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"Breast Cancer Management Guidelines. A Consensus Statement by The Society of Surgeons® and Surgical Oncology Society of Pakistan®"

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"BREAST CANCER MANAGEMENT CONSENSUS BY THE SOCIETY OF SURGEONS AND SURGICAL ONCOLOGY SOCIETY OF PAKISTAN"

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"Society of Surgeons of Pakistan, Lahore Chapter"

Dr. Ruqayya Naheed Khan_

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Breast cancer remains as the the most common cancer among females globally. Despite scientists' endeavors to curtail this, it continues to rise rapidly in Pakistan. A multimodality approach remains the hallmark for the optimum management of breast cancer. Treatment paradigms are unfortunately limited to larger tertiary care centers around Pakistan, reasoned by an objective lack of specialist training and in-adherence of regulations and perhaps to some extent due to a paucity of economic resources.

Despite the availability of standard international guidelines such as NCCN, ESMO and ASCO, there continues a lack of compliance across many centers of care. Keeping in consideration of the local and cultural limitations, we have felt a growing need to establish a more relevant system of guidelines applicable to Pakistan. The ultimate aim of these guidelines is to provide objective consistency in delivering care across all realms of facilities.

To that end, we established a cohesive committee to assist with the draft of our preliminary guidelines. An initial core committee was formed comprising experts in the speciality of Surgical & Medical Oncology from Lahore tertiary care hospitals.

Further expansion of these guidelines followed at national centers of excellence across Pakistan.
After careful deliberation, the final guidelines are being presented here. Our recommendations here are evidence based, clinically approved and consistent with current standards of international guidelines.

With the benefit of this framework as a leading standard for management of breast cancer, we endeavor to improve patient care across a broader range of district level facilities.

I am in-debt to the enthusiasm of a dedicated team of experts who devoted their valuable personal and professional time to contribute to the ultimate formation and implementation of these guidelines.

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Fellowship Breast Surgery (Shaukat Khanum Memorial Cancer Hospital & Research Center)
Fellow of the European Board of Breast Surgery (Belgium)
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FOREWORD

Dr. Muhammad Farooq Afzal_
PRESIDENT, SOCIETY OF SURGEONS OF PAKISTAN, LAHORE CHAPTER

Breast cancer is both a global and local public health issue. According to the World Health Organization (WHO), breast cancer is the most common cancer among women worldwide, with an estimated 2.3 million new cases diagnosed in 2020. It is also the leading cause of cancer death among women, accounting for 685,000 deaths in the same year.

Similarly, in Pakistan, this is the commonest cancer among women and a leading cause of death. As per Global cancer observatory (GCO), the breast cancer related mortality is 13 per 100000.This higher mortality could be due to a number of factors, including late diagnosis, lack of access to quality treatment, and cultural barriers to seeking medical care. Therefore, there is a need for more research on breast cancer in Pakistan to better understand the risk factors, improve early detection and treatment, and reduce the mortality rate.

The development of clinical practice guidelines is one such effort to improve the management of breast cancer in Pakistan. It is with great enthusiasm that I introduce the Clinical Practice Guidelines for the Management of Breast Cancer, a pivotal resource crafted for surgeons, surgical oncologists, and all dedicated healthcare professionals intricately involved in the comprehensive care of breast cancer patients.

Though we lack authentic local research but efforts are being made to incorporate consensus as per our local needs. These guidelines represent a collective effort to distill the latest scientific evidence and clinical best practices into a cohesive framework.

The primary audience for these guidelines is you—the skilled surgeons, the surgical oncologists, and committed healthcare practitioners who daily confront the challenges posed by breast cancer and the health administration at Governmental level. Grounded in evidence-based recommendations, the guidelines aim to empower you with a comprehensive roadmap, facilitating informed decision-making and enhancing the quality. These guidelines provide a valuable tool to standardize practices, foster collaboration, and ultimately improve patient outcomes.

Looking forward, these guidelines should be viewed as a living document, adaptable to the evolving landscape of medical knowledge. Your insights, experiences, and feedback will be crucial in refining and updating the guidelines, ensuring their continued relevance and efficacy in the ever-advancing field of breast cancer management.

