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SYSTEMATIC REVIEWS

Adaptation of international coronavirus disease 2019 and breast cancer guidelines to local context

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Abstract

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (a novel coronavirus), which was first identified amid an outbreak of respiratory illness cases in Wuhan, China and declared a global health emergency, is currently considered an additional challenge in the management of patients with breast cancer (BC). Cancer patients are more vulnerable to becoming infected with severe acute respiratory syndrome coronavirus 2 and are more likely to suffer additional complications that can increase mortality. Identifying those BC patients who require more urgent therapy than others in the current situation is essential. These recommendations are based on and have been adapted from those similarly published by

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international scientific societies for BC management. They are divided mainly by clinical stage (early, advanced), subtype [luminal, human epidermal growth factor receptor 2 (HER2), triple-negative], or type of medical treatment and setting (neoadjuvant, adjuvant, metastatic). Recommendations for HER2 and triple-negative subtypes are similar, whereas in luminal subtype there are various options of management. The objective is to adapt guidelines to local context through relevant decision-makers, avoiding duplication of efforts and optimizing use or resources. We hope that these recommendations will help medical oncologists provide the best quality care to BC patients during the COVID-19 pandemic with information tailored to our healthcare system.

AIM
To establish and adapt recommendations from those published by international scientific societies for BC management.

METHODS
The Peruvian Society of Medical Oncology developed a consensus and propose here a manuscript with recommendations for oncological medical treatment of BC during the COVID-19 pandemic. The Peruvian Society of Medical Oncology invited a panel of experts and opinion leaders on BC working in major health care systems around Peru. Panel experts selected three international clinical practice guidelines (National Comprehensive Cancer Network, European Society for Medical Oncology, Spanish Foundation Research Group in Breast Cancer), considering that these are more representative in COVID-19 management. Also, the panel agreed to include at least one European and American clinical practice guideline.

RESULTS
Recommendations about BC management during the COVID-19 pandemic were divided mainly by clinical stage (early, advanced), subtype (luminal, HER2, triple-negative), or type of medical treatment and setting (neoadjuvant, adjuvant, metastatic). Recommendations for HER2 and triple-negative subtypes were similar between clinical practice guidelines, whereas in luminal subtype there were various options of management. One hundred twelve recommendations were reviewed, adapted, and voted. A consensus was made in order to provide best decisions of management, avoid duplication of efforts, and optimize medical resources, considering health care system reality. These recommendations are not intended to replace clinical judgment.

CONCLUSION
Most of recommendations are similar, mainly in high-risk subtypes (HER2, triple-negative). Certain societies adapt them to deal with different situations involving the best decision in the management of BC patients.

Key Words: Breast cancer; COVID-19; Guidelines; Recommendations; Oncology; Medical treatment

Core Tip: This manuscript includes some recommendations about oncological medical treatment of breast cancer in coronavirus disease 2019 pandemic that were selected from three international clinical practice guidelines. These were reviewed and adapted to local context by a panel of experts from Peru invited by the Peruvian Society of Medical Oncology using levels of prioritization. Consensus was made, including a vote, in order to provide best decisions of management, avoid duplication of efforts and optimize medical resources, considering health care system reality. These recommendations are not intended to replace clinical judgment.

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INTRODUCTION

The rapid escalation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to a pandemic has required a fast mechanism of prioritization of health services globally, to identify and select correctly actions that assure the best management of the breast cancer (BC) patient. The risk of worse outcomes needs to be weighed against the risk of patients and health workers to SARS-CoV-2 infection[1,2].

The need for priority mechanisms is mandatory since there are more restrictions, especially in systems with impaired availability or accessibility (including limited human resources and lack of access to medicines). The prioritization is established according to clinical practice guidelines, which are based on the highest-level available evidence[3-5].

MATERIALS AND METHODS

The Peruvian Society of Medical Oncology (SPOM, Lima-Peru) developed a consensus and proposed a manuscript with recommendations for oncological medical treatment of BC during the coronavirus disease 2019 (COVID-19) pandemic. SPOM invited a panel of experts and opinion leaders on BC working in major health care systems around Peru (nine in total). Panel experts selected three international clinical practice guidelines (National Comprehensive Cancer Network, European Society for Medical Oncology, Spanish Foundation Research Group in Breast Cancer), considering that these are more representative in the COVID-19 management. Also, the panel agreed to include at least one European and American clinical practice guideline. Previously, in an attempt to reduce debate and discuss controversial questions, panelists *via* teleconference had reviewed and exchanged recommendations.

By vote, panel of experts defined and adapted three levels of prioritization from European Society for Medical Oncology: High, medium and low priority; to support the best decision of care in oncological medical treatment, adapting treatment recommendations to the local context.

The consensus (Friday, June 19, 2020) was held in Lima, Peru *via* teleconference. A moderator chaired the panel discussion and the voting. One hundred twelve recommendations were reviewed, adapted, and voted. Panelists were asked to cast their vote using three possible answers: Yes, no, abstain. "Abstain" was used in cases of insufficient data, lack of expertise on the issue in question, or panelist's conflict of interest. A percentage greater than 70% was considered a unanimous decision. Furthermore, some additional comments were added on each topic under discussion.

