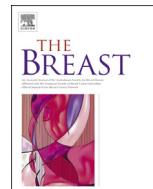




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Original article

Carcinoma in situ of the breast in New South Wales, Australia: Current status and trends over the last 40 year

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ABSTRACT

Background: The incidence of non-invasive breast cancer has increased substantially over time. We aim to describe temporal trends in the incidence of carcinoma in situ of the breast in New South Wales (NSW), Australia.

Methods: Descriptive study of trends in the incidence of ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) in women who received a diagnosis from 1972 to 2012, recorded in the NSW Cancer Registry.

Results: Carcinoma in situ as a proportion of all breast cancer was 0.4% during the prescreen in the Oxford dictionary prescreening period 1972 to 1987 and is currently 14.1% (2006 to 2012). Among 10,810 women diagnosed with DCIS, incidence across all ages rose from 0.15 per 100,000 during 1972 to 1983 to 16.81 per 100,000 over 2006 to 2012, representing a 100-fold increase (IRR 113.10; 95% CI 81.94 to 156.08). Among women in the target age group for screening (50–69 years) incidence rose from 0.27 per 100,000 to 51.96 over the same period (IRR 195.50; 95% CI 117.26 to 325.89). DCIS incidence peaks in women aged 60–69 years. DCIS incidence has not stabilized despite screening being well established for over 20 years, and participation rates in the target age range remaining stable.

Conclusions: Our findings raise questions about the value of the increasing detection of DCIS and aggressive treatment of these lesions, especially among older women, and support trials of de-escalated treatment.

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1. Introduction

Incidence rates of both ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) have risen over the past few decades with the advent of breast imaging. After the introduction of widespread screening mammography in developed countries, the proportion of detected breast tumors that were carcinoma in situ increased from 1 to 3% [1], to 10 to 17% [2–6], the vast majority being DCIS. Internationally, DCIS accounts for approximately 20% of all screen-detected breast cancers [7–10]. Although most women

diagnosed with carcinoma in situ are labelled as having cancer and those with DCIS receive treatment [11–13], reported breast cancer statistics only capture invasive disease [14]. While women with carcinoma in situ are at increased risk of developing a second primary breast cancer (in situ or invasive), there is evidence that their risk of dying from breast cancer is low [15].

Many studies describe the epidemiology of carcinoma in situ [1,2,4,5,7,16–25], but few include historical population data before the introduction of mammography [2,16,22,25], or examine LCIS [16,20]. Further, with the transition from analog film to digital mammography internationally, more contemporary estimates are required. There is a growing interest and need to understand trends in DCIS better to help inform management, including options for de-escalation of treatment such as active surveillance instead of immediate surgery and adjuvant therapy. This is especially

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important given improvements in mammographic sensitivity [26].

Since 1988, free biennial screening mammography has been offered to Australian women aged 40 years and older. We aim to describe the temporal trends in carcinoma in situ over the past 40 years in women and explore the influence of widespread screening mammography in NSW.

2. Methods

2.1. Study design and setting

This descriptive study took place in the state of NSW, Australia, where around one-third of Australia's female population resides. In 1984, diagnostic mammography became reimbursable by Medicare, Australia's universal health insurance scheme. In 1988, free biennial screening using two-view mammography, with double-reading, became available to NSW women over age 40 through BreastScreen NSW [27]. Since 1991, women aged 50–69 years have been specifically targeted via letters of invitation, with recruitment of women outside the target age range via advertising and other methods.

2.2. Data sources

We obtained de-identified individual data for all cases of female breast cancer from the NSW Cancer Registry diagnosed from 1972 to 2012. The NSW Cancer Registry contains records of all new diagnoses of cancer in residents of NSW. The Registry has been collecting cancer data since 1972 with mandatory pathology reporting from 1986 and almost 100% coverage. Carcinoma in situ is histologically verified for over 99% of cases. The NSW Cancer Registry is the only cancer registry in Australia that contains information on the stage of breast cancer (degree of spread) from 1972 onwards. Carcinoma in situ of the breast has been notifiable in NSW since 1992 and completeness of data before then has been estimated to be around 90% [28]. Female population estimates were obtained from the Australian Bureau of Statistics [29]. Our research protocol was approved by the research ethics board of the NSW Population & Health Services Research Ethics Committee.

