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The management of women with ductal carcinoma in situ of the breast in Australia and New Zealand between 2007 and 2016

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Abstract

Background: The incidence of detected ductal carcinoma in situ (DCIS) continues to increase and now accounts for 14% of all breast cancer, and 20%–25% of screen-detected cases. Treatment trends of DCIS are important in order to inform the ongoing debate about possible overdiagnosis and overtreatment, but have not been investigated for over a decade in Australia and New Zealand. Against this background, we aimed to describe the temporal trends in management of DCIS in Australian and New Zealander women.

Methods: Using the BreastSurgANZ Quality Audit (BQA) database, we conducted a descriptive study of the trends of management of DCIS in Australia and New Zealand from 2007 to 2016. We assessed the frequency of surgical treatments, adjuvant therapies, and axillary surgery conducted in women with pure DCIS.

Results: There were 17 883 cases of pure DCIS in 2007–2016 in Australia and New Zealand recorded in the BQA database. The treatment patterns were consistent with no changes over time. The most common surgical treatment was breast-conserving surgery (66%), followed by mastectomy (37%), and 36% of women with DCIS received sentinel node biopsy (SNB).

Conclusion: The clinical management of women diagnosed with DCIS in Australia and New Zealand, appears stable over time. A substantial proportion of women with DCIS receive SNB and this aspect of surgical care warrants further exploration to determine whether it represents appropriate care. These results, alongside the outcomes of the ongoing clinical trials on the management of DCIS, will help inform if any changes to best practice treatment are required.

Introduction

DCIS, ductal carcinoma in situ, indicates an abnormal growth of epithelial cells within breast ducts and lobules.1 Unlike invasive breast cancer, DCIS does not invade surrounding tissue or spread to other places of the body and long term mortality is low.2 Together with small, invasive breast cancer, DCIS may be categorized as early breast cancer and is notifiable to Australian cancer registries.3

Mammographic screening aims to find breast cancer at an early stage to decrease breast cancer mortality, as well as improve surgical outcomes and reduce unnecessary treatment.4 Since the introduction of breast cancer screening programs, mammography has detected more DCIS due to the visible characteristic calcifications,3,5,6 (Fig. 1). DCIS was considered rare prior to the introduction of screening. In contrast, today, DCIS makes up about 20%–25% of the screen-detected cancers,4,7 and 14% of all breast cancer.5 In addition, mammographic screening has become more sensitive due to the improvements in technology. These step-wise advances have seen analog film replaced by digital mammography and 3D mammography (tomosynthesis), and commensurate with the practice shift, the majority of the increased detection has been in screen-detected DCIS.3 As such, DCIS rates continue to rise in Australia.3

The national breast screening program in Australia, BreastScreen Australia, started in 1991.8 Mammographic screening in Australia is recommended every 2 years for women aged 50–74.9 In Australia, women receive invitations to attend screening when they
turn 50 years of age; however, women can attend screening starting at age 40. Screening may be recommended to women before age 50 if they are at a greater risk of breast cancer. The biennial screening program in New Zealand, BreastScreen Aotearoa, was rolled out nationwide in 1998. In 2004, the age range of BreastScreen Aotearoa was extended from 50–64 to 45–69 years old, nearly doubling the number of women being screened each year.

Overdiagnosis of breast cancer occurs when mammography screening leads to the detection of a cancer that would never have presented clinically if the woman had not been screened. Over-diagnosis may lead to overtreatment. Concerns about overtreatment of DCIS have led to the establishment of several trials of treatment de-escalation for low-risk DCIS to investigate active monitoring as an alternative to surgery. In current clinical practice, however, surgery remains the mainstay of clinical management of DCIS, pending results of the de-escalation trials. Furthermore, in contrast to invasive breast cancer, surgical guidance for treatment of DCIS is limited or lacking and as such it is unclear to what extent variation in surgical practice may exist currently in Australia and NZ.

Against this background it is timely to analyze patterns of surgical treatment of DCIS, examining temporal trends over the past decade. The most recent analysis of DCIS management in Australia and New Zealand was conducted more than a decade ago and, as such, we considered an updated analysis would be informative. The aim of this study therefore was to describe temporal trends in the management of DCIS of the breast in Australian and New Zealand women over the decade 2007–2016.

Methods

Study design

We conducted a retrospective study using data sourced from a clinical breast cancer database, the BreastSurgANZ Quality Audit (BQA). Surgeons, members of the specialist society, Breast Surgeons of Australia and New Zealand, contribute to this database to capture data on the management and treatment of breast cancer. The study was approved by HUMAN RESEARCH ETHICS COMMITTEE at Sydney University, project number 2019/086.