RESULTS

General recommendations for the management of BC during the COVID-19 pandemic

During the pandemic, it is recommended to choose regimens and therapeutic sequences that are the most consistent with the current situation to reduce the risk of SARS-CoV-2 infection in patients and health workers, without compromising the prognosis of patients (Yes: 100%, No: 0%). In addition, there should be a differentiated triage for COVID-19 in all cancer centers before entrance, where patients and family members are questioned about their symptoms, history contacts, as wells as a record of body temperature for fever. In case of suspected COVID-19 infection, patients and/or companions should not have contact with other patients and/or health workers and should be managed according to protocols of each institution (Yes: 100%, No: 0%).

It is important to leave a medical register (informed consent) specifying explicitly the discussion with the patient of risk/benefits of treatments in the context of a pandemic as well as therapeutic decisions and alternatives available (Yes: 78%, No:

22%). In addition, individualizing the need for blood transfusions when strictly necessary (Yes: 100%, No: 0%) (Table 1).

Priorities of outpatient visits for BC during the COVID-19 pandemic

Events that require immediate in-person visit or evaluation and/or treatment (high priority) are, for example, unstable postsurgical patients (hematoma, infection, bleeding) (Yes: 100%, No: 0%) and oncological emergencies (febrile neutropenia, uncontrolled pain, symptomatic brain metastases) (Yes: 100%, No: 0%). Other conditions to evaluate in-person are BC diagnosis during pregnancy (Yes: 100%, No: 0%) and *de novo* locally advanced BC with aggressive phenotypes [human epidermal growth factor receptor 2 (HER2) positive, triple-negative] (Yes: 78%, No: 22%).

De novo invasive BC (Yes: 89%, No: 11%), intercurrences on-treatment patients (new signs/symptoms, abnormal findings during the physical examination, adverse events) (Yes: 100%, No: 0%), patients on active intravenous chemotherapy (Yes: 78%, No: 22%), and clinically stable routine postsurgical patients are examples of medium priorities (Table 2).

Priorities for telemedicine

Recommendations about telemedicine are generally classified as medium or low priority. The majority of patients could be evaluated remotely *via* telemedicine (if feasible) (Yes: 100%, No: 0%). In-person visits can be converted evaluating the risks of viral transmission to patients and health workers. Examples of patients with BC who can be evaluated with telemedicine are patients completing neoadjuvant chemotherapy and waiting for surgery (Yes: 89%, No: 11%), patients eligible for radiotherapy (first visit) (Yes: 89%, No: 11%), and patients receiving oral chemotherapy or endocrine therapy + targeted therapy (Yes: 78%, No: 22%).

Low priority patients are those for whom certain treatments or interventions can be deferred until pandemic is over; for example, routine evaluation in patients who are in periodic controls (observation) or endocrine therapy (Yes: 78%, No: 22%) and survivorship follow-up (Yes: 100%, No: 0%) (Table 3).

Priorities for breast disease: Diagnostics and imaging

As a high priority, clinical diagnosis of a mass or lump in the breast (with auto examination) or another sign with high suspicion of malignancy should be immediately evaluated (Yes: 100%, No: 0%). Similarly, patient should be evaluated when there is clinical evidence of relapsed locoregional disease (Yes: 100%, No: 0%). There are urgent situations that require imaging (Yes: 100%, No: 0%). It is recommended to perform additional images upon abnormal mammogram results (*e.g.*, Breast Imaging Reporting and Database System score 5) or suspected BC signs/symptoms (Yes: 89%, Abst: 11%) and for patients experiencing relapsed BC (Yes: 100%, No: 0%). Pathologic evaluation (cytopathology or histopathology) for abnormal mammograms or symptoms in the breast or symptomatic metastatic relapse is considered high priority (Yes: 100%, No: 0%).

Examples of medium priority in imaging include: Performing mammograms additionally with abnormal result in asymptomatic patients (Yes: 100%, No: 0%) and monitoring of treatments with echocardiograms (every 6 mo, if feasible) in patients who require treatment based in anthracyclines or anti-HER2 agents as a regular assessment of cardiac function (Yes: 78%, No: 22%). In the case of histopathologic diagnosis, examples of medium priority are biopsies for Breast Imaging Reporting and Database System score 4 or 5 Lesions (Yes: 100%, No: 0%) and image-guided (or clinically) biopsy to determine a metastatic relapse (Yes: 100%, No: 0%).

Screening and follow-up are classically considered as low priority. It is safe to deliver these scenarios during the pandemic[6,7] (Yes: 100%, No: 0%) (Table 4).

Priorities for early BC

As high priority in early BC (EBC), all subtypes should complete their regimens that have already started[8]. It is reasonable to consider shorter regimens or dose-modifications (Yes: 100%, No: 0%). Patients with clinical stage (CS) I-II (including N1) and those with intermediate/low grade, "low risk" genetic profile or classified as luminal A subtype do not benefit from neo/adjuvant chemotherapy. These patients can receive endocrine therapy alone (Yes: 100%, No: 0%)[9,10]. Recommendations about subtype are shown in Table 5[8-20].

