mentioned guidelines and protocols. The used search engines were Google Scholar, PubMed, Scopus, and journals that had released articles about COVID-19 in a fast setting, including the New England Journal of Medicine (NEJM) and the Lancet. Issues that had resulted from our search as well as our comments were collected and organized as follows.

RESULTS

Proceeding through the method described above, we delineated the following headings and subheadings as the mainstays of our discussion frame: General and preventive measures for patients (in the

outpatient clinic, the waiting room and the inpatient ward), and for health care professionals; breast cancer screening (in the general population, in high-risk groups); visits and procedures for breast signs and symptoms; visits and procedures for breast imaging findings (centered on BIRADS); benign breast disease surgery (grouped as priority and non-priority surgeries); breast cancer staging; breast cancer surgery [(timing of surgery, pre-operative assessment), types of surgery (early breast cancer, locally-advanced breast cancer, metastatic breast cancer, risk-reducing surgery, delayed breast reconstruction, oncoplastic surgery revision, others), intra-operative concerns, postoperative care and patient discharge]; follow-up after breast cancer treatment (in newly treated patients and in breast cancer survivors), palliative care, and telemedicine. The general outline organized and approved as the structure for the directive, and the acknowledged best recommendations are presented in the discussion.

DISCUSSION

Up to April 16, 2020, a number of 310,340 COVID-19 tests have been carried out in Iran. Out of these, 77995 have been positive. Up to date, the number of health care staff that have undergone COVID-19 test or had positive results has not been reported in official national statistics. However, screening hospital personnel for COVID-19 via PCR tests has begun in some centers. In our mother center at Imam Khomeini Hospital, 440 screening tests have been performed during the recent four weeks, and 52 out of them have been reported as positive. This is a high percentage; so, we shall also consider the health status of health care workers when defining indications of surgery during the outbreak. Our recommendations are described as follows.

COVID-19-RELATED GENERAL AND PREVENTIVE MEASURES IN THE HOSPITAL

For patients

- **In the outpatient clinic and waiting room**

The following measures should be undertaken to minimize the spread of COVID-19:

1. Body temperature of all patients and companions should be checked at the entrance. If fever is detected, they should be referred elsewhere according to the "COVID-19 prevention and care guidelines for cancer patients and their family, directors, and personnel of health care centers"²¹⁻²³.
2. Patients are asked to attend without any companion as far as possible, or with one companion only when necessary (such as non-self-sufficient patients)²⁶.
3. Personal protection equipment (PPE) including appropriate facial masks and gloves should be offered to all patients at the entrance, except if the center is faced with a deficit of PPE. In this case, patients are asked to bring these with them.
4. Patients should be encouraged to wash their hands with soap for at least 15-20 seconds or use hand sanitizer at the first entry to the clinic, before leaving the clinic, and at regular intervals if waiting for a long time.
5. Distance of at least 1.5 meters should be maintained in the waiting room. If seats are available, 2 seats must be left empty between every 2 patients and companions.
6. COVID-19-related instruction packages should be provided for all patients^{21,22}.
7. Instructions about not touching the surfaces of any equipment or furniture and avoiding touching the face should be repeatedly given to all patients.
8. All these instructions must also be written and provided in available panels across the clinic.
9. The center must manage to shorten the waiting time of patients as much as possible.

- **In the inpatient ward**

Since priority should be given to the management of the pandemic, equipment and facilities should be re-allocated to prevent shortages for COVID-19 patients. In addition, cancer patients should be well protected against the infection. Therefore, modifications should be accepted for hospitalized breast cancer patients:

1. The wards for cancer patients should be completely detached from the COVID-19 ward.
2. Fewer beds may be dedicated to breast cancer patients.
3. Hospital stay should be shortened as far as possible.
4. Blood transfer thresholds should be lowered because of predictable blood supply shortages. For example, a threshold of 10,000 or even 5,000 can be considered for platelet transfusion in patients who are stable. Also, when blood products are not available, erythropoietin use can be considered in severe anemia when there is no contraindication²⁷.
5. Procedures that necessitate higher usage of PPE for nurses should be restricted, e.g. measurements of urine output.
6. Visitor entry to the ward should be minimized and preferably prohibited.
7. Number of staff entering the ward and patients' rooms should be limited²⁰.



- **For health care professionals**

Education and appropriate training of all medical staff about preventive measures and PPE use, as well as presentation of COVID-19 for self-evaluation should be held and repeated regularly^{20,23}.

