

Overview of Breast Cancer Therapy



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KEYWORDS

- Breast cancer therapy • Local therapy • Adjuvant therapy • Breast-conserving therapy
- Mastectomy • Neoadjuvant chemotherapy • Breast cancer surveillance • Endocrine therapy

KEY POINTS

- Breast-conserving therapy and mastectomy are well-established local therapies for early-stage invasive breast cancer and have equivalent survival and recurrence outcomes with multimodal therapy.
- Neoadjuvant chemotherapy is increasingly used to downstage disease in the breast and axilla, allowing breast conservation and avoiding axillary lymph node dissection, and is most likely to be successful in a unicentric, human epidermal growth factor receptor 2–positive or triple negative breast cancer.
- Adjuvant medical therapies are given after breast surgery to eradicate clinically and radiographically occult micrometastatic disease that may develop into frank metastases if untreated.
- Disease burden and biology determine patients' risk of recurrence, which guides the selection of appropriate adjuvant medical therapies.

The diagnosis and treatment of invasive breast cancer requires a collaborative effort among multiple subspecialties. Diagnostic imaging workup and biopsy play a key role in establishing a diagnosis and informing surgical decisions on management of the primary tumor, staging of the axilla, and the sequence of therapy. Once a diagnosis of breast cancer is established, the extent of disease is assessed, which, for the most part, determines whether or not preoperative (neoadjuvant) systemic therapy is indicated. Confirmed stage IV breast cancer is considered incurable; it is treated with systemic therapy alone unless there is an indication for palliative resection of the primary tumor and is not discussed further. An important part of the initial clinical evaluation of patients with nonmetastatic breast cancer is to identify

clinical criteria of inoperability, which necessitate the use of neoadjuvant therapy. These criteria include inflammatory carcinoma, fixation of the tumor to the bony chest wall (ribs, sternum), extensive skin involvement with ulceration or satellite skin nodules, fixed/matted axillary lymphadenopathy, involvement of neurovascular structures of the axilla, or lymphedema of the ipsilateral arm. All of these findings are readily identifiable on physical examination and should prompt an imaging evaluation for distant metastases. In these cases, systemic therapy is administered as initial treatment to reduce tumor volume and will render approximately 80% of patients operable.¹ In those patients who present with operable disease, the sequence of surgical resection and systemic therapy is variable. Preoperative systemic therapy

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may be used to reduce tumor volume in the breast, allowing breast conservation when mastectomy would otherwise be necessary, and to decrease the need for axillary lymph node dissection (ALND). In most patients presenting with stage I and II disease, resection of the tumor is the initial step in management, and patients have the option of breast conservation or mastectomy (Fig. 1).

LOCAL THERAPY FOR INVASIVE BREAST CANCER: BREAST-CONSERVING THERAPY AND MASTECTOMY

Breast-conserving therapy (BCT) and mastectomy are both well-established local therapies for invasive breast cancer. Multiple randomized clinical trials with a follow-up of up to 20 years have demonstrated that BCT is safe and has survival outcomes equivalent to mastectomy in stage I and II breast cancer.^{2–6} Although a few earlier trials reported higher rates of locoregional recurrence (LRR) following BCT than were seen after mastectomy (10%–22%),^{2,4,7} much lower LRR rates are reported in contemporary studies. The decrease in LRR can be attributed to the implementation of microscopic confirmation of negative resection margins and the widespread use of systemic therapy. In a study of LRR in patients with node-negative and node-positive breast cancer receiving systemic therapy after BCT in 5 National Surgical Adjuvant Breast and Bowel Project protocols, 10-year local recurrence rates were 5.2% and 8.7%, respectively.^{8,9} These rates are comparable with observed 10-year rates of isolated local recurrence after mastectomy of approximately 8%.¹⁰ It is now understood that local control is not solely a function of disease burden and extent of surgery, but varies with tumor molecular subtype and administration of systemic therapy. Rates of local recurrence differ significantly among breast cancer subtypes, regardless of whether patients are treated with mastectomy or BCT. Local recurrence rates are highest among patients with hormone receptor (HR)–negative, human epidermal growth factor receptor 2 (HER2)–negative cancers (triple negative), and lowest among patients with HR-positive, HER2-negative cancers.^{11,12} This understanding eliminates the rationale for treating biologically aggressive cancers with mastectomy, and most patients with stage I and II disease are candidates for BCT.

BREAST-CONSERVING THERAPY

BCT involves excision of the tumor (lumpectomy) followed by adjuvant whole-breast irradiation (WBI). In order to perform BCT, it must be possible

to excise the tumor to negative margins with an acceptable cosmetic outcome, patients must be able to receive radiotherapy, and the breast must be suitable for follow-up to allow prompt detection of local recurrence. The contraindications to BCT arise logically from these requirements. Contraindications to BCT include the presence of diffuse suspicious or malignant-appearing calcifications, disease that cannot be resected to negative margins with a satisfactory cosmetic result, and the presence of contraindications to delivery of radiation, such as prior treatment of the breast field or active scleroderma.¹³ A negative margin is defined as “no ink on the tumor.”^{13,14} More widely clear margins do not improve local control in invasive breast cancer and are not required for BCT.¹⁵ If negative margins can be achieved with an acceptable cosmetic outcome, then lumpectomy can be performed irrespective of tumor size. In women with large tumors relative to breast size, neoadjuvant chemotherapy (NAC) can be used to downstage the tumor (see later discussion). Young age, aggressive tumor subtype (HER2-positive and triple negative), and lobular histology are not contraindications to BCT. In patients with BRCA1/2 mutations, bilateral mastectomy is a consideration, as the risk of a new primary breast cancer development can range from 26% to 40% over the 20 years following diagnosis depending on the age of onset of the initial cancer, performance of oophorectomy, and use of endocrine therapy.¹⁶ Despite this higher risk, a BRCA mutation is not an absolute contraindication to breast conservation, and patient preference must also be considered.

Physical examination, mammography, and diagnostic ultrasound are the imaging modalities in standard use to select patients for BCT. In a population-based study of 1984 women with ductal carcinoma in situ and stage I and II invasive cancers, 88% of those attempting BCT successfully had the procedure. This figure is probably an underestimate of the number of women eligible for BCT because many were converted to mastectomy without an attempt at reexcision.¹⁷ The use of MR imaging in the preoperative setting is controversial. MR imaging is more sensitive than mammography or ultrasound, detecting additional disease in 16% of patients in a meta-analysis.¹⁸ It was hoped that MR imaging would improve selection of lumpectomy candidates and decrease rates of reoperation. However, multiple studies of preoperative MR imaging have demonstrated an increase in both ipsilateral mastectomy for the index tumor and contralateral prophylactic mastectomy rates without an accompanying reduction in reoperation and recurrence rates.^{19–26}

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