In closing, I extend my sincere appreciation to all those who have contributed to the development of these guidelines. It is my earnest hope that they serve as a valuable companion in your daily practice, enhancing the standard of care and reaffirming our shared commitment to excellence in the management of breast cancer. I also expect the department of health to ensure their dissemination and implementation in the provinces and all corners of Pakistan.

Dr Muhammad Farooq Afzal
FCPS FRCS FACS MCPS(HPE) MBA
Professor of Surgery
President Society of Surgeons of Pakistan Lahore chapter (2019-2022)

GUIDELINES

Breast Cancer Management Consensus By The Society of Surgeons and Surgical Oncology Society of Pakistan

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Abstract

The Society of Surgeons of Pakistan and The Society of Surgical Oncology of Pakistan with factions from various major centres comprising of surgical oncology, medical and radiation oncology collaborated to reach consensus on breast cancer management guidelines and a framework of "good practice" minimum standards of care. The aim of the task force was to enhance treatment standards, which have a direct correlation with improving patient mortality and morbidity and long-term survival whilst taking into consideration economic limitations of access to leading centers of excellence as well as minimum expertise required in health care. These multi-disciplinary guidelines, whilst not exhaustive, aim to provide an algorithm of care for breast cancer patients at tertiary care centres and district level hospitals to provide most appropriate treatment.

Keywords: Breast cancer, Chemotherapy, Radiotherapy, Lower and Middle Income Country, Safe Practice, Surgery, Management.

Introduction

Breast cancer is the most common cancer among women globally, however it remains less common in males. In 2020, there were 2.3 million women diagnosed with breast cancer and 685000 deaths globally. As of the end of 2020, there were 7.8 million women alive who were diagnosed with breast cancer in the past 5 years, making it the world's most prevalent cancer.[1]

Like many other developing countries, the cancer incidence is increasing in Pakistan being one of the most populous countries of the world. Shaukat Khanum Memorial Cancer Hospital & Research Center in 2021 reported breast cancer as the leading cancer with 1699 cases which constitute 24.6% of total cancer burden.[2] Another comprehensive report of cancer statistics in Pakistan from 2015 to 2019 showed breast cancer as the most common cancer constituting 38.8%.[3]

Early detection of breast cancer is the key to reduce morbidity and mortality however, we lack screening facilities. We are still struggling to initiate and maintain reliable cancer registry to pick up high risk patients. On the other hand, breast cancer awareness is increasing due to many awareness programmes which is a positive step towards restricting this disease.

Breast cancer should be managed according to standard guidelines by various societies such as National Comprehensive Cancer Network (NCCN)[4], European Society of Medical Oncology (ESMO)[5] or American Society of Clinical Oncology[6] to have uniformity of care. The optimum management of breast cancer requires a multimodality approach which is limited to some of the bigger tertiary care centers in Pakistan due to lack of resources and training.

The Society of Surgeons of Pakistan (Lahore chapter) along with the Surgical Oncology Society of Pakistan made a committee comprising of general surgeons, surgical oncologists, medical and radiation oncologists from different parts of Pakistan to form breast cancer management guidelines with mutual consensus for tertiary care hospitals with limited resources and district level hospitals to provide most appropriate treatment for

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breast cancer patients. This would also increase patient compliance and save them from travelling to far off specialised centers. These guidelines were made keeping in view all the international guidelines and well known clinical trials.[4-11]

The recommendations in these guidelines represent the view of the committee members , derived after multiple meetings and careful consideration of the evidence available. The professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients and to make decisions appropriate to the circumstances of the individual.

A. Diagnosis of Breast Cancer

A combination of clinical examination, radiological imaging (mammography, ultrasonography) and pathology called as triple assessment test is used to accurately diagnose all palpable breast lumps.

