Ductal Carcinoma In Situ

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KEYWORDS

• Ductal carcinoma in situ • Incidence • Mortality • Radiation therapy
• Hormonal therapy • Breast cancer

KEY POINTS

- Ductal carcinoma in situ has been stable in incidence over the past decade and has an excellent prognosis within a multidisciplinary treatment approach.
- Breast conservation therapy is a safe and effective surgical treatment for most Ductal carcinoma in situ patients at the current time.
- Adjuvant whole breast radiation therapy is recommended to reduce the risk of local recurrence in ductal carcinoma in situ undergoing breast conservation therapy.
- Accelerated partial breast irradiation is a promising alternative for some selected patients to decreased toxicity and improve cosmetic results.

EPIDEMIOLOGY AND ETIOLOGY

Ductal carcinoma in situ (DCIS) of the breast is characterized by abnormal ductal epithelial cells that have not yet invaded through the myoepithelial cells overlying the ductal basement membrane and, thus, is by definition noninvasive. The incidence of DCIS has increased dramatically over the last few decades, thought to be largely attributable to the widespread adoption and use of population-based mammographic screening for breast cancer in the United States.[1] Before 1982, the incidence of DCIS was relatively stable at approximately 12 per 100,000, comprising less than 1% to 2% of diagnosed breast cancer.[2] With the increased use of mammographic screening between 1982 and 1991, its incidence reached approximately 30 per 100,000. After 1991, the age-standardized incidence of DCIS continued to increase to 50 per 100,000 women in 1999, and then stabilized.[1] In the United States, DCIS accounts for 20% of all newly diagnosed breast cancers and about 1 in 33 women will be diagnosed with breast carcinoma in situ in their lifetime.[3] In 2015, there were an estimated 60,000 diagnosed cases of breast carcinoma in situ, representing 25% of all breast cancer diagnoses, with most of them (83%) being DCIS.[4]

The authors have nothing to disclose.

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The incidence of DCIS varies according to both age and ethnicity. Because mammographic screening for women younger than 40 years of age is not routinely recommended, DCIS is rarely identified in young women.[5] In women over 40 years of age, DCIS incidence tends to increase rapidly with increasing age and peaks in the 70 to 79 years of age range.[4] With regard to ethnicity, the incidence of DCIS is nearly equal for non-Hispanic white and black women, lower for Asian/Pacific Islander and Hispanic women, and lowest for American Indian and Alaska Native women.[4]

The long-term prognosis of DCIS is excellent, with mortality rates at 10 years being less than 5%. Recently, a large retrospective study using Surveillance, Epidemiology, and End Results (SEER) data investigated the 10- and 20-year breast cancer-specific survival in 956 patients after a diagnosis of DCIS.[6] They found a 20-year cause-specific DCIS mortality rate of 3.3% (95% confidence interval [CI], 3.0%-3.6%), which decreased to 1.7% when contralateral recurrence was excluded. The breast cancer-specific survival of DCIS was associated with age at diagnosis, ethnicity, tumor size, tumor grade, and estrogen receptor (ER) status. Among patients who received breast conservation therapy (BCT)/lumpectomy and whole breast radiation therapy (WBRT), there was an associated reduction in risk of ipsilateral invasive recurrence at 10 years (2.5% vs 4.9%; adjusted hazard ratio [HR], 0.47; 95% CI, 0.42–0.53), but not of breast cancer-specific survival at 10 years (0.8% vs 0.9%; HR, 0.86; 95% CI, 0.67–1.10).[6] This study has been criticized for its absence of central pathology review to exclude occult invasive breast cancer, its retrospective nature with inherent selection bias, and its survival statistical methods.[7–9] Despite these limitations, the study clearly demonstrates the excellent prognosis of DCIS when treated appropriately.

DCIS is generally considered as the nonobligate precursor lesion of invasive ductal carcinoma (IDC), but its own etiology is poorly understood compared with IDC. Epidemiologic studies indicate that both DCIS and IDC share similar environmental risk factors, which include reproductive risk factors, such as age at menarche, parity, age at first birth, and age at menopause, as well as nonreproductive risk factors, such as family history, alcohol intake, and hormone replacement therapy.[10–18] Interestingly, the association of body mass index (BMI) with DCIS remains unclear. Longnecker and colleagues[11] found that increasing BMI was inversely related to the risk of DCIS (excluding 11 lobular carcinoma in situ cases), but was unrelated to the risk of developing IDC. Conversely, Reinier and colleagues[19] demonstrated that BMI was associated with an increased risk of IDC in postmenopausal women, but was not related to DCIS regardless of menopausal status. Similarly, a much larger study found that BMI was positively associated with the risk of invasive breast cancer but not DCIS (relative risks [RR] per 5 kg/m^2 = 1.20 and 1.01, respectively; P for heterogeneity = .002).[17] Further study is needed to more clearly define the association between BMI and DCIS.

Germline mutations in *BRCA1* and *BRCA2* are associated with a significantly increased risk of both invasive breast cancer and DCIS. It is reported that about 3.2% of patients with DCIS have mutations in one of these two genes.[20] Patients with DCIS with a family history of ovarian cancer or a first-degree relative with breast cancer are much more likely to be BRCA mutation carriers.[20,21] Most BRCA1-associated DCIS cases have triple negative receptor status, whereas most BRCA2-associated DCIS cases are ER and/or progesterone receptor (PR) positive, similar to invasive breast cancer.[22]

Outside of BRCA mutations, few studies have attempted to search the low-risk common loci predisposing a patient to DCIS in comparison with invasive breast cancer. One study of 873 women with DCIS and 4959 women with IDC reported that locus rs1982073 on TGFB1 was associated with a per-allele relative risk of 0.93 (95% CI, 0.84–1.03) for DCIS and 1.03 (95% CI, 0.98–1.09) for IDC (P = .05).[17] Campa and