DCIS episodes were available from the start of the collection in 1998 through end of 2018. We used only episodes where the histology report showed pure DCIS, excluding any type of invasive breast cancer. We measured the capture rate of the BQA data for both Australia and New Zealand by comparing reported cases of DCIS to the national cancer registries in both countries, AIHW and Ministry of Health NZ. We set an a priori threshold for adequate capture at 60%, that is at least 60% of DCIS registered on cancer registries were included in the BQA dataset for that year. The years 2007–2016 were the most recent 10-year period with a capture rate for all years for both countries above our a priori cutoff of 60%. An episode in the database is defined as the diagnosis and treatment period for a woman with DCIS. Women who had more than one episode recorded either had more than one primary tumor site, or a DCIS recurrence 3 months after surgery with clear margins. Only the first episode for each woman was included in order to avoid over-counting of a single woman’s treatment experience. (Fig. 2).
Data analysis

We combined records from Australia and New Zealand, acknowledging that contributing members from both jurisdictions are required to submit their total caseload to the audit and are benchmarked by the same key performance indicators. We measured time trends of the type of surgery, adjuvant therapy, and axillary surgery conducted using descriptive statistics. Surgery and treatment included: mastectomy, breast-conserving surgery (BCS), open biopsy, re-excision, reconstruction, no surgery, radiotherapy, tamoxifen, sentinel node biopsy (SNB), axillary surgery (i.e. level 1, 2, or 3 axillary lymph node dissection), and no axillary surgery. Additionally, we stratified data by patient age, menopausal status, histological grade of the tumor, and tumor size based on histopathology. Chi-squared analysis was used to test significance between subgroups and the Mantel–Haenszel method was used to test for trend over time (SAS 9.4).

Results

Study population and characteristics of women with DCIS

A total of 17,883 cases of DCIS were recorded in the BQA database in Australia and New Zealand from 2007 to 2016; 14,278 cases (overall capture rate 69%) from Australia and 3,925 cases (overall capture rate 78% New Zealand) (Table 1).

In both countries, the highest percentages of women diagnosed with DCIS were among women aged 50–69 years. DCIS was more common among women aged 40–49 in New Zealand than in Australia. Conversely, among women aged 70–74 years, DCIS was more common in Australia than in New Zealand. Most of the women diagnosed with DCIS in New Zealand were diagnosed and treated in the public health care system (66.0%), while in Australia more women were treated privately (62%). The most common referral source was from screening programs (57.8%). The remaining women were either symptomatic (29.1%), that is, they were referred to the breast surgeon after presenting to a GP or other physician, or were referred from other sources (13.1%) including private screening. Most cases were among postmenopausal women, although a sizeable minority (19–28%) was premenopausal (higher in New Zealand). Most cases were intermediate or high-grade histology, and ≤20 mm.

Surgical procedures

The most common type of surgery was BCS (65.5%, mastectomy 36.6%). Open biopsy was conducted among 12.3%, re-excision in 18.2% and reconstruction in 12.6% of women. Of women who had a mastectomy, 33.4% had reconstruction. Less than 1% of women (0.4%) did not undergo any form of surgery (n = 74).

Rates of surgical procedures were generally stable over time (Fig. 3), except for SNB which increased (described in detail below). Small fluctuations over time were statistically significant for all the surgical procedures except for reconstruction and no surgery (for which fewer events occurred) but are not of clinical significance.

Axillary procedures

SNB was conducted among 36.0% of women. An increase in SNB was observed over time: 27.5% of women had SNB in 2007, compared to 36.2% in 2016 (p < 0.0001) (Table 2, Fig. 3). Women with high-grade DCIS had the highest frequency of SNB (44.9%), whereas a smaller percentage of women with intermediate-grade (29.8%) and low-grade (19.6%) DCIS had SNB. Among women who had a mastectomy, 71.2% had a SNB, whereas 18% of women who had BCS also had SNB (Table S1). Of women with tumor size less than or equal to 20 mm, 16.1% had SNB compared to 21.4% of women with tumors greater than 20 mm. (Table 3).

Axillary lymph node dissection (ALND) was performed in 4.1% of women, with a slight decrease over time: 7.1% of the women with DCIS had ALND in 2007, while 2.9% of the women had ALND in 2016 (p < 0.0001) (Table 2). Of the ALND performed, 11.2% had positive axillary lymph nodes (n = 82).

Variation in surgical procedures by women’s and tumor characteristics

Statistically significant differences were observed according to age, histological grade, tumor size, and menopausal status (Table 3). Age was consistently associated with differences in treatment options. Most women aged 15–39 underwent mastectomy (62.4%), while fewer women aged 40–49 years (46%) and over 50 years (<40%) had mastectomy, while the opposite trend was observed for BCS. Immediate reconstruction was more commonly performed among younger women diagnosed with DCIS (15–39, 36.2%, 40–49, 25.4%), and it decreased steadily with age. More women in the younger age groups (15–39, 53.9%, 40–49,
42.3%) had SNBs, compared to women 50 and older (30–35%) (Table 3). Patterns according to menopausal statuses reflected those for age.