History:

1. Presenting symptoms
- Breast mass
- Skin changes like erythema/thickening
- Breast pain (cyclical/acyclical)
- Nipple discharge
- Nipple or skin retraction
- Axillary mass or pain
- Arm swelling
- Symptoms with reference to possible metastatic spread
- Prior biopsies

2. Past medical history of breast diseases
3. Family history of breast cancer, ovarian cancer, uterine cancer, other cancers
4. Reproductive history
- Menstrual history
- Age at first live pregnancy
- Number of pregnancies, children and miscarriages
- Age at onset of menopause
- Breast-feeding
- History of hormonal treatment including contraceptive pills and hormone replacement therapy (Type and duration)

5. Past medical history
- Hypertension
- Diabetes Mellitus
- Asthma
- Ischaemic
- Heart Diseases
- Skin diseases

Physical Examination:

1. Local examination: This should be carried out in both sitting and supine position. Both breasts and axilla should be examined.
- Size of breast compared to opposite breast
- Breast mass (Size/location specified by clock position/shape/ consistency/fixation to muscle and skin)
- Skin changes (Erythema / Oedema /Dimpling / Infiltration / Ulceration)
- Satellite nodules
- Nipple changes (Retraction/Erythema/Erosion and Ulceration)
- Nipple discharge (specify)
- Axillary nodes
- Supraclavicular nodes / Cervical nodes

2. Systemic examination

Radiological Investigations:

1.Ultrasound bilateral breast and axilla to be performed with a linear high frequency probe. (Lesion size/position/ solid or cystic/BIRADS/ multifocality/multicentricity/ suspicion of lymph node involvement like cortical thickness and loss of fatty hilum)

2. Bilateral breast mammogram:
- No age limit for performing mammogram if required in patients with highly suspicious breast lump, positive family history or biopsy proven breast cancer.
- In non-suspicious breast lump, mammography to be performed only if age more than or equal to 35years.
- In patients with age less than 35years (excluding above), ultrasound guided biopsy should be performed first. Mammography later if suspicion of malignancy.
- Mammogram can be omitted, if ipsilateral side is fungating.
- Report to include description after additional ultrasound breast.

3. Magnetic resonance imaging (MRI) Breast:

The routine use of MRI of the breast is not recommended. It should be considered in the following circumstances:
- If there is a discrepancy regarding the extent of disease between clinical examination, mammography and ultrasound assessment and accurate assessment of tumour size is required in treatment planning.
- Increased breast density precluding accurate mammographic assessment.
- To assess the tumour size in invasive lobular cancer if breast conservation is planned.

- Suspicious lump in the background of multiple fibroadenomas.
- In patients with occult breast cancer (axillary node metastasis but no lesion identified in breast on mammogram or ultrasound)
- Palpable lump but not picked up by ultrasound or mammogram.
- In younger BRCA (Breast Cancer Gene) positive patients for screening
- For screening patients having breast implants
- In some patients with positive margins after breast conserving surgery to assess the extent of residual disease (after 4 weeks of surgery). Magnetic Resonance Imaging should be carried out in the mid-portion of menstrual cycle.

5. Metastatic screening:
- Chest x-ray and ultrasound abdomen and pelvis should be advised to all patients
- If there is clinical suspicion of metastatic disease, the type of imaging will depend on the presentation.
- Bone scan should be advised to all patients with stage 2 or higher disease.
- Computed Tomography (CT) Chest, abdomen, pelvis and neck should be performed on every patient with N2, N3, T3 and T4 disease or any patient going for neoadjuvant treatment.
- Contrast enhanced CT head is imaging of choice for neurological symptoms.
- Positron Emission Tomography (PET) scan is optional.

