Short Communication

Age-Specific Incidence Rates of In situ Breast Carcinomas by Histologic Type, 1980 to 2001

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Abstract

Incidence rates of ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) have increased rapidly over the past several decades largely due to the increased use of mammography. However, recent data from 1987 to 1999 indicate that invasive ductal carcinoma incidence rates have remained essentially constant, whereas rates of invasive lobular carcinoma have increased 65%, with greater increases observed among postmenopausal women. Data on recent trends in DCIS and LCIS incidence rates, particularly age-specific trends, are lacking. We evaluated trends in the incidence rates of DCIS overall, noncomedo DCIS, comedo DCIS, and LCIS using data from nine Surveillance, Epidemiology, and End Results cancer registries. DCIS incidence rates increased 7.2-fold [95% confidence interval (95% CI), 6.8-7.7] from 1980 to 2001, 1.8-fold (95% CI, 1.7-1.9) over the past 10 years (1992-2001), and 1.1-fold (95% CI, 1.0-1.2) over the past 5 years (1997-2001). The magnitudes of these increases were highest among women ages ≥50 years. Furthermore, over the past 10- and 5-year periods, rates of noncomedo DCIS have generally increased across all age groups, whereas rates of comedo DCIS held constant or decreased. LCIS incidence rates increased 2.6-fold (95% CI, 2.3-2.9) from 1980 to 2001, 1.3-fold (95% CI, 1.2-1.5) over the past 10 years, and 1.1-fold (95% CI, 1.0-1.3) over the past 5 years. Similar to invasive lobular carcinoma, but unlike invasive ductal carcinoma, incidence rates of both DCIS and LCIS continue to increase in the United States primarily among older women. These trends present important public health and clinical challenges. (Cancer Epidemiol Biomarkers Prev 2005;14(4):1008–11)

Introduction

Incidence rates of both ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) have risen sharply over the past few decades in the United States. DCIS rates increased 18.1% per year from 1983 to 1992 among women ages ≥50 years (1), and LCIS rates increased a total of 300% from 1978 to 1998 (2). Similar increases have been observed in other Western countries including Australia (3), Italy (4), and Switzerland (5). These increases have primarily been attributed to the increasing numbers of mammograms and biopsies of suspicious lesions that are being done. However, recent U.S. data from 1987 to 1999 indicate that invasive ductal carcinoma (IDC) incidence rates have remained essentially constant, whereas rates of invasive lobular carcinoma (ILC) have increased 65% (6). Trends in ILC rates also vary by age; as from 1987 to 1999, they increased 61% to 109% among women ages ≥50 years but increased only 28% to 44% among women ages 30 to 49 years. The observation that these changes in ILC incidence occurred over a period in which the use of combined estrogen and progestin hormones among postmenopausal women had also increased, led to the hypothesis that hormone use was more strongly related to IDC than to ILC risk. This hypothesis has been substantiated in seven observational studies that each found that use of estrogen and progestin increases ILC risk 2.0- to 3.9-fold, whereas having a more modest effect on IDC risk (7-13). Given that incidence rates of in situ carcinoma are increasing and that DCIS currently accounts for >14% of all breast cancers diagnosed in the United States, these tumors are of growing public health importance.

Whereas data from 1992 through 1999 indicate that similar to ILC, DCIS rates have increased 73% (14), data on age-specific trends are lacking. An evaluation of how trends in these incidence rates by histologic type vary by age is needed to enhance our understanding of their effect. In addition, similar to the link between estrogen and progestin use and risk of ILC that was suggested based on assessments of age-specific incidence trends (15), an evaluation of age-specific trends in in situ carcinoma incidence may point to factors underlying these trends.