In the clinic, in the ward and in the operating theatres, health care providers should follow the general guidelines regarding the use of PPE and observance of hygienic measures as instructed in the “COVID-19 prevention and care guidelines for cancer patients and their family, directors, and personnel of health care centers” and the “Guidelines to encounter COVID-19 in cancer patients and bone marrow recipients” issued by the Ministry of Health and Medical Education of Iran²¹⁻²³.

Breast cancer screening

- **In the general population**

To appropriately maintain available health system resources and decrease non-essential patient contacts with medical centers, all breast cancer screening measures including regular scheduled breast exam, mammography, and other types of imaging should be postponed^{17,25,28}.

However, a temporary schedule should be considered for the patients according to predicted future circumstances regarding the outbreak. These can be rescheduled later if the epidemic unexpectedly gets worse^{23,26}.

- **In high-risk groups**

Every measure intended for screening purposes only, including breast examination, mammography, magnetic resonance imaging (MRI) or ultrasound scanning should be withheld until the epidemic is controlled^{15,28}. However, appointments should be rescheduled consistent with the expected slow-down curve of the outbreak^{23,26}.

Visits and procedures for breast signs and symptoms

Every visit should be postponed or performed via telemedicine, except for symptoms suspicious for breast cancer, which need to undergo a breast exam. In these cases, imaging is requested as indicated based on patient conditions^{15,28}.

Biopsies should be performed in cases which are suspicious for breast cancer.

Drainage of breast abscesses and large or enlarging hematomas should be done, but preferably in the outpatient setting.

Visits and procedures for breast imaging findings

- **BIRADS: B1, B2, B3**

Any visit and procedure should be postponed.

- **BIRADS: B0, B4, B5**

1. For B0, additional imaging is postponed if the clinical estimate is in favor of benign lesions.
2. For B4a lesions, biopsy should be postponed.
3. For B4b, B4c and B5 lesions, biopsy should be performed as indicated for non-epidemic, usual circumstances.

Benign breast disease surgery

- **Priority surgeries**

Breast abscess and enlarging hematomas should undergo surgery in case of failure of conservative management (aspiration)^{14,15}.

- **Non-priority surgeries**

All other surgeries for benign lesions should be deferred, including the following:

1. Benign nodules like fibroadenomas
2. Duct excision
3. When the discordant histologic result of a biopsy is most likely to be benign.
4. Lesions that are considered high risk for malignancy such as papillomas and atypias^{14,15}.

Breast cancer staging

Staging procedures should be reduced wherever possible in order to lessen patients' contact with probably infected medical areas and save human and equipment resources^{17,25}. We recommend discussing measures such as insertion of markers to localize tumor bed or positive lymph nodes prior to neoadjuvant chemotherapy in a multidisciplinary setting in order to decide whether to perform them (so that further breast conservative surgery could be possible), or to omit them (and carry out mastectomy later). Imaging processes that are usually requested for detection of metastases can also be obviated in T0-3, N0-1 breast cancer^{25,29}.

Breast cancer treatment

Treatment of breast cancer should be planned in a multidisciplinary team whenever possible. When making decisions on treating newly diagnosed breast cancer or modifying the previous treatment plan based on COVID-19 conditions, the physician should explain the causes of these choices as well as the benefits and harms of any plan for the patients and their families²³.

One important point is whether breast cancer treatment should be carried out, or previous therapy should be continued, in patients affected by the 2019 Novel coronavirus. Present data are insufficient for evidence-based decision-making, but existing knowledge about the severity of COVID-19 in pa-

tients under cancer treatment implies postponement of current or new therapy until resolution of symptoms of the viral disease^{17,30}.

Establishment of a telephone call or web-based virtual triage system before attending the hospital can effectively support the system in this regard²³.

• Surgery

Generally, surgeries must be planned based on the risk of transmission of the 2019 Novel coronavirus during hospitalization, the need to prioritize the use of hospital supplies, and the benefits and harms of immediate or delayed operation. Thus, curative surgeries whose benefits outweigh risks of COVID-19 infection and those that could compromise patient survival or disease prognosis when delayed, are carried out during the outbreak^{14,23}.

• Timing of surgery

Since a patient's length of stay in the hospital is usually longer for surgery of breast cancer than for its chemotherapy, sequences of these two modalities can sometimes be exchanged at the time of COVID-19 outbreak; therefore, the operation can be scheduled for a later time. This is explained further in "Types of surgery".