Women with high-grade DCIS were more likely to be treated by mastectomy and were more likely to undergo SNB. The majority of women, 53.3% with a DCIS lesion greater than 20 mm, had a SNB and 58.0% (n = 4453) had a mastectomy. Among women with a tumor size less than or equal to 20 mm, 23.2% (n = 2239) had a SNB conducted and 20.1% (n = 1940) had a mastectomy.

Women who had a mastectomy were more likely to have a SNB and/or an open biopsy than women who had BCS, whereas more women who had BCS had a re-excision (Table S1).

Adjuvant therapies
The most common adjuvant therapy was radiotherapy (42.0%). Of women who had BCS, 64.9% had radiotherapy. Tamoxifen was used among 8.4% of women and Aromatase inhibitors in 5.1% of women (Table S2).

Discussion
Summary of main findings
The majority (~60%) of DCIS cases were among women aged 50–69 years, consistent with screening mammography programs.
operating in both countries. However, DCIS was more common in women 40–49 years in New Zealand, and more common in women 70–79 years in Australia, consistent with the different policies on age groups targeted for screening (45–69 vs. 50–74).

Management of DCIS in Australia and New Zealand appears to have been stable over the years 2007–2016, with no major changes in surgery, including axillary surgery, or adjuvant therapy being observed. BCS followed by radiation therapy was more common than mastectomy, particularly in women over 50 years. In contrast, mastectomy was the most common surgical procedure in women younger than 40 years. Mastectomy was also more common among women with larger tumors—for example, a tumor size greater than 20 mm more than doubled the chance of mastectomy—and among women with high-grade DCIS. Breast reconstruction was performed among 12.6% of the women, mainly among younger women, and a trend of decreasing reconstruction with age was observed. Around one-third of the women diagnosed with DCIS had a SNB (36.0%), with a slight increase in SNB rate over time, accompanied by a slight decrease in the rate of ALND. SNB was associated with type of surgery, with more women who were treated with mastectomy receiving a SNB (71.2%) compared to women receiving BCS (18.0% had SNB). These temporal trends were not altered when adjusting for age, referral source, histological grade, and menopausal status.

Findings in context

Most of the findings are expected and in line with current best surgical practice. BCS followed by radiation therapy has become more common than mastectomy, to minimize surgical intervention with equally good outcomes. BCS gives a better cosmetic outcome, but total mastectomy may be needed for multifocal or widespread DCIS. International studies, as well as the previous study conducted in this population, have reported similar trends, with BCS followed by radiotherapy as the most common treatment approach. Younger women have an increased risk of a second invasive event of breast cancer than older women with DCIS. A higher percentage among younger women could be expected to have a more extensive disease, since they are below screening age and most likely detected outside of screening. The treatment of DCIS among younger women has tended to include more intensive surgery such as total mastectomy and in some prophylactic contralateral mastectomy. However, the long-term mortality rates of these younger women do not indicate an improved prognosis following the more extensive treatments, compared to BCS with adjuvant therapy.

 Mastectomy is usually selected as a treatment when DCIS appears multifocal or large, indicating more extensive or widespread disease. Our findings accord with this. While size and grade have been associated with treatment decision, these indicators do not perfectly correlate with whether DCIS will advance to an invasive disease or not. Further research on the biology of DCIS, biological markers, and gene profiling of DCIS pathology will increasingly inform decisions about management. While our results

| Year | Total | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |
|------|-------|------|------|------|------|------|------|------|------|------|------|
| **Surgery** | | | | | | | | | | | |
| Mastectomy | 553 (37.1) | 528 (35.6) | 699 (39.5) | 644 (36.3) | 637 (38.3) | 677 (38.7) | 741 (39.3) | 716 (34.1) | 776 (36.6) | 673 (32.3) | 202 (13.6) |
| BCS | 696 (43.7) | 668 (44.1) | 819 (44.7) | 772 (43.1) | 765 (45.5) | 797 (44.5) | 851 (43.2) | 826 (38.9) | 886 (40.6) | 788 (37.4) | 231 (15.3) |
| Reoperation | 267 (17.5) | 238 (16.1) | 289 (15.7) | 252 (14.3) | 236 (14.1) | 245 (13.8) | 254 (13.2) | 251 (12.1) | 253 (11.6) | 223 (10.8) | 74 (4.2) |
| Reconstruction | 160 (10.5) | 163 (10.8) | 183 (10.0) | 173 (9.7) | 176 (10.2) | 190 (10.7) | 223 (11.4) | 239 (11.3) | 249 (12.2) | 217 (11.0) | 92 (5.7) |
| No surgery | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| **Axillary intervention** | | | | | | | | | | | |
| SNB | 374 (24.7) | 437 (29.3) | 585 (32.4) | 617 (35.0) | 647 (38.6) | 699 (38.7) | 755 (38.5) | 682 (32.0) | 755 (36.6) | 755 (36.6) | 646 (45.0) |
| ALND | 97 (6.3) | 81 (5.4) | 73 (4.