Materials and Methods

We restricted our analysis to women ages ≥30 years with no prior history of any type of cancer (excluding nonmelanoma skin cancer). We identified 32,990 DCIS cases, including 26,278 noncomedo DCIS cases (defined using International Classification of Diseases for Oncology, Third Edition codes: 8201, 8230, 8500, 8503, 8507, and 8523) and 6,712 comedo DCIS cases (International Classification of Diseases for Oncology, Third Edition code: 8501), and 5,462 LCIS cases (International Classification of Diseases for Oncology, Third Edition codes: 8520 and 8524) meeting these criteria who were diagnosed from 1980 through 2001 in one of nine U.S. population-based cancer registries that participate in the Surveillance, Epidemiology, and End Results (SEER) Program (16). The registries included were those serving the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound. The total size of the underlying population of women across these registries increased from 5,658,379 in 1980 to 8,195,377 in 2001.

Individual patient medical records are the source of all SEER data on patient and tumor characteristics, including age at diagnosis and histopathologic type. The standard for
ascertainment of cases of cancer in the SEER registries is 98% (16). Informed consent was not obtained from subjects included in this study because cancer is a reportable disease by law, and release of information regarding all diagnoses made is mandatory in the areas covered by each of the SEER registries. As a whole, the SEER population is representative of the whole United States with regard to socioeconomic status and education level, although it includes higher proportions of people living in urban areas and who are foreign born (17).

Using SEER*Stat 5.2.2 (National Cancer Institute, Bethesda, MD issued April 2004), we calculated incidence rates of DCIS overall, noncomedo DCIS, comedo DCIS, and LCIS from 1980 through 2001 that were age-adjusted to the 2000 U.S. population. In addition to considering women of all ages together, we analyzed women ages <50 and ≥50 years separately and six other age groups separately: 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79, and ≥80 years. Using negative binomial regression, we estimated linear trends in incidence rates by histology over three time periods, 1980 to 2001 (the entire 22-year period of our study), 1992 to 2001 (the last 10 years for which data are available), and 1997 to 2001 (the last 5 years for which data are available), calculated as proportional changes over each time period with their associated 95% confidence intervals (95% CI; ref. 18). All analyses were adjusted for age at diagnosis (categories: 30-39, 40-49, 50-59, 60-69, 70-79, and ≥80 years), race (categories: White, Black, and other), and SEER registry.

Results

Overall, rates of DCIS increased sharply from 1983 to 1998 and then plateaued (Fig. 1). Specifically, they increased 7.2-fold (95% CI, 6.8-7.7) over the entire study period (1980-2001), 1.8-fold (95% CI, 1.7-1.9) over the past 10 years (1992-2001), and 1.1-fold (95% CI, 1.0-1.2) over the past 5 years (1997-2001; Table 1). Rates of noncomedo DCIS also began to increase in 1983, but then they plateaued from 1987 to 1993 before increasing sharply again through 1998 when the rate of increase slowed. These rates increased 6.1-fold (95% CI, 5.7-6.5) over the entire study period, 2.1-fold (95% CI, 2.0-2.3) over the last 10 years, and 1.2-fold (95% CI, 1.1-1.2) over the last 5 years. Rates of comedo DCIS increased from 1980 through 1995, although mostly sharply during the late 1980s through the early 1990s. Since 1995, rates of comedo DCIS have declined, decreasing 0.9-fold (95% CI, 0.9-1.0) over the past 10 years and 0.8-fold (95% CI, 0.8-0.9) over the past 5 years. Rates of LCIS increased from 1980 through 1987 and held fairly constant through the mid-1990s when they began to increase again slightly. From 1980 to 2001, LCIS rates increased 2.6-fold (95% CI, 2.3-2.9), and increased 1.3-fold (95% CI, 1.2-1.5) and 1.1-fold (95% CI, 1.0-1.3) over the past 10 and 5 years, respectively.

Incidence rates of both DCIS overall and noncomedo DCIS increased over the periods 1980 to 2001 and 1992 to 2001, but these increases were more pronounced among women ages ≥50 years (Fig. 2). For example, among women ages ≥50 years, rates of DCIS overall increased 1.8- to 1.9-fold from 1992 to 2001, whereas rates increased 1.4- to 1.6-fold among women ages 30 to 49 years (Table 1). With respect to the decline in comedo DCIS rates over the past 5 years, this decline was only observed among women ages 30 to 59 years as rates remained essentially unchanged among women ages ≥60 years. Finally, from 1980 through 2001, rates of LCIS increased 2.5- to 3.8-fold among women ages ≥50 years whereas increasing only 1.4-fold among women ages 40 to 49 years and remaining essentially constant among women ages 30 to 39 years. Rates of LCIS increased 1.4- to 2.0-fold among women over the age of 50 over the past 10 years, and 1.3- to 1.4-fold among women ages 50 to 69 years (and decreased 0.5-fold among women ages 30-39 years) over the past 5 years.