• Pre-operative assessment

When surgery is necessary, the patient should be investigated for COVID-19 in the pre-operative examination: asking questions about the history of related symptoms as well as recent contact with affected patients and measurement of body temperature should take place. A chest CT scan and laboratory assessment of the virus before elective surgery when available, or patient isolation for two weeks prior to proceeding with the operation, has been advised by Chinese surgeons^{10,31,32}; we recommend these measures in patients who are suspected for COVID-19 based on their history or examination result. Other pre-operative tests are performed according to existing guidelines, but proper planning should minimize the patient's entry to medical centers. For example, cardiac and anesthetic consult can be undertaken via telemedicine before patient's admission, and be completed afterward.

Patients should be made aware of the increased risk of COVID-19 transmission during hospitalization despite protective measures.

• Types of surgery

The priority is to perform surgeries with shorter lengths of stay and lower complication rates. Consequently, it is recommended to carry out breast conserving surgery rather than mastectomy and modified or simple mastectomy instead of subcutaneous or nipple-sparing mastectomy. Also, our trend is to defer surgeries which can be performed later without a high risk of early relapse¹⁴.

Early breast cancer

1. For ductal carcinoma *in situ* (DCIS), estrogen receptor (ER) positive tumors, surgery should be postponed, and endocrine therapy should be initiated.
2. For DCIS, ER negative tumors, surgery is better to be performed in cases that are suspicious to have an invasive component; these include high grade, palpable, and large tumors, as well as DCIS with microinvasion in the biopsy specimen. When the tumor lacks the latter criteria, surgery should be postponed; in this setting, vacuum-assisted excision is recommended as a temporary treatment. Monthly monitoring should be subsequently held via telemedicine until the time of surgery.
3. For hormone receptor positive, human epidermal growth factor receptor 2 (HER2) negative tumors with T2-3 tumors or N1 axillary status, surgery should be performed.
4. For hormone receptor positive, HER2 negative tumors with T0-1, N0 tumors surgery can be postponed. In this case, endocrine therapy should be initiated. If the patient is stressed out about postponing the operation, surgery can be performed.
5. For triple negative or HER2 positive T0-1, N0 tumors, either surgery or neoadjuvant chemotherapy can be performed. Whenever accurate localization of the lesion cannot be achieved prior to chemotherapy while breast conserving surgery is planned, the surgeon is worried about immunosuppression caused by chemotherapy, or the patient is stressful about postponing the operation, surgery should be prioritized. Otherwise, neoadjuvant chemotherapy is recommended. Multidisciplinary decision-making would be of great assistance in these cases.
6. For a tumor that has undergone excisional biopsy and the histologic exam shows malignancy, but axillary sampling has not been performed, axillary sentinel lymph node biopsy can be postponed if lymph nodes are not involved in clinical exam and imaging¹⁴.

Locally advanced breast cancer

1. For patients who have undergone and finished their neoadjuvant treatment, surgery should be performed.
2. For hormone receptor positive, HER2 negative tumors with T3-4 tumors or N2-3 axillary status, neoadjuvant systemic therapy should be initiated, and surgery should be deferred.
3. For triple negative or HER2 positive tumors and inflammatory breast cancer, neoadjuvant chemotherapy should be initiated, and surgery should be deferred.



Metastatic breast cancer

1. Resection of the primary tumor should be postponed in the metastatic setting except for local complications which need care in the hospital, such as an ulcerative bleeding in the breast.
2. Any metastasectomy that was planned to be performed in oligometastatic patients should be postponed, except when the operation is expected to effectively improve the quality of life of the patient.

Others

Surgery should be performed without delay in the following conditions:

1. When the histologic exam of a biopsy is benign but discordant with the clinical and imaging finding and is most likely to be malignant.
2. In loco-regional recurrence, especially for hormone receptor positive, HER2 negative tumors.
3. In cases that progress under systemic therapy.
4. In malignant phyllodes tumors.
5. In breast angiosarcoma or other rare sarcomas¹⁴.

• Intraoperative concerns

General measures regarding suitable PPE use for operating room staff at the time of COVID-19 epidemic should be observed. It is of utmost importance to keep the patient distant from rooms dedicated to COVID-19 surgeries and to minimize staff entry in the room especially those that have been recently exposed to infected patients, when allowable regarding circumstances of human resources in the hospital.