Examples of medium priority involve situations in HER2 (+) EBC and luminal patients. In BC HER2 (+), anti-HER2 therapy can be restarted after remitting SARS-CoV-2 infection, following a discussion and approval by a multidisciplinary team (Yes:

Table 1 General recommendations for the management of breast cancer

High priority	Comments
(1) Choose regimens and therapeutic sequences consistent with the current situation to reduce the risk of COVID-19 in patients and health workers (Yes: 100%, No: 0%); (2) Differentiated triage for COVID-19 in all cancer centers before entrance (Yes: 100%, No: 0%); (3) Leave a medical register (informed consent) about the discussion of risk/benefits of treatments as well as therapeutic decisions and alternatives available (Yes: 78%, No: 22%); and (4) Individualize the need for blood transfusions when strictly necessary (Yes: 89%, No: 11%)	(1) These recommendations will be adapted according to the reality of each oncological center; (2) Treatment decisions are based on protocols (international/local) about the management of COVID-19; and (3) Multidisciplinary web meetings are recommended to decide the best choices of treatments and outcomes

COVID-19: Coronavirus disease 2019.

Table 2 Priorities of outpatient visits for breast cancer during the coronavirus disease 2019 pandemic

High priority	Medium priority	Comments
(1) Unstable postsurgical patients (hematoma, infection, bleeding) (Yes: 100%, No: 0%); (2) Oncological emergencies (febrile neutropenia, uncontrolled pain, symptomatic brain metastases) (Yes: 100%, No: 0%); (3) BC diagnosis during pregnancy (Yes: 100%, No: 0%); and (4) *De novo* locally advanced BC with aggressive phenotypes (HER2, TNBC) (Yes: 78%, No: 22%)	(1) *De novo* invasive BC (during the multidisciplinary evaluation, priority is guided by tumor biology and clinical stage) (Yes: 89%, No: 11%); (2) Intercurrences on-treatment patients (new signs/symptoms, abnormal findings during physical examination, adverse events (Yes: 100%, No: 0%); (3) Patients on active intravenous chemotherapy (Yes: 78%, No: 22%); and (4) Stable routine postsurgical patients (Yes: 100%, No: 0%)	In patients requiring urgent clinical evaluation, consider converting to telemedicine for follow-up, according to medical evolution

BC: Breast cancer; HER2: Human epidermal growth factor receptor 2; TNBC: Triple-negative BC.

Table 3 Priorities for telemedicine

Medium priority	Low priority	Comments
(1) During the pandemic, most patients could be evaluated using telemedicine (if feasible) (Yes: 100%, No: 0%); and (2) BC patients who can be evaluated with telemedicine: (a) Patients completing neoadjuvant chemotherapy and waiting for surgery (Yes: 89%, No: 11%); (b) Patients eligible for radiotherapy (Yes: 89%, Abst: 11%); and (c) Patients receiving oral chemotherapy or endocrine therapy + targeted therapy (Yes: 78%, No: 22%)	Patients can be evaluated with telemedicine (including after pandemic is over): (a) Routine evaluations in patients who are in periodic controls (observation) or endocrine therapy (Yes: 78%, No: 22%); (b) Survivorship follow-up (Yes: 100%, No: 0%); (c) Psychological visits (Yes: 100%, No: 0%); and (d) New diagnosis of non-invasive BC (Yes: 100%, No: 0%)	(1) During follow-up of patients with high-risk of recurrence, an in-person visit can be assessed according to evolution (if necessary); and (2) In some oncological centers, it is possible to evaluate in-person oral treatments of continuing patients (including whom with adjuvant therapy)

BC: Breast cancer.

78%, No: 22%). In luminal EBC in postmenopausal CS I patients with low/intermediate grade tumors or lobular breast histology variants, endocrine therapy may be started when surgery is deferred (up to 6-12 mo) as indicated in clinical practice guidelines (Yes: 100%, No: 0%). For patients with low-risk genomic score/signature, endocrine therapy should be started alone (Yes: 89%, No: 11%).

Priorities for neoadjuvant medical treatment of BC

All the recommendations in these settings are considered high priority. BC patients initiating therapy or ongoing neo/adjuvant chemotherapy and who present suspected symptoms of infection or contact history with an infected person are recommended to get tested (polymerase chain reaction) before starting or continuing it. In the case of a positive result, defer treatment until confirmation of negative result with a new test (polymerase chain reaction), which could be performed between 2-3 wk later, and with previous evaluation from the Infectious Disease Department (Yes: 67%, No: 33%).

Neoadjuvant treatment according to subtypes: A multidisciplinary team (using web platforms) should evaluate patients with invasive BC for the decision to initiate neoadjuvant therapy during the pandemic (Yes: 100%, No: 0%). Neoadjuvant treatment in BC with "high risk" [triple-negative, HER2 (+), luminal B with "high risk"] is recommended (Yes: 100%, No: 0%)[21,22]. In patients with HR (+) BC, neoadjuvant endocrine therapy allows deferring definitive surgery[23-25] (Yes: 100%, No: 0%). Recommendations about subtypes are included in Table 6[26].