Data on annual numbers of screening mammography examinations for women aged 40 years and older were obtained from BreastScreen NSW for 1988 to 2012 (Fig. 1A). These data did not include private screening, and in 2012 around 7% of NSW women aged 50–69 years had a government-funded bilateral mammogram through Medicare, many of whom were likely to be asymptomatic and the mammography performed for screening purposes [30]. To capture this private screening outside of the program, we obtained data on the number of bilateral mammograms in NSW reimbursed by Medicare from the Department of Human Services since 1984 (Medicare Benefits Schedule item number 2734 for 1984 to 1991 and 59300 for 30 November 1991 onwards). The rate of Medicare screening peaked around 1991, declined until 1996, and has been relatively stable since (Fig. 1B). The proportion of government-funded bilateral mammograms in women aged 50–69 years that are non-diagnostic (i.e. performed for screening purposes) has been estimated to be around 53% [30].

2.3. Population

We identified 133,658 NSW women with breast cancer diagnosed from 1972 to 2012 and extracted cases of first diagnosis of primary female carcinoma in situ of the breast. From this, we selected women who had a diagnosis of DCIS or LCIS. Information included: year of birth, year of diagnosis, age at diagnosis, anatomical site and cell type (ICD-10-AM Topography Code),

histology (4 digit ICD-0-3 Morphology Code), behavior code, and best basis of diagnosis. We identified 12,218 women with first primary stage 0 breast cancer. DCIS cases were defined based on the following International Classification of Diseases for Oncology (ICDO-3) codes: 8201/2, 8230/2, 8500/2, 8501/2, 8503/2, 8507/2, 8521/2, 8522/2 and 8523/2 ($n = 10,905$) [6,31]. LCIS cases were defined based on the ICDO-3 codes 8519/2 and 8520/2 ($n = 1093$). We excluded 127 women with the following histologic subtypes: 8010/2, 8050/2, 8070/2, 8140/2, 8480/2 because these are non-epithelial cancers or unspecified categories. We excluded 93 women with histological subtypes that have traditionally been considered variants of DCIS, but recent studies suggest some of these lesions lack surrounding myoepithelial cells and are low-grade invasive carcinoma (8504/2, 8508/2, 8509/2) [32]. From the remaining 11,998 subjects we identified 11,893 women with histologically confirmed DCIS ($n = 10,810$) and LCIS ($n = 1083$).

2.4. Statistical analyses

We divided the study into five intervals, which represent important periods for screening mammography in NSW. 1972 to 1983 was the period where there was no government-funded mammography and women were unexposed to mass screening. 1984 to 1987 saw the introduction of government-funded diagnostic mammography through Medicare and opportunistic screening. From 1988 to 1995 population-based screening was gradually introduced via BreastScreen NSW. 1996 to 2005 was the period where BreastScreen had full geographical coverage and reached a steady state (where all women in the target population were invited). 2006 to 2012 saw the gradual replacement of film with digital mammography, with roll-out complete by 2010 [33]. In each period, and for individual years over the entire study period from 1972 to 2012, we calculated the stage-specific incidence rate, standardized to the Australian 2001 population [34]. We used Poisson regression to analyze trends in incidence by time period for relevant age groups. We compared incidence rates (IR) and incidence rate ratios (IRR) across the different periods for each age group. The annual percentage changes in rates were estimated in Poisson models with terms for age group and year of diagnosis.

We used SAS software for the statistical analyses [35]. We assumed that the number of cases for a specific time period would follow a Poisson distribution from which 95% confidence intervals (CIs) were estimated [36]. For scatter plots we used penalized B-splines to fit a smooth curve through trend points using the PBSPLINE statement in the SGPLOT procedure.

3. Results

Of the 11,893 women diagnosed with carcinoma in situ of the breast between 1972 and 2012, 90% were diagnosed with DCIS. The median (range) age at diagnosis of DCIS was 58 (20–97) years and for LCIS was 53 (22–90) years. Carcinoma in situ is less common than invasive breast cancer, but the marked increase in the incidence of DCIS in the late 1980's mirrors that of invasive breast cancer (Fig. 2). Diagnosis of carcinoma in situ of the breast is rare among women younger than 40 years, the age at which women are eligible to start screening in NSW (Fig. 3). DCIS incidence rates increase with age and peak at ages 60–69 years, whereas LCIS incidence rates peak at ages 50–54 years (Fig. 4).

3.1. DCIS

DCIS as a proportion of all breast cancer was, on average, 0.2% during the prescreening period 1972 to 1983, 0.9% during the government-funded mammography period (1984–1987), 5.1%

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