

QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF BREAST CANCER

(Third Edition)



Ministry of Health
Malaysia



Academy of
Medicine Malaysia

KEY MESSAGES

1. Breast cancer is the most important cancer among women in Malaysia. Regardless of gender, it contributed to 19.0% of all new cancer cases diagnosed in 2012 - 2016.
2. Nearly half of the breast cancer patients are diagnosed at stage III & IV (47.9%). Thus, increasing awareness is important for early detection.
3. Screening mammography for breast cancer may be performed biennially in women aged 50 - 74 years in the general population. For those with high risk, offer screening from 30 years of age.
4. Patients with symptoms & signs of breast cancer should be referred to breast clinic within 2 weeks.
5. Triple assessment which consists of clinical assessment, imaging [ultrasound (US) and/or mammography] & pathology (histology and/or cytology) is required in breast cancer diagnosis.
6. Multidisciplinary team approach should be considered in the management of breast cancer to improve clinical outcomes.
7. Surgery is the mainstay of treatment for early breast cancer, consists of breast conserving surgery (BCS) or mastectomy with sentinel lymph node (LN) biopsy or axillary dissection.
8. Breast cancer is a systemic disease. Hence, systemic therapy and/or radiotherapy have an established role in eradicating micro-metastasis to improve survival.
9. Fertility preservation should be discussed with all breast cancer patients in the reproductive age group & suitable patients should be referred to the fertility specialist.
10. Individuals suspected of having hereditary breast and/or ovarian cancers should have initial risk evaluation in order to determine if formal risk assessment in a cancer genetics clinic should be undertaken.

This Quick Reference provides key messages & a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Breast Cancer (Third Edition).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia: www.moh.gov.my

Academy of Medicine Malaysia: www.acadmed.org.my

CLINICAL PRACTICE GUIDELINES SECRETARIAT

Malaysian Health Technology Assessment Section (MaHTAS)

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RISK FACTORS

- The cause of the vast majority of breast cancers remains unknown. However, established risk factors include:

Non-modifiable	Modifiable
<ul style="list-style-type: none"> Increasing age Female Family history of breast cancer at a young age A carrier of pathogenic or likely pathogenic variants in genes e.g. BRCA1, BRCA2, PALB2, ATM & CHEK2 Early menarche (≤ 12 years old) or late menopause (≥ 50 years old) History of neoplastic disease of breast Increased mammographic density 	<ul style="list-style-type: none"> Nulliparity Lack of breastfeeding Hormonal factors: oral contraceptives, hormone replacement therapy, unopposed oestrogen use in hysterectomised women, etc. Lifestyle: overweight, lower level of physical activity, etc. Radiation exposure

CRITERIA FOR EARLY REFERRAL

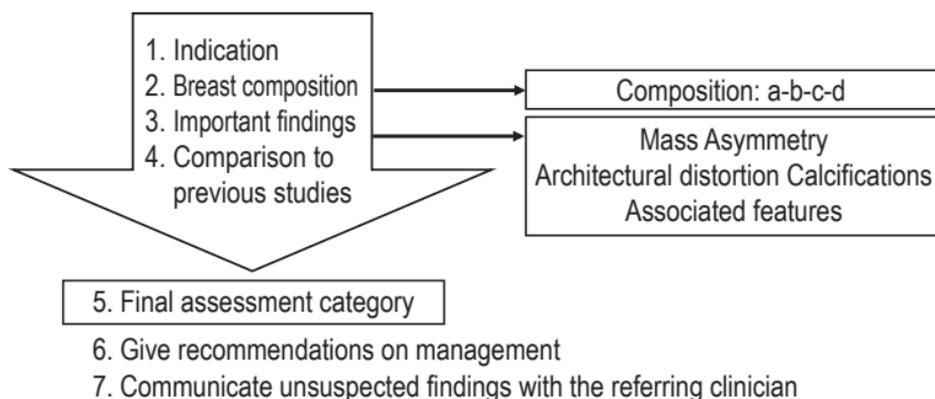
- Patients with any of the following conditions should be referred early (within 2 weeks) to breast or surgical clinic for further evaluation:
 - women aged >35 years with signs and symptoms
 - high risk group with signs and symptoms
 - patients with clinical signs of malignancy

ASSESSMENT AND DIAGNOSIS

i. Radiological Reporting

- Breast Imaging Reporting and Data System (BI-RADS®) is the preferred reporting method in the management of breast cancer.