Table 4 Priorities for diagnostic and imaging of breast cancer

High priority	Medium priority	Low priority	Comments
(1) Clinical diagnosis: (a) Diagnosis of a mass or lump (auto examination) or other signs with high suspicion of malignancy (Yes: 100%, No: 0%); and (b) Clinical evidence of relapsed locoregional disease (Yes: 100%, No: 0%); (2) Imaging: (a) Urgent situations that require imaging (oncological emergencies, serious postsurgical complications, *etc*.) (Yes: 100%, No: 0%); (b) Perform additional images upon abnormal mammogram results or suspected metastasis (depending on clinical stage and tumor biology) (Yes: 89%, Abst: 11%); and (c) Images for relapsed BC (Yes: 100%, No: 0%); and (3) Pathological diagnosis: Pathologic evaluation (cytopathology or histopathology) for abnormal mammograms or symptoms in the breast or symptomatic metastatic relapse (Yes: 100%, No: 0%)	(1) Imaging: (a) Perform additional images upon abnormal mammogram results or suspected metastasis (depending on the clinical stage and tumor biology) (Yes: 100%, No: 0%); and (b) Echocardiograms (every 6 mo, if feasible) in patients who require treatment based in anthracyclines or anti-HER2 agents (Yes: 78%, No: 22%); (2) Pathological: (a) Biopsy for BIRADS 4 or 5 lesions (Yes: 100%, No: 0%); and (b) Image-guided (or clinically) biopsy to determine a metastatic relapse (note: metastatic relapses should not be 100% biopsies) (Yes: 100%, No: 0%)	(1) Screening: All screening exams (mammograms or images) for symptomatic patients (*e.g.*, ultrasound or MRI) may be performed after pandemic (Yes: 100%, No: 0%)—BRCA mutated carriers < 40 yr may be considered for screening if delays or more than 6 mo are expected[6,7]; and (2) Follow-up: (a) EBC patients that require images, reevaluation of disease, echocardiograms, and bone scans, should be deferred if patients are clinically asymptomatic (Yes: 100%, No: 0%); and (b) In MBC patients, follow-up oriented to symptoms is recommended. Images, disease reevaluation, echocardiograms may be deferred in large intervals (Yes: 100%, No: 0%)	All patients with a new mass lump with a high suspicion of malignancy or who have already undergone imaging with a high suspicion for malignancy (*e.g.*, BIRDAS 5 in mammogram) should be immediately referred for histological diagnosis and imaging, as a high priority

BC: Breast cancer; BIRADS: Breast Imaging Reporting and Database System score; EBC: Early BC; MBC: Metastatic BC; MRI: Magnetic resonance imaging.

Table 5 Prioritization for early breast cancer

High priority	Medium priority	Comments
(1) General considerations: (a) All subtypes should complete their regimens that have already started[8]. Consider shorter regimens or dose-modifications (Yes: 100%, No: 0%); and (b) Patients with CS I-II (including N1) and those with intermediate/low grade, "low risk" genetic profile, or classified as luminal A subtype do not benefit from neo/adjuvant chemotherapy. They can receive endocrine therapy alone[9,10] (Yes: 100%, No: 0%); (2) TNBC EBC: (a) Chemotherapy neo/adjuvant is recommended. Sequential treatment with one agent reduces complications[11] (Yes: 100%, No: 0%); and (b) Adjuvant capecitabine is recommended in post-neoadjuvant residual disease (Yes: 100%, No: 0%); (3) HER2 (+) EBC: (a) Neo/adjuvant systemic therapy + targeted therapy anti-HER2 is recommended (Yes: 100%, No: 0%); (b) Complete neo/adjuvant chemotherapy (+/- anti-HER2 therapy) for HER2 (+) EBC (Yes: 100%, No: 0%); (c) Trastuzumab-based adjuvant therapy could be reduced from 12 mo to 6 mo without affecting outcomes[12,13] (Yes: 100%, No: 0%); (d) Consider the use of T-DM1 (+/- pertuzumab) in the neo/adjuvant scenario (reduces risk of neutropenia, hospital admissions, use of corticosteroids)[14-16] (Yes: 67%, No: 22%, Abst: 11%); and (e) Continue with T-DM1 in HER2 (+) patients as an adjuvant therapy for post-neoadjuvant residual disease[17,18] (Yes: 100%, No: 0%); and (4) Luminal EBC: (a) Neo/adjuvant endocrine therapy +/- chemotherapy for HR (+)/HER2 (-) BC is recommended (Yes: 100%, No: 0%); (b) Continue standard adjuvant endocrine therapy in pre and postmenopausal patients (use telemedicine to manage potential toxicities reported by patients) (Yes: 100%, No: 0%); and (c) Neoadjuvant endocrine therapy is an option for HR (+)/HER2 (-) BC patients allowing to defer surgery between 6-12 mo in BC with CS I or II (Yes: 100%, No: 0%)	(1) HER2 (+) EBC: Anti-HER2 therapy can be restarted after remitting SARS-CoV-2 infection, following a discussion, and approval by a multidisciplinary team (Yes: 78%, No: 22%); and (2) Luminal EBC: (a) In postmenopausal CS I patients with low/intermediate grade tumors or lobular BC, endocrine therapy may be started when surgery is deferred (Yes: 100%, No: 0%); and (b) For patients with low-risk genomic score/signature, endocrine therapy should be started alone (Yes: 89%, No: 11%)	(1) In patients with active infection due to COVID-19, stopping treatment is recommended; (2) Antihormonal therapy: Endocrine therapy (tamoxifen, AI, LHRH agonists) is safe (does not affect the immune system) and can be continued during the COVID-19 pandemic. LHRH analogs can be administered every 3 mo (although home administration of LHRH analogs is the preferred recommendation); however, fulvestrant requires intramuscular monthly application[19]; (3) Chemotherapy: schedules can be modified to reduce admissions (every 2 or 3 wks' doses can be used instead of a weekly dose with selected agents). Consider the use of concomitant colony-stimulating factor (G-CSF), preferably pegfilgrastim for single-dose administration)[20]; and (4) Bone modifying agents (denosumab or bisphosphonates) can be deferred or administrated every 3 mo (without hypercalcemia), both for adjuvant therapy or in long-term treatments