• Postoperative care and patient discharge

In the postoperative period, the patient must be hospitalized in a non-COVID-19 ward. Hospital staff that is not suspicious of being infected with the virus should take care of the patient. Both patients and medical staff should use PPE and observe hygienic rules. Other measures to be taken are not different for non-epidemic conditions. The patient should be discharged as soon as possible. When possible and legally acknowledged, home care services can provide a great part of postoperative support²³.

Instructions regarding preventive measures about COVID-19 should be repeated before discharge³³. Relevant instructions are cited in the "COVID-19 prevention and care guidelines for cancer patients and their family, directors and personnel of health care centers" issued by the Ministry of Health and Medical Education of Iran²¹⁻²³.

Follow-up after breast cancer treatment

• In newly treated patients

Every postoperative visit should be performed via phone call or telemedicine, except for symptoms in favor of complications that need physical exam or intervention.

• In breast cancer survivors

Every visit should be postponed to a time when the outbreak is under control²³ or performed via telemedicine; except for symptoms suspicious for recurrence which need to undergo breast exam.

Every imaging should be postponed except for patients with new findings suspicious for recurrence.

When existing guidelines offer frequency ranges for visits and procedures (such as recommending a 3 to 6 months interval), it seems logical to postpone them to the latest advised time¹⁷.

Other breast surgeries

• Risk-reducing surgery

These should be postponed and performed after complete control of the outbreak.

• Delayed breast reconstruction

These should not be performed during the outbreak. Scheduled procedures should be cancelled and deferred until the outbreak is under control.

• Oncoplastic surgery revision

If a cosmetic revision is needed, it should be postponed and performed after complete control of the outbreak. For a positive margin, these are not emergent procedures, and complementary treatments including adjuvant treatments should be carried out. Thereafter, depending on the bulk of positive margin, radiation might be enough, or surgery can be completed after chemotherapy.

Palliative care

Surgical and chemotherapy options are better to be postponed^{15,21,22} except for any life-threatening condition such as severe bleeding, or when a delay in treatment would have negative consequences for patient's quality of life and there is no substitute for these therapeutic modalities²³. However, this policy may result in a subsequent uncontrollable status of the symptoms, which would increase urgent admissions in a later phase. This sequence would, in turn, worsen the public conditions regarding human and equipment resources²⁰. Thus, careful and even individualized planning should be set based on

circumstances of every center and each patient. For conditions and treatments that are authorized to be provided at home by the official national directions, home care facilities can offer part of palliative management if the service is accessible²³.

Telemedicine

So far, telemedicine has been rather inactive in Iran. However, initiation of various possibilities for telecommunication about medical issues can assist the proper management of breast cancer patients in present COVID-19 conditions²⁵. Accordingly, many practitioners and medical centers have been available to patients' concerns via social media and phone calls since the beginning of the epidemic.

Instructing people about breast cancer presentation and management as well as COVID-19 presentation and prevention, visiting patients when physical exam is not necessary, monitoring treatment response and post-treatment status, and psychological support of the survivors and the new patients can all be directed via telemedicine. These should be organized in every center according to their capacities.

Other remarks

A best approach to the current problems would be to foresee the course of the epidemic. This can be achieved through calculations assisted by artificial intelligence and machine learning. In this way, the probable time when the outbreak would be under control might be predicted, and thus re-scheduling the postponed visits and procedures would be reasonably planned³⁴.

CONCLUSIONS

Every visit and follow up should be rescheduled to a later time except for findings suspicious for cancer and management of a new malignant disease. Even in this setting, telemedicine should be prioritized over the presence of the patient in the hospital. Appropriate protective, preventive, and instructive measures about COVID-19 should be observed in the hospital outpatient and inpatient departments for patients, companions, and health care providers. Staging procedures for breast cancer should be limited to the least necessary. Surgeries of non-malignant breast lesions as well as reconstructive and cosmetic operations are deferred to a time when COVID-19 epidemic is under control. Breast cancer surgery should be accomplished when it positively affects the outcome of the disease. When breast cancer surgery can

be substituted by non-operative treatments without negative consequences on the prognosis of the disease and the quality of life of the patient, it should be postponed. When surgery is the best choice, less extensive procedures with shorter length of stay and lower complication rates should be favored.

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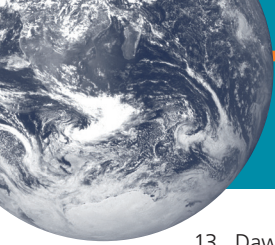
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CONFLICT OF INTEREST:

The authors declare no conflict of interest

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