Standard Reporting



Final Assessment Categories			
	Category	Management	Likelihood of Cancer
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	Not applicable
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably benign	Short interval follow-up (6 months) or continued surveillance	>0% but ≤2%
4	Suspicious	Tissue diagnosis	4a. low suspicion of malignancy (>2% to ≤10%) 4b. moderate suspicion of malignancy (>10% to ≤50%) 4c. high suspicion of malignancy (>50% to <95%)
5	Highly suggestive of malignancy	Tissue diagnosis	≥95%
6	Known biopsy-proven	Surgical excision when clinical appropriate	Not applicable

ii. Tissue Sampling

- Minimally invasive biopsy technique (MIBT) with core needle is the preferred diagnostic technique for both palpable and non-palpable breast lesions.
- Repeat image-guided MIBT or consider surgical excision when the initial core biopsy results are non-diagnostic or discordant with the imaging findings.

iii. Histopathological Examination

Adequate surgical pathology reporting of breast cancer using standard proforma with minimum dataset should have:

- maximum diameter of invasive tumour
- location (side & quadrant), multifocality/multicentricity
- tumour type (histology according to WHO classification)
- histological grade
- LN involvement and total number of nodes examined
- resection margins
- lymphovascular invasion
- non-neoplastic breast changes
- hormone receptor status: ER/PR
- HER2/c-erb B2 assessment

- Estrogen receptor (ER) & progesterone receptor (PR) status should be assessed in all cases of breast cancer.
- Human Epidermal Growth Factor Receptor 2 (HER2) test using immunohistochemistry should be performed on all invasive breast cancer specimens.
- In-situ hybridisation test should be done only in equivocal HER2 (immunohistochemistry 2+) on invasive breast cancer specimens.

- The staging of breast cancer is based on Tumor Nodes Metastasis (TNM) Classification of The American Joint Committee on Cancer (AJCC)
- Early breast cancer includes cancer of stage I, stage IIA & stage IIB.

SURGICAL MARGIN

- No tumour at ink margin on histopathological examination is adequate for BCS in invasive breast carcinoma.
- In women treated with BCS for ductal carcinoma in situ of <2 mm margin, the benefits & risks of further treatment (surgery or radiotherapy) should be discussed to reduce the risk of local recurrence.

SYSTEMIC THERAPY

Neoadjuvant Therapy

- Inoperable breast cancer should be referred for neoadjuvant systemic therapy prior to surgical intervention.
- Neoadjuvant chemotherapy may be offered to patients with triple negative or HER2-positive early breast cancer to enable BCS but its benefits & risks need to be discussed with the patients.

Adjuvant Therapy

- Adjuvant therapy should be offered based on assessment of risks & benefits (refer table on risk categories).
- Taxane-based adjuvant chemotherapy should be offered in patients requiring adjuvant chemotherapy especially in node positive breast cancer.
- Adjuvant extended endocrine therapy may be offered to hormone receptor-positive breast cancer.
- Trastuzumab should be given to women with HER2-positive breast cancer having adjuvant chemotherapy.

Risk categories of breast cancer for adjuvant systemic therapy

Low risk	Intermediate risk	High risk
<p>pN0 and all of the following criteria:</p> <ul style="list-style-type: none"> • size of tumour maximum 2 cm • Grade 1 • no vessel invasion • ER/PR+ • HER2-negative • age ≥ 35 years old 	<p>pN0 and at least 1 further criterion:</p> <ul style="list-style-type: none"> • size of tumour >2 cm • Grade 2/3 • vessel invasion • HER2 overexpression • age <35 years old • pN+ (N1 - 3) and HER2-negative 	<p>pN+ (N1 - 3) and HER2 overexpression or pN+(N\geq4)</p>

Systemic therapy for metastatic disease

- Endocrine therapy should be considered as first-line treatment in hormone-receptor positive, HER2-negative metastatic breast cancer unless there is evidence of visceral crisis or endocrine resistance.
- Combination chemotherapy may be considered in fit metastatic breast cancer patients with impending visceral crisis or when rapid resolution of symptoms is required.
- Bisphosphonates may be offered in breast cancer patients with bone metastases to reduce skeletal-related events.

RADIOTHERAPY

- Indication for adjuvant radiotherapy:
 - i. BCS with clear margin
 - ii. Post-mastectomy
 - ≥ 1 LN positive
 - positive margin not amenable for surgery
 - LN negative in T3 or T4

FAMILIAL BREAST CANCER

Comprehensive guidelines for genetic testing are contained in the CPG. However, the simplified Mainstreaming Cancer Genetics Cancer-Based Criteria below may be used as a guide to identify at-risk individuals for evaluation of genetic testing.

1. Ovarian cancer (epithelial non-mucinous ovarian cancer)
2. Breast cancer in patient diagnosed ≤ 45 years old
3. Two primary breast cancers, both diagnosed ≤ 60 years old
4. Triple-negative breast cancer, diagnosed ≤ 60 years old
5. Male breast cancer
6. Breast cancer plus parent, sibling or child with any of the above criteria

- Individuals with pathogenic/likely pathogenic variants in BRCA1 & BRCA2 have an increased risk of breast, ovarian & a number of related cancers. Hence these individuals warrant consideration of earlier & more intensive screening plus preventive strategies.

FOLLOW-UP

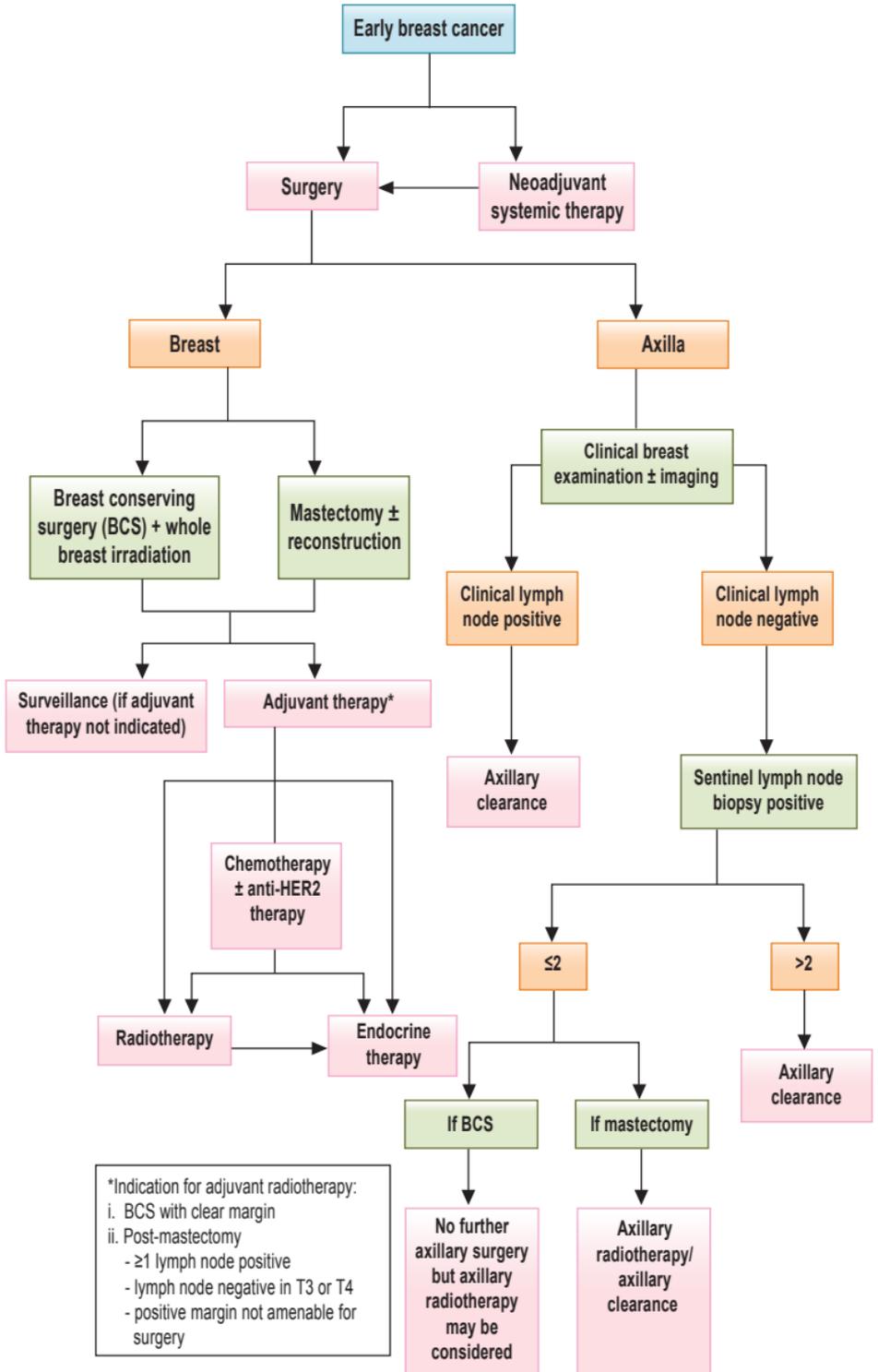
- Regular follow-up visits are recommended every 3 - 4 months in the first 2 years, every 6 - 8 months from subsequent years 3 - 5 & annually thereafter. The interval of visits should be adapted to the risk of relapse & patients' needs.

SUPPORTIVE TREATMENT

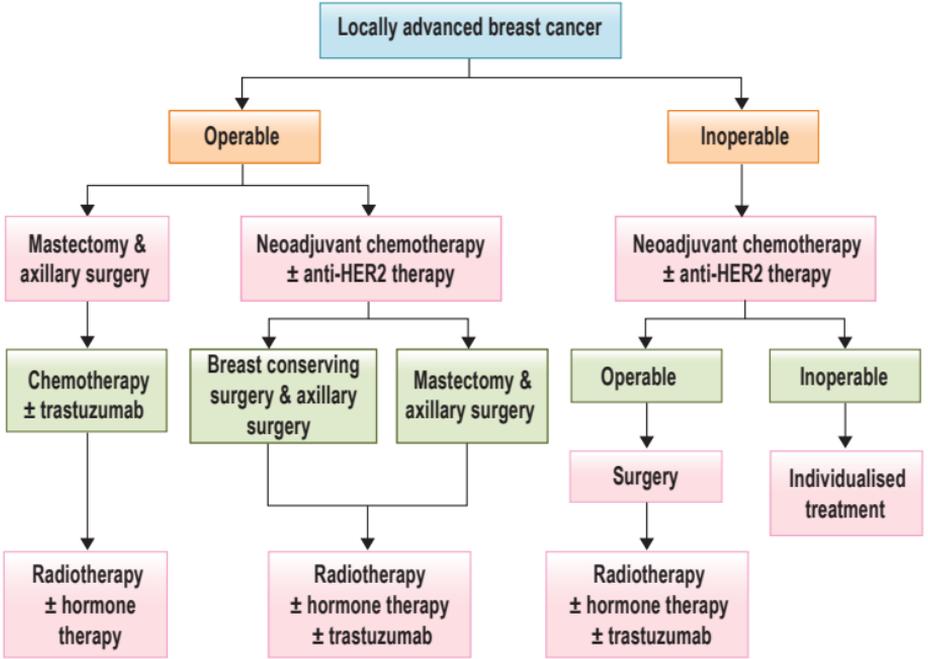
The following additional management is important & should be considered for breast cancer patients when indicated:

- psychosocial assessment & intervention
- palliative care
- breast care nurse
- patient navigation programme
- lifestyle modifications
- breast cancer patient support groups

ALGORITHM 1. MANAGEMENT OF EARLY BREAST CANCER



ALGORITHM 2. MANAGEMENT OF LOCALLY ADVANCED BREAST CANCER



ALGORITHM 3. MANAGEMENT OF METASTATIC BREAST CANCER