AI: Aromatase inhibitor; BC: Breast cancer; COVID-19: Coronavirus disease 2019; CS: Clinical stage; EBC: Early BC; G-CSF: Granulocyte-colony stimulating factor; HER2: Human epidermal growth factor receptor 2; HR: Hormone receptor; LHRH: Luteinizing hormone-releasing hormone; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Priorities for adjuvant medical treatment of BC

Similar to neoadjuvant therapy for BC, all the recommendations for adjuvant therapy are the same and considered as high priority (Yes: 100%, No: 0%). Recommendations are mentioned in Table 7.

Priorities for medical treatment in metastatic BC

The goals of treatment in metastatic BC (MBC) are palliative: Improvement of quality of life and prolong survival as well as minimizing adverse effects due to therapy (Yes: 100%, No: 0%). The medical criteria demand the best decision where a delay can result in fatal outcomes (*e.g.*, a patient with visceral crisis needs to start promptly

Table 6 Prioritization for neoadjuvant medical treatment of breast cancer

High priority	Comments
(1) General recommendations: Patients with BC initiating therapy or ongoing neo/adjuvant chemotherapy and who present suspected symptoms of infection or contact history with an infected person is recommended to get tested (PCR) before starting or continuing it. In the case of positive results, defer treatment until confirmation of negative result with a new test (PCR) which could be performed between 2-3 wk later, and with previous evaluation from the Infectious Disease Department (Yes: 67%, No: 33%); (2) Neoadjuvant treatment according to subtypes: (a) A multidisciplinary team (using web platforms) should evaluate patients with invasive BC for the decision to initiate neoadjuvant therapy during the pandemic (Yes: 100%, No: 0%); (b) Neoadjuvant treatment in BC with "high risk" (TNBC, HER2 (+), luminal B with "high risk") is recommended (Yes: 100%, No: 0%); and (c) In patients with HR (+) BC, neoadjuvant endocrine therapy allows deferring definitive surgery (Yes: 100%, No: 0%); (3) TNBC: (a) Standard neoadjuvant chemotherapy is recommended during the pandemic, although regimens that further reduce exposure and toxicity can be accepted (shorter duration, lower risk of immunosuppression and with an interval of every 3 wk) (Yes: 100%, No: 0%); (b) Consider the use of G-CSF (preferably pelfilgastrim for single-dose administration) in conjunction with chemotherapy (Yes: 89%, No: 11%); (c) The reduction of chemotherapy dose does not seem acceptable to reduce the risk of myelosuppression (Yes: 89%, No: 11%); (d) In older patients > 70 yr, the risk/benefit of neoadjuvant chemotherapy should be discussed. Initial surgery (as long as it is available) is an option, hoping that in 4-5 wk the situation improves to start chemotherapy (it should not be postponed more that period) (Yes: 89%, Abst: 11%); and (e) In patients < 70 yr who reject neoadjuvant chemotherapy for fear of COVID-19, initial surgery may be an option (if available) (Yes: 89%, Abst: 11%); (4) HER2 (+): (a) Neoadjuvant chemotherapy associated with anti-HER2 monoclonal antibodies is strongly recommended (Yes: 100%, No: 0%); and (b) A neoadjuvant regimen with dual anti-HER2 blocking for six courses without anthracyclines can be considered[26] (Yes: 67%, No: 11%, Abst: 22%); and (5) Luminal: (a) In those patients who do not accept surgery (initial therapy), the use of neoadjuvant endocrine therapy is considered to delay surgery until the pandemic is over, especially in patients > 70 yr, tumors with high expression of HR and low ki67 (Yes: 100%, No: 0%); (b) In luminal tumors, the benefit of adding neo/adjuvant chemotherapy to endocrine therapy can be estimated by clinic pathological factors: Tumors with histological grade 3, elevated ki67, or axillary involvement benefit more from chemotherapy (Yes: 100%, No: 0%); (c) Genomic platforms (oncotype, mammaprint, prosigna, endopredict) and online tools like ePrognosis provide additional value in establishing the need for chemotherapy (Yes: 100%, No: 0%); (d) In high-risk luminal tumors, neoadjuvant chemotherapy may provide benefits (*e.g.*, an increased rate of conservative surgery) but not increased survival. This should be analyzed with the risk of SARS-CoV-2 infection and the availability of surgery (Yes: 100%, No: 0%); and (e) Recommendations of the use of neoadjuvant chemotherapy are the same as those described for TNBC subtype (Yes: 100%, No: 0%)	In patients with HER2 (+) EBC, trastuzumab can be restarted for up to 6 mo after stopping treatment