Pathological Diagnosis:
- A non-operative breast cancer diagnosis is always preferable (clinical and radiological assessment followed by core biopsy and/or fine needle aspiration [FNAC]).
- Core biopsy is preferable due to the additional information it can provide however the possibility of utilizing FNAC as the alternative investigation for tissue diagnosis in patients less than 30yrs of age with no family history and clinically benign looking lumps can be considered.
- Image guided core biopsy should be performed in non-palpable or vaguely palpable lumps.
- Incisional biopsy can be considered in Paget's disease (wedge resection), fungating mass or in patients with inconclusive core.
- All clinically positive axillary lymph nodes should be biopsied (FNAC or core biopsy).
- ER, PR, Her2Neu and Ki67 should be performed on all specimens of proven cancers.
- Any patient with suspicious lesion but negative core biopsy should be advised to have upto 2 repetitive biopsies. If still negative for any malignancy, offer excision of the lesion to high risk patient or close follow up if patient refuses.
- Clinical staging should be done according to TNM classification[12].

One-Stop Breast Clinic Proforma:
A proforma should be designed for documenting history, clinical examination, investigations and MDT recommendations to bring uniformity to assessment and for accurate data collection.

B. Multidisciplinary Care
The breast multidisciplinary team (MDT):
It is worldwide accepted that breast cancer treatment should be provided by breast cancer specialists and that multidisciplinary teams form the basis for best practice. MDT meeting should take place before treatment options are discussed with the patient. The minimum requirement is the core membership.

Core Members of MDT:
- Breast Surgeon, Oncoplastic Breast Surgeon or a Consultant General Surgeon with an interest in breast disease.
- Specialist Radiologist
- Pathologist (Cytopathologist and/or Histopathologist)
- Medical Oncologist
- Radiation Oncologist
- Breast Care Nurse / Navigator (Highly recommended. He/she will work as MDT co-ordinator as well)

Extended members of the MDT may include;
- Medical Geneticist
- Clinical Psychologist
- Palliative Care Team
- Reconstructive Surgeon

Extended members are usually not available even in tertiary care but is highly recommended to develop these services and make them part of MDT.

Multidisciplinary team meetings:
All consultants and other team members within the breast unit must have fixed clinical commitment to attend MDT. It should be made compulsory for the trainees within breast surgery unit and other medical staff in the related disciplines to attend the MDT meeting. This should be a part of trainee's log book. The management plan of

PROFORMA

Name: ———————————————— DOB: ————————————
Age/Sex: ———————————— Hospital No: ————————————
Marital status: ————————- CNIC No: ————————————
Address: ————————————————————————————
Co-morbidities:
_____
_____

History:
Presenting Complaints: (duration, progression, pain)
_____
_____
_____
_____
_____

Nipple discharge:
_____
_____
_____

Skin change: ———————————— Nipple retraction: ————————————-
Other palpable masses:
_____
_____
_____

Past History:
_____
_____
_____

Family History: (Breast, ovarian, uterine and other cancers)
_____
_____
_____

Age of Menarche: ———— Age of Menopause: ————————
G P A: ———————————— Age at first pregnancy: ————————————-
LMP: ————————— Pregnancy: ————————————-

Breast Feeding: _____

History of OCPS(Oral/injectable) / Emergency Contraceptive Pills / Infertility treatment / HRT:

_____

_____

Clinical Examination:

Right breast:

_____

_____

_____

Right Axilla:

_____

_____

_____

Left Breast:

_____

_____

_____

Left Axilla:

_____

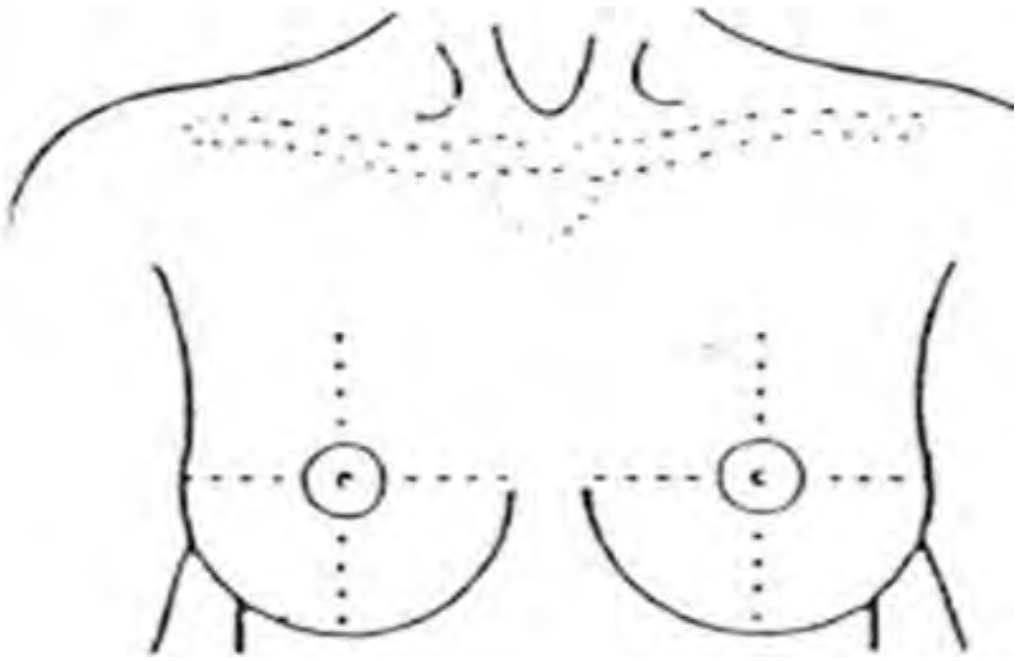
_____

_____

Other lymph nodes (Supra-clavicular / Cervical):

_____

_____



Systemic Examination:
_____
_____
_____

Investigations:
Ultrasound bilateral breast and axilla:
_____
_____
_____

Bilateral Mammogram:
_____
_____
_____

MRI Breast:
_____
_____
_____

Chest X-Ray:
_____
_____
_____

Ultrasound Abdomen / Pelvis:
_____
_____
_____

CT Thorax, Abdomen and Pelvis:
_____
_____
_____

Bone Scan:
_____
_____
_____

Other Investigations:
_____
_____
_____

Histopathology/Cytology:
Trucut Right Breast:
_____

Trucut/Fine Needle Aspiration Cytology,(FNAC) Right Axilla:
_____

Receptors: ER ———— PR ———— Her2Neu: ————
FISH (If Her2 Equivocal): ———— Ki67: ————

Trucut Left Breast:
_____

Trucut/FNAC Left Axilla:
_____

Receptors: ER _____ PR _____ Her2Neu: _____
FISH (If Her2 Equivocal 2+): _____ Ki67: _____

Other biopsies:
_____
_____
_____

Multidisciplinary Team Recommendations:
_____
_____
_____

Signature: _____
Date: _____

_____

patient discussion should be recorded in the case notes and coordinated by a designated member (MDT-coordinator).

All new patients should be discussed in MDT within 2 weeks of presentation. Results / post MDT clinic should be done no later than 1 week of MDT. All additional investigations (If recommended in MDT) should be done within 2 weeks of MDT. Definitive upfront surgery or neo-adjuvant treatment (after MDT) should not be delayed for more than two weeks.

C. Treatment Planning and Patient Communication

Each institution should have written guidelines for breast cancer treatment and should be followed by the MDT team however there can be circumstances where there may be reasonable exceptions which should be discussed at the MDT meeting and documented and later discussed with the patient. Patient should always be encouraged to bring a close relative, next of kin or a friend with them when the results are being discussed. Environment should be peaceful with adequate privacy. They should be given adequate time to ask questions and make decisions regarding their treatment. All the possible options agreed at MDT should be discussed.

- Operable early breast cancer: Most of the screen detected cancers and symptomatic patients with early presentation will fall into this category. Surgery will usually be the first treatment option.
- Inflammatory and locally advanced primary breast cancer: It will initially require staging investigations once the diagnosis have been made. In most patient's medical treatment (hormonal/chemotherapy/ targeted) will be the most appropriate initial treatment.
- Metastatic breast cancer: The aim should be to palliate symptoms and maintain quality of life. The average life expectancy is approximately 2 years in metastatic breast cancer with virtually all patients eventually dying from breast cancer. The role of surgeons come late if and when systemic disease is under control. Oligometastatic cancer can be treated with curative intent. Recurrent breast cancer: All such patients should be restaged prior to MDT discussion and definitive management. Tumor markers should be repeated on re-biopsy specimen.
- Patients who do not respond to neo-adjuvant treatment and patients who had some equivocal findings like lung nodules should be re-staged prior to surgery. PET -CT if available can be used as a tool for assessment and re-staging.