Discussion

Before interpreting our results, it is important to acknowledge this study’s limitations. The histologic categorizations used were based on diagnoses made by pathologists from multiple institutions, and diagnostic criteria likely vary across pathologists resulting in a certain degree of misclassification error. In particular, SEER captures data on DCIS but not on atypical ductal hyperplasia, and distinguishing between these two lesions can be quite challenging given the somewhat vague criteria used for their diagnoses. This same problem is also present for the distinction between LCIS and atypical lobular hyperplasias (which are also not recorded by SEER). Studies evaluating the concordance between tumors classified as DCIS or LCIS by SEER and those classified through a centralized pathology review are needed to quantify the magnitude of this misclassification, as none have been reported in the literature. In addition, we lacked information on factors that could influence these trends such as access to health care and mammography utilization rates.

Rates of IDC (the most common histologic type of invasive breast cancer) have remained essentially unchanged since 1987, but rates of ILC have increased 65% from 1987 to 1999 (6). Similar to ILC incidence rates, noncomedo DCIS rates have continued to increase through 2001 (increasing 110% over the past 10 years and 20% over the past 5 years) and LCIS rates have continued to increase through 1998 (increasing 30% over the past 10 years and 10% over the past 5 years). Alternatively, comedo DCIS rates have decreased 20% over the past 5 years. These findings are consistent with previous studies that have also observed that noncomedo DCIS (14) and LCIS (15) rates have been increasing, albeit more slowly in recent years, whereas comedo DCIS rates have been decreasing (14).

However, our data indicate important differences in these trends by age, as rates of noncomedo DCIS have increased over the past 5 years only among women ages ≥50 years, rates of comedo DCIS have only decreased among women ages <60 years, and rates of LCIS have only increased among women ages 50 to 69 years. The rising incidence rates of noncomedo DCIS (the most common histologic type of DCIS) may be largely attributed to the increased utilization of mammography, which is thought to explain the rising rates of both in situ and invasive breast carcinomas overall in the United States over the past several decades (1, 2, 15). Because DCIS has clearly been shown a precursor lesion of invasive breast cancer (19, 20), the observational data on noncomedo DCIS trends presented here, taken in conjunction with the previously...
published data on IDC trends, suggest that mammography has been effective in shifting the stage distributions of breast cancers so that fewer invasive and more in situ lesions are being diagnosed in the current era of widespread mammography use. This is substantiated by our observation that noncomedo DCIS rates increased during the past 5 years only among the women who are most likely to receive mammographic screening, those ages ≥50 years. The reasons why comedo DCIS rates are declining are less clear, but this may be due to changes in pathologic criteria used to diagnosis DCIS (14). In addition though, there is some pathologic evidence that high grade DCIS (which is commonly comedo DCIS) arises from low grade DCIS (which is commonly noncomedo DCIS; ref. 21). Thus, the increase in noncomedo DCIS and the parallel decline in comedo DCIS incidence rates may represent another form of “down-staging” related to increased mammographic screening, in that more noncomedo DCIS lesions may be being detected before their possible progression to comedo DCIS. The increases in LCIS rates are also likely related to mammography utilization given that LCIS lacks both clinical