BC: Breast cancer; EBC: Early BC; HR: Hormone receptor; PCR: Polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; TNBC: Triple-negative BC.

Table 7 Prioritization for adjuvant medical treatment of breast cancer

High priority	Comments
(1) General recommendations: (a) Recommendations in the neoadjuvant setting are similar to adjuvant therapy (Yes: 100%, No: 0%); (b) In patients > 70 yr, the evaluation of performance status for estimating the risk/benefit of chemotherapy is mandatory. Online tools (such ePrognosis) and genomic profiles can be useful (Yes: 100%, No: 0%); and (c) It is valid to defer the start of adjuvant chemotherapy until the pandemic is over, although decisions should be individualized according to the patient risk and tumoral subtypes (Yes: 100%, No: 0%); (2) TNBC: (a) Adjuvant chemotherapy must be administered in the most effective way (Yes: 100%, No: 0%); (b) It is recommended to initiate adjuvant chemotherapy up to 2 mo after surgery (Yes: 100%, No: 0%); (c) In patients with age > 70 yr, discuss risk/benefits of using adjuvant chemotherapy; consider a regimen less immunosuppressive to avoid hospital admissions (Yes: 100%, No: 0%); (d) Consider the use of concomitant G-CSF to reduce the risk of infections (Yes: 89%, No: 11%); and (e) The use of adjuvant capecitabine, during 6-8 mo, in patients with no PCR after neoadjuvant chemotherapy is recommended (Yes: 100%, No: 0%); (3) HER2 (+): (a) Adjuvant chemotherapy associated with anti-HER2 therapy is recommended (Yes: 100%, No: 0%); (b) Subcutaneous trastuzumab is an alternative to reduce time to hospital admission. (Yes: 100%, No: 0%); (c) In selected patients (low risk, CS I-II, with PCR after neoadjuvant chemotherapy and surgery), it is valid to consider a shorter time of treatment with adjuvant trastuzumab (6 mo) to reduce hospital admission (Yes: 100%, No: 0%); (d) In the case of completing neoadjuvant chemotherapy associated with anti-HER2 therapy, it is reasonable to continue anti-HER2 therapy until surgery (Yes: 89%, No: 11%); and (e) The use of T-DM1 in those patients who cannot reach pCR after neoadjuvant chemotherapy is recommended. Moreover, the use of T-DM1 can be delayed after surgery (Yes: 100%, No: 0%); and (4) Luminal: (a) In "high risk" luminal patients, it is recommended to assess a clinical risk and/or use of genomic platforms (including tumors with lymph node involvement) to limit the use of adjuvant chemotherapy, according to institutional clinical practice guidelines (Yes: 100%, No: 0%); (b) The assessment of clinical risk with online tools (such as Predict) to estimate the risk of recurrence and the benefit of adjuvant chemotherapy is recommended (Yes: 100%, No: 0%); and (c) If adjuvant chemotherapy is necessary (risk/benefit previous evaluation), its initiation can be delayed up to a maximum of 3 mo after surgery (without reducing efficacy) (Yes: 89%, No: 11%)	(1) Delaying adjuvant chemotherapy in TNBC is associated with an increased risk of relapse and death; and (2) To limit the use of adjuvant chemotherapy, luminal BC should be assessed by clinical and/or genomic risks

BC: Breast cancer; CS: Clinical stage; G-CSF: Granulocyte-colony stimulating factor; PCR: Polymerase chain reaction; TNBC: Triple-negative BC.

chemotherapy). The election of chemotherapy, endocrine therapy, targeted therapy, or immunotherapy should be delivered in a selected population [*e.g.*, dual blockade anti-HER2 therapy + chemotherapy in HER2 (+) MBC, if accessible]. Most recommendations are classified as a medium priority in the MBC scenario. Recommendations for medical treatment in MBC are mentioned in Table 8[27-30].