D. Surgery for Invasive Breast Cancer and Ductal Carcinoma in Situ

Surgery is the mainstay of treatment in early breast cancer and involves breast conservation or mastectomy depending on the following selection criteria:

Indications for Breast Conservation Surgery:

- Patient's choice provided they are given all the evidence based guidance.
- Favourable breast to tumour size ratio (Luminal A and B type cancers) to achieve an acceptable outcome. BCT is not a contraindication if they are not involving NAC. Tumours involving < 20% of breast tissue can undergo BCT while > 20 % can still undergo BCT with oncoplastic techniques.
- Central tumours depending on size, site and involvement of NAC
- Multi-focal tumour (distance in lesions < 2cm) restricted to a single breast quadrant
- If no contraindications to radiotherapy such as active connective tissue disease (scleroderma, Systemic lupus erythematosus etc) with significant vasculitis.
- Breast conservation can be offered to post neo adjuvant responsive tumours or larger tumours in combination with oncoplastic procedures.
- Unresponsive larger tumours such as DCIS can still have breast conservation surgery with oncoplastic procedures.

Indications for mastectomy:

- Patient's choice, provided they are given all the evidence based guidance
- Multi-centric (distance in lesions > 2cm) breast tumours
- Contraindication to radiotherapy
- Inflammatory breast cancer
- Extensive DCIS with or without invasive cancer
- Locally advanced breast cancer (e.g. not responding to neo adjuvant systemic therapy or ulcerated growth involving skin and chest wall)
- Local recurrence or positive margins after wide local excision where further wide local excision is not feasible
- Where breast conservation is unlikely to result in an acceptable cosmetic outcome (e.g. larger tumour in a small breast) though in most cases it can be down staged except large tumours with mostly DCIS does not respond to neo-adjuvant treatment.

Margins of excision:

- Excision of lump should be done in total
- All margins should be marked
- The incidence of local recurrence following breast conservation surgery can be reduced by attaining adequate clear margins. No ink on tumour margin for invasive disease and at least 2 mm margin for DCIS (except low grade DCIS) is acceptable and this is the minimal margin that will be accepted in all patients undergoing breast conserving surgery.
- Patients with a margin of less than 1 mm should be offered re-excision. However uni-focal involvement as per pathology report does not require re-excision.

Marking of surgical cavities in breast conservation surgery:

Consistent and accurate localisation of tumour bed in BCT with metal clips is vital for planning and delivery of radiotherapy and future surveillance. This is even more important in patients where oncoplastic techniques are used.

E. Axillary Management in Invasive Breast Cancer and Ductal Carcinoma in Situ

- Most powerful prognostic determinant in primary operable breast cancer is involvement of axillary lymph nodes for which histological confirmation is required.
- They can be clinically accessed or seen on an ultrasound prior to surgery. Fine needle aspiration cytology or core biopsy is done. Core biopsy of lymph node is mandatory in occult breast cancers.
- In case of positive node, patient will proceed with level II axillary dissection. In case of negative node, a sentinel lymph node biopsy is performed using blue dye or radio-isotope. In case sentinel lymph node biopsy cannot be performed due to lack of resources, axillary sampling should be carried out with at least 4 lymph nodes. Routine use of axillary clearance for staging purpose is an over treatment. ACOSOG Z0011 trial9 should be followed for the management of axilla in patients undergoing upfront breast conservation surgery in early breast cancer and sentinel lymph node biopsy. In patients with macro metastases, particularly if more than two nodes are involved, an axillary node clearance will be recommended.
- In patients undergoing upfront breast conserving surgery or mastectomy with a single micro metastasis, assessed by either immunohistochemistry or histopathology, an axillary node dissection can be avoided.
- Isolated tumour cells in axillary lymph nodes should be regarded as lymph node negative and does not require axillary clearance.
- In patients undergoing mastectomy, axillary clearance is recommended even with single positive node.
- In post chemotherapy patients, if nodes are positive for metastasis before chemotherapy, they will proceed to ALND. However, if they are negative before chemotherapy they will undergo sentinel lymph node biopsy ideally with dual tracer and will proceed to ALND even with a single positive node. A minimum of 3 nodes should be removed to decrease false negative rates.
- Axillary surgery should be avoided in DCIS except in patients requiring mastectomy or BCT for large (5cm or more) high grade lesion or patients with evidence of micro invasion on core. SLNBx or axillary sampling should be recommended in these patients.

