

Table 23-4 American Joint Committee on Cancer and Union Contre Le Cancer Staging*

Stage	T: Primary Cancer	N: Lymph Nodes	M: Distant Metastasis	10-Year Survival (%)
0	DCIS or LCIS	No metastases	Absent	92
I	Invasive carcinoma ≤2 cm	No metastases or only micrometastases	Absent	87
II	Invasive carcinoma >2 cm	1 to 3 positive LNs	Absent	65
	Invasive carcinoma >5 cm but ≤5 cm	0 to 3 positive LNs	Absent	
III	Invasive carcinoma >5 cm	Negative or positive LNs	Absent	40
	Any size invasive carcinoma	≥4 positive LNs	Absent	
	Invasive carcinoma with skin or chest wall involvement or inflammatory carcinoma	Negative or positive LNs	Absent	
IV	Any size invasive carcinoma	Negative or positive lymph nodes	Present	5

DCIS, Ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

*The groups listed in the table are based on the characteristics of the primary carcinoma and the axillary lymph nodes. For rare women with involved internal mammary lymph nodes or supraclavicular lymph nodes, there are additional staging criteria.

type is more strongly correlated with prognosis than the molecular type.

- **Histologic grade.** All invasive carcinomas are graded using the Nottingham Histologic Score (already described). Nuclear grade, tubule formation, and mitotic rate classify invasive carcinomas into three groups that are highly correlated with disease free and overall survival.
- **Proliferative rate.** Proliferation can be measured by mitotic counts (e.g., as part of histologic grading), by immunohistochemical detection of proteins that are specifically expressed by actively dividing cells (e.g., cyclins, Ki-67). Proliferation is primarily important for ER-positive, HER2-negative carcinomas, as the majority of ER-negative and/or HER2 positive carcinomas have high proliferative rates. Carcinomas with high proliferation rates have a poorer prognosis but may respond better to chemotherapy.
- **Estrogen and progesterone receptors.** Eighty percent of carcinomas that are both ER- and PR-positive respond to hormonal manipulation, whereas only about 40% of those positive for only ER or PR respond. Strongly ER-positive cancers are less likely to respond to chemotherapy. Conversely, cancers that fail to express either ER or PR have a less than 10% likelihood of responding to hormonal therapy but are more likely to respond to chemotherapy.
- **HER2.** HER2 overexpression is associated with poorer survival, but its main importance is as a predictor of response to agents that target this receptor.

For decades, the prognosis of breast cancer patients has been estimated by gauging the extent of disease in the breast, the involvement of regional lymph nodes, and the presence of distant metastases. The five stages (0 to IV) defined by the American Joint Committee on Cancer (AJCC) and Union Contre Le Cancer (UICC) are highly correlated with survival (Table 23-4 and Fig. 23-25). More recently, insights gained by studying the molecular biology of breast cancers has improved outcome prediction (Fig. 23-26).

In the absence of adequate surgery, the majority of patients with breast cancer die with extensive local disease causing ulceration of the skin. *Carcinoma en cuirasse* (literally “carcinoma of the breastplate”) is a dreaded

complication that must be prevented in order to maintain the best possible quality of life, even in women with distant metastatic disease. Unfortunately, it remains a common presentation for women living in areas with limited resources. With earlier detection, local control of the disease can be achieved in the majority of women with breast conserving surgery and radiation. Carcinoma in situ and small node negative invasive carcinomas are often cured by this treatment alone. For those who require mastectomy, skin- and nipple-sparing procedures provide cosmetically superior results.

KEY CONCEPTS

Types of Carcinoma, Prognostic Factors

- DCIS is treated locally, as subsequent invasive carcinomas usually occur at the same site, whereas LCIS confers bilateral risk.
- Invasive carcinomas can be classified into molecular types based on expression of hormone receptors and HER2 along with proliferative rate.
- Molecular types have important clinical, biologic, and therapeutic associations.
- Special histologic types of carcinomas tend to have distinctive pathways of tumorigenesis and are providing additional clues linking biologic changes to clinical behavior.
- Prognosis is dependent on both the biologic type of cancer (molecular or histologic type) and the extent of cancer at the time of diagnosis (stage).
- Effective treatment requires both local and systemic control of disease.
- Improvements in treatment are being made as new targeted therapies are being developed and response to treatment is better understood.

Stromal Tumors

The two types of stroma in the breast, intralobular and interlobular give rise to distinct types of neoplasms. The breast-specific biphasic tumors fibroadenoma and phyllodes tumor arise from intralobular stroma. This