DISCUSSION

The importance to divide recommendations into priorities is a complex challenge in

Table 8 Priorities for medical treatment of metastatic breast cancer

High priority	Medium priority	Low priority	Comments
HER2 (+) MBC: Dual anti-HER2 therapy (pertuzumab/trastuzumab) + chemotherapy is recommended in first-line HER2 (+) MBC (Yes: 100%, No: 0%)	(1) General considerations: (a) Goals for treatment in MBC: improvement of QoL, prolong survival (Yes: 100%, No: 0%); and (b) In absence of clinical infection for SARS-CoV-2, there is no specific recommendation to test a patient who initiates therapy (Yes: 89%, No: 11%); (2) Chemotherapy: (a) Consider the use of less toxic regimens (capecitabine, CM – cyclophosphamide/methotrexate) (Yes: 100%, No: 0%); and (b) If an anthracycline, a taxane, or eribulin is used, consider the concomitant use of G-CSF (Yes: 89%, No: 11%); (3) iCDK 4/6: (a) Offer clinical benefit in the first or second line in luminal MBC. They should be considered according to resources available and institutional practices[27] (Yes: 100%, No: 0%); (b) iCDK 4/6 can be deferred in selected patients if there is a high chance of controlling the disease with endocrine therapy alone (*e.g.*, *de novo* luminal MBC with a low burden of disease without visceral metastases) (Yes: 100%, No: 0%); and (c) Palbociclib dose reduction does not reduce efficacy (Yes: 100%, No: 0%)[28,29]; (4) Visceral crisis: (a) In the case of a suspected visceral crisis, clinical practice guidelines recommend the use of chemotherapy immediately (Yes: 100%, No: 0%); and (b) In an established visceral crisis, chemotherapy is the treatment of choice, but this concept is actually in revision due to the use of iCDK 4/6 in clinical practice (Yes: 100%, No: 0%); (5) Luminal MBC: (a) There should be an analysis of the benefits of using iCDK 4/6 *vs* the risk of adverse events. Dose reduction can reduce treatment related toxicities (Yes: 100%, No: 0%); (b) In the case of premenopausal women, it is recommended to induce ovarian suppression with LHRH analogs monthly or quarterly in selected cases, to reduce hospital admissions (Yes: 100%, No: 0%); (c) First line of treatment: currently, there is insufficient evidence to discontinue treatment with iCDK 4/6 in patients with luminal MBC (Yes: 100%, No: 0%); (d) The second line of treatment: after progression to iCDK 4/6, moving to another endocrine therapy is recommended (*e.g.*, AI or fulvestrant) (Yes: 100%, No: 0%); and (e) Other targeted therapies in luminal MBC: in second-line, consider avoiding or deferring the addition of mTOR inhibitors (everolimus induces immunosuppression and mucositis) or PIK3CA inhibitors (alpelisib induces hyperglycemia and risk of diabetes) to endocrine therapy, especially in elderly and/or comorbid patients (Yes: 100%, No: 0%); (6) HER2 (+) MBC: (a) In patients with more than 2 yr of disease control and minimal tumor burden with trastuzumab-based regimens, discontinuation of maintenance therapy may be considered[30] (Yes: 100%, No: 0%); (b) HR (+)/HER2 (+) MBC: (b1) Patients who initiate first-line treatment: Two options according to age—(i) patients < 70 yr: Consider less toxic regimens (paclitaxel every 3 wk + dual anti-HER2 blockade as a treatment option). If using docetaxel, consider the use of G-CSF from first cycle (Yes: 89%, No: 11%); and (ii) patients > 70 yr: Consider less toxic regimens (capecitabine) + dual anti-HER2 blockade. The option of using endocrine therapy associated to anti-HER2 therapy is valid if there is a low tumoral burden (Yes: 89%, No: 11%); and (b2) patients with controlled disease: Discontinuation of chemotherapy and use of oral therapy with AI +/- LHRH analogs (in premenopausal patients) may be considered as maintenance of anti-HER2 blockade (Yes: 100%, No: 0%); and (c) HR (-)/HER2 (+) MBC: (c1) In first-line setting (where an overall survival > 5 yr is expected) with a patient < 70 yr and symptomatic: Initiate taxanes every 3 wk and/or vinorelbine or capecitabine associated with anti-HER2 blockade (pertuzumab +/- trastuzumab). If using myelosuppressive regimens, consider G-CSF to reduce the risk of neutropenia (Yes: 89%, No: 11%); and (c2) Cases where the disease is in response with one line of chemotherapy + anti-HER2 therapy, in patients classified as "high groups for COVID-19" (*e.g.*, > 65-70 yr and/or comorbidity (diabetes, hypertension, *etc.*): Consider maintaining anti-HER2 therapy as maintenance (Yes: 89%, No: 11%); (7) mTNBC: (a) Recommendations with use of chemotherapy: (a1) Use regimens less frequently and with less toxicity (*e.g.*, use paclitaxel every 2 wk - Q2W- instead of docetaxel Q3W (Yes: 78%, No: 22%); (a2) Consider G-CSF to minimize the risk of neutropenia and reduce the use of corticosteroids (Yes: 89%, No: 11%); (a3) Prefer oral chemotherapy regimens (such as capecitabine) as an alternative to the EV route (if possible) (Yes: 100%, No: 0%); (a4) Consider less immunosuppressive regimens, with a preference for monotherapy regimens rather than combinations (Yes: 100%, No: 0%); and (b) For treatment with targeted therapies, it is recommended: (b1) Immunotherapy: Consider atezolizumab + chemotherapy in patients with PD-L1 (+) mTNBC (Yes: 100%, No: 0%); and (b2) PARP inhibitors (olaparib, talazoparib): Evaluate risk/benefit (myelotoxicity) and drug interactions (Yes: 100%, No: 0%); and (8) Second-line and subsequent lines: (a) Offer second-line, third-line, or subsequent lines of treatment when therapy can deliver clinical benefit and impact on outcomes (Yes: 100%, No: 0%); (b) In HER2 (+) MBC, after progression with trastuzumab, evaluate treatment with T-DM1 and/or other available therapies, always maintaining anti-HER2 blockade (Yes: 100%, No: 0%); (c) Some doses may be deferred to minimize risk of infection during the COVID-19 pandemic (Yes: 100%, No: 0%); and (d) In MBC, after a multidisciplinary discussion and according to the patient's preferences, terms such as "therapeutic rest", palliative therapy or maintenance regimens with dose reduction can be offered, depending on the case (Yes: 89%, No: 11%)	Bone agent therapy: Denosumab and zoledronic acid are no urgently needed (except in cases of hypercalcemia). It can be administered every 3 mo. Bone agents for patients with bone metastases should be deferred (Yes: 100%, No: 0%)	The rapidly evolving nature of the COVID-19 pandemic may change some recommendations. These will evolve over time with continuous updates