F. Breast Reconstruction

- All women undergoing mastectomy should be offered reconstruction.
- Women must be fully informed of all available options for breast reconstruction at the time of planning initial surgical treatment so that they can make informed decisions, even if it is their personal preference to have a delayed reconstruction or no reconstruction at all.
- Delayed reconstruction is a better option in patients who require radiotherapy due to increased rate of capsular contraction.
- It should be performed by surgeons trained in reconstruction or patient should be referred to a tertiary care centre if required.

G. Neo Adjuvant Treatment

- All patients should receive neo adjuvant chemotherapy who are triple negative, Her2 enriched (if tumour is 2cm or above), inflammatory breast cancer, all N2, N3 patients and most patients with N1 nodal disease or where tumour size needs to be reduced for BCT and/or T2-T4 tumours.
- Clip localization and axillary biopsy should be done in all patients planned for BCT before

starting chemotherapy. If MRI is required, place clip after MRI as MRI compatible clips are expensive and not easily available.
- Women who are single or have not completed their family should be started on LHRH agonists at commencement of neo- adjuvant chemotherapy and throughout treatment to increase the chances of conception.

Assessment of response to treatment:
- Periodic clinical evaluation during systemic treatment should be carried out to assess response to treatment. Radiological evaluation should be done at the end of neo-adjuvant treatment.
- Surgery should be offered before completion of chemotherapy if poor response and can be completed later on. Patient should be restaged before surgery. PET CT can be used if available for re-staging.

H. Adjuvant Treatment
- Adjuvant chemotherapy or radiotherapy should be started as soon as clinically possible and certainly within 4-6 weeks of surgery.
- Radiotherapy: Indications are as follow;
- All patients who have had BCT for invasive breast cancer with clear margins.
- High grade DCIS following breast conservation surgery.
- Radiotherapy after mastectomy for invasive breast cancer should be given in patients with high risk of recurrence (tumour size more than 5cm, 4 or more positive lymph nodes or close / involved margins).
- There is no role of radiotherapy in patients undergoing mastectomy for DCIS.
- Axillary radiotherapy is not indicated in negative lymph nodes for metastasis.
- Axillary and supra-clavicular node radiotherapy should be considered in patients where axillary lymph nodes dissection is omitted following positive SLNBx or axillary sampling.

Endocrine treatment:
- Patients with ER positive invasive breast cancer potentially benefit from at least 5 years of anti-oestrogen therapy.
- Extended use of endocrine treatment for 10 years is recommended.
- Endocrine treatment is not recommended whilst patient is on chemotherapy.
- LH-RH (Luteinizing hormone – releasing hormone) agonists should be added in young premenopausal women for fertility prevention.
- Male breast cancer patients who are ER positive should be given tamoxifen for 5 years.
- It can be used in DCIS for risk reduction.
- Herceptin should be offered to all patients who are Her2 positive for a minimum of 6-12 months. Locally advanced Her2 positive patients with nodal metastasis should be offered dual Her 2 therapy. If after surgery there is still residual disease, patient can receive TDM1 (Transtuzumab emtansine).

I. Breast Cancer in Pregnancy
- Stay in close liaison with gynaecologist for antenatal care during treatment and a planned delivery.
- For axillary staging low dose radioactive agent to be used for sentinel lymph node biopsy. Blue dye is contraindicated in pregnancy.

