and computed tomographic (CT) scanning of the chest and abdomen. In the absence of signs or symptoms suggestive of metastatic disease, patients with smaller tumors and negative lymph node involvement usually do not require further imaging. Fewer than 10% of women have metastatic breast cancer at diagnosis.

PATHOLOGY

Because of the increasing utilization and sophistication of breast cancer screening, ductal carcinoma in situ (DCIS) is being reported more frequently; however, it is infrequently invasive. Most invasive breast cancers are infiltrating ductal carcinomas, and a smaller proportion are infiltrating lobular carcinomas. Tubular and mucinous carcinomas, a subtype of infiltrating ductal cancers, are associated with a better prognosis. Inflammatory breast cancer is on the other end of the spectrum, frequently denoting a poor prognosis. Inflammatory breast cancer remains a clinical diagnosis: it is recognized by breast skin changes such as edema and erythema of the skin (peau d'orange), often in the absence of a palpable mass.

At the time of breast biopsy and definitive surgery, the estrogen and progesterone receptor status of the primary tumor should be routinely assessed. Overexpression of the human epidermal growth factor receptor HER2/neu or its gene amplification is critical for treatment selection and prognosis and should also be assessed. So-called triple-negative tumors—those that are negative for the estrogen and progesterone receptors and for amplification of the *HER2 [ERBB2]* oncogene—are associated with a poorer prognosis and offer fewer treatment options. Triple-negative tumors are more commonly found in women who have the *BRCA* breast cancer susceptibility gene. In women with hormone receptor–positive tumors, gene expression assays may provide additional prognostic information to guide treatment decision making.

TREATMENT

The appropriate care of patients with early-stage breast cancer is multidisciplinary, involving a radiologist, pathologist, surgeon, medical oncologist, radiation oncologist and often others. Breast-conserving therapy with lumpectomy followed by radiation therapy represents the current standard of care for most women with small invasive breast cancers. Women with large tumors may be considered for mastectomy with or without breast reconstruction. Currently, many such patients are considered for neoadjuvant (preoperative) chemotherapy; this may allow breast conservation in these women who would otherwise not be able to undergo a lumpectomy, and it also provides an objective assessment of tumor response to systemic therapy. Women who have had previous radiation to the breast for breast cancer or another malignancy, are usually treated with mastectomy. Frail patients with hormone receptor–positive tumors may be considered for primary hormonal therapy rather than radiation therapy; surgical treatment is usually indicated for these patients.

Adjuvant therapy with chemotherapy and hormonal therapy following definitive surgery improves relapse-free and overall survival rates in premenopausal and postmenopausal women. Subsequent adjuvant therapy for 1 year with the monoclonal antibody trastuzumab improves disease-free survival in patients with tumors that demonstrate overexpression of the HER2 oncoprotein or amplification of its *HER2 (ERBB2)* oncogene. DCIS is treated with either lumpectomy followed by radiation therapy or with mastectomy alone. Women with larger or multifocal DCIS should have assessment of their lymph node status to exclude lymph node involvement associated with occult invasive cancer. In the absence of invasive disease, adjuvant chemotherapy is not indicated for DCIS.

The risks and benefits associated with tamoxifen for chemoprevention in patients with higher risk features should be discussed. Women with the *BRCA1* or *BRCA2* breast cancer susceptibility genes should be offered prophylactic bilateral mastectomy and oophorectomy given their high risk for development of invasive breast cancer as well as ovarian cancer at a relatively young age. Close surveillance with breast clinical examinations as well as screening mammography and breast MRI should be offered to those patients with *BRCA* susceptibility genes who elect a nonsurgical approach. Oophorectomy or antiestrogen therapy can help decrease the risk of breast cancer in these women and others at high risk for the disease.

Breast cancer most commonly recurs with metastases in the bone, liver, lung, and central nervous system, but it can recur in any organ system. Rates of breast cancer recurrence and mortality are greater among African American women than white women; those of other ethnicities have lower mortality rates (see Fig. 59-2). Although women with metastatic breast cancer have an average life expectancy of years rather than months, the disease remains incurable. The decision to offer systemic therapy in women with metastatic breast cancer is based on extent and sites of disease, severity of symptoms, patient physical functioning, previous treatment, comorbid conditions, and especially the tumor molecular characteristics of hormone receptor and *HER2* status. Although tumor hormonal status and *HER2* status may change over the treatment course in a patient with metastatic breast cancer, life expectancy is typically longer in women with hormone-responsive (receptor-positive) disease and when the sites of metastases are lymph nodes or bone rather than liver, lung, or central nervous system. Patients with hormone-responsive metastatic breast cancer may live for many years, often responding to hormonal therapy for years before requiring chemotherapy for disease control.

In patients with HER2-positive tumors, trastuzumab may be used in combination with chemotherapy or hormonal therapy. Several novel anti-HER2 therapies have been developed that are changing and expanding the therapeutic options and improving the prognostic outlook of these patients. Many chemotherapeutic agents (singly or in combination), including the anthracyclines, taxanes, alkylating agents, fluoropyrimidines, vinca alkaloids, gemcitabine, and epithilones, demonstrate activity against breast cancer. Bisphosphonates, such as zoledronate and pamidronate, are given intravenously to decrease the pain associated with bone metastases and the risk for fracture in women with skeletal metastases.

PROGNOSIS

Most women with early-stage breast cancer survive for many years after their initial diagnosis and treatment, and many enjoy