AI: Aromatase inhibitor; COVID-19: Coronavirus disease 2019; G-CSF: Granulocyte-colony stimulating factor; HR: Hormone receptor; LHRH: Luteinizing hormone-releasing hormone; MBC: Metastatic BC.

clinical decision-making. The purpose of this guideline is to prioritize patient scenarios by the urgency of treatment and make recommendations based on these priorities without compromising outcomes. This manuscript must be interpreted and adapted according to each oncologist's necessity, prioritizing physician judgment, and is not intended to replace institutional health policies or local guidelines. The goal of this manuscript is to orient and guide health workers related to medical oncology in the development of action plans to maintain the best outcomes for BC patients in the COVID-19 era. Recommendations about "high risk" subtypes (HER2, triple-negative) were similar in guidelines. Conversely, there was certain discordance in luminal subtype, with more flexible options of oncological medical treatment in each scenario (neoadjuvant, adjuvant, early, metastatic). For example, consider the assessment of clinical criteria or genomic platforms for the final decision of therapy in early BC. Consensus was made in order to avoid discordances. The goal of this manuscript is adapting guidelines to local context through relevant decision-makers in order to avoid duplication of efforts and optimize use of medical resources according to the national system[31].

This manuscript was adapted to a Latin America health system. For example, SPOM used some recommendations in order to generate best decisions of oncological medical treatment in Peru.

CONCLUSION

The COVID-19 pandemic represents a unique challenge for patients, clinicians, and the healthcare system. During the COVID-19 pandemic, minimization of exposure risk and preservation of resources are mandatory because there is a need of recommendations according to national realities and possibilities of health services access, without affecting the health of cancer patients. International clinical practice guidelines have formulated guidelines for the management of BC in the COVID-19 era involving all scenarios, most recommendations are similar, mainly in high-risk subtypes (HER2, triple-negative). Certain societies haven adapted these recommendations, including a panel vote with percentages, to deal with different situations involving the best decision in the management of BC patients. This manuscript has used and summarized three clinical practice guidelines, showing a broad vision (American, European) of BC management using different approaches and generating a consensus for adapting to our health system reality.

ARTICLE HIGHLIGHTS

Research background

The evaluation of the reality of access to health services in our country (Peru) is mandatory in coronavirus disease 2019 (COVID-19) era as is the prioritization of different approaches to determine which patients with cancer [in this case with breast cancer (BC)] need immediate treatment or those in which treatment can be deferred until pandemic is over. BC is one of the most frequent tumors in Peru, similar to other countries of Latin America and globally.

Research motivation

In Peru there is no information about a consensus or local guidelines of BC and COVID-19 management.

Research objectives

The main objective is to adapt international clinical practice guidelines to local context through best decision-makers, avoid duplication of efforts, and optimize medical resources, since Peru has many limitations to access a optimal health care attention.

Research methods

Peruvian Society of Medical Oncology invited an expert panel (including nine medical oncologists, opinion leaders in Peru) who reviewed and were asked to cast their vote. Decisions were discussed with a consensus though teleconference. One hundred twelve recommendations were reviewed, and priority categories were defined and adapted in three levels based on the severity and urgency of an individual patient's

conditions or treatments. Finally, some comments were allowed in each topic discussed.

Research results

Recommendations about human epidermal growth factor receptor 2 and triple-negative subtypes were quite similar, but in the luminal subtype there are more options for clinical decisions since treatment of different scenarios (mainly metastatic BC) has evolved in the last few years.

Research conclusions

Majority of recommendations were reviewed and adapted from international clinical practice guidelines to local context.

Research perspectives

The authors believe that this manuscript will be useful for other Latin America countries to adapt health policies in the COVID-19 era.

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