First trimester:
- Surgery is the only recommended treatment.
- No neo adjuvant systemic therapy.
- In case of precious pregnancy, it may be allowed to continue after discussing the effects with patient. Otherwise it should be terminated after discussion with the patient. Treatment is given according to the stage of the disease.
- Radiotherapy and endocrine treatment are contraindicated.
- If patient is a candidate for neo-adjuvant chemotherapy and 1-2 weeks are left before she starts her second trimester, it is recommended to wait till then.

Second trimester:
- Neo adjuvant systemic therapy (anthracycline based chemotherapy, taxanes are better avoided) and surgery both are recommended. A pregnancy is to be continued after explaining the possible hazards to the patient.
- Radiotherapy and endocrine treatment is contraindicated.

Third trimester:
- Neo adjuvant systemic therapy and surgery both are recommended. A pregnancy is to be continued after explaining the possible hazards to the patient.
- Radiotherapy and endocrine treatment is contraindicated.

J. Paget's Disease

Paget's disease, without an associated lump, is to be treated as intra-ductal carcinoma. When a lump is present, treatment should be according to the TNM classification.

K. Male Breast Cancer

The classification of male breast cancer is the same as in females and is treated on the same guidelines. Early involvement of skin and pectoralis muscle occurs due to lack of breast tissue.

L. Clinical Follow up

- After completion of treatment, patient should be followed every 6 months for clinical examination and ultrasound if required.
- Bilateral yearly mammogram in case of BCT and in case of mastectomy, unilateral mammogram of the opposite breast and ultrasound of the mastectomy site should be performed.
- Patient should be followed up for at least 5 years but ideally 10 years.

M. Genetic Counselling and Testing:

- It should be offered to breast cancer patients less then 50 years age, triple negative and strong family history of breast and ovarian cancers.
- Breast surgeons are well positioned to be a resource for identifying patients who will benefit from genetic testing which mainly includes BRCA 1/ BRCA 2.

N. Institutional Guidelines

The criteria for a centre to treat breast cancer patients remains same as international institutional guidelines for both tertiary care and cancer hospitals. Since we have a large population and geographically it is not always possible for patients to travel to specialised health care centre, it is important to empower district level hospitals to at least be able to manage initial stages of breast cancer so there is no compromise on patient care. However if a centre is unable to provide optimum care, they should always refer the patient to a tertiary care centre. Specialist centres should have the following facilities to implement these guidelines;

- Development of dedicated breast surgery unit
- One stop breast clinic
- Pathology department with facility for immunohistochemistry and frozen sections to report breast biopsy as per College of American Pathologists guidelines.[13]
- Radiology department with facility of mammogram, stereotactic core biopsy, ultrasound machines (High frequency probe), MRI, clipping and wire localization of lesions. Mammogram and ultrasound to be reported by BIRAD categorisation.
- Facility for sentinel lymph node biopsy
- Isotope injections / Blue dye (Patent V)
- Department of Medical and Radiation oncology
- Plastic surgeon
- Psychologist
- Physiotherapy
- Breast care navigator
- Genetic counselling
- Appropriate data management resources should be available to record follow up and outcome data.

Conclusion:

These multidisciplinary guidelines have attempted to simplify things to understand and follow for the practicing surgeons to achieve standardised patient management. The guidelines are endorsed by the 'Society of Surgeons - Lahore Chapter" & 'Surgical Oncology Society of Pakistan" with intent of revision and updating periodically.

Abbreviations:

- ER: Estrogen Receptor
- PR: Progesterone Receptor
- Her2Neu: Human Epidermal Growth Factor Receptor 2
- Ki67: A monoclonal antibody
- ALND: Axillary Lymph Node Dissection
- SLNBx: Sentinel Lymph Node Biopsy
- DCIS: Ductal Carcinoma in Situ
- NAC: Nipple Areola Complex
- BCT: Breast Conserving Therapy
- PET-CT: Positron Emission Tomography and Computed Tomography
- FISH: Fluorescent in-situ Hybridisation

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