<table>
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<tr>
<th>Age (y)</th>
<th>Proportional change (95% CI)*</th>
<th>DCIS, overall</th>
<th>DCIS, noncomedo</th>
<th>DCIS, comedo</th>
<th>LCIS</th>
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<td>60-69</td>
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<td>7.7 (6.6-8.9)</td>
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<td>1.2 (1.1-1.4)</td>
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<td>1.4 (1.0-1.9)</td>
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<td>70-79</td>
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<td>1980-2001</td>
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<td>6.4 (5.5-7.4)</td>
<td>16.0 (11.3-22.7)</td>
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<td>1992-2001</td>
<td>1.9 (1.7-2.1)</td>
<td>2.2 (1.9-2.5)</td>
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<td>1.4 (1.0-2.1)</td>
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<td>1997-2001</td>
<td>1.2 (1.0-1.4)</td>
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<td>1.2 (0.7-1.8)</td>
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<td>≥80</td>
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<td>5.5 (4.5-6.7)</td>
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<td>2.1 (1.7-2.5)</td>
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<td>3.0 (1.3-6.9)</td>
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<td>1997-2001</td>
<td>1.2 (1.0-1.5)</td>
<td>1.3 (1.0-1.6)</td>
<td>1.0 (0.7-1.6)</td>
<td>1.8 (0.7-4.7)</td>
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*Proportional changes estimated using negative binomial regression and adjusted for age at diagnosis, race, and SEER registry.

1P < 0.05.

Figure 2. Incidence rates of in situ breast carcinoma by histologic type and age, 1980 to 2001. ■, age ≥50 years; ○, age 30 to 49 years.
signs and is almost always an incidental finding in breast biopsies done for another reason, such as a suspicious mammogram. Whereas LCIS has long been thought not to be associated with any specific mammographic findings, more recent data indicate that calcifications are seen in 21% to 67% of LCIS cases (22-24). Our observation that increases in LCIS rates over the past 5 years were only observed among women ages 50 to 69 years, the age group of women most likely to receive regular mammograms, supports the notion that these increases are related to changes in mammography utilization rates. Because the use of menopausal hormones has been associated with an increased risk of ILC (7-13) and because ILC and LCIS share certain molecular features (ref. 25; suggesting that LCIS is a true precursor rather than just a risk factor for ILC), one might also hypothesize that the use of menopausal hormones may be related to LCIS risk. However, no prior studies have evaluated this hypothesis, and thus further studies aimed at identifying LCIS risk factors are needed.

Given that women diagnosed with DCIS have a 2.0- to 8.6-fold increased risk of invasive breast cancer compared with women in the general population, and that women diagnosed with LCIS have a 3.0- to 4.2-fold increased risk (26-29), the increasing incidence rates of noncomedo DCIS and LCIS pose important public health and clinical challenges. It is important to acknowledge though that the changes in incidence rates reported here are likely largely due to several factors, including more widespread screening, technical improvements in screening, improved training and skills of radiologists, multimodal screening, and increases in breast biopsy rates, rather than to “true” increases in these rates independent of these factors. Nevertheless, the increasing number of women diagnosed with DCIS and LCIS present a clinical problem because we do not have effective means of distinguishing between which of these patients will and will not develop invasive breast cancer. Current clinical recommendations indicate that DCIS patients should be treated either with a total mastectomy or with a lumpectomy with radiation, although axillary surgery is not routinely indicated (30). However, a recent meta-analysis reported that local recurrence rates were higher for women with DCIS who were treated with lumpectomy alone and lumpectomy with radiation compared with women treated with a mastectomy (31). Then again, there is also some controversy as to whether or not treatment with a total mastectomy or a lumpectomy with radiation may constitute overtreatment, given that the majority of DCIS patients will not develop invasive disease (32, 33). Women with LCIS are also in a quandary. LCIS is generally treated as a nonsurgical disease because studies published from 1974 to 1991 consistently indicated that LCIS patients are equally likely to develop invasive tumors in the breast ipsilateral to their LCIS as they are in the breast contralateral to their LCIS (34-37). Thus, it has been argued that the only logical operation for LCIS would be a bilateral mastectomy, an operation that would be unnecessary for an estimated 80% of women with LCIS. Thus, given that rates of DCIS and LCIS continue to increase in the United States, clinically useful tools that improve our abilities to stratify these patients based on their risk of invasive breast cancer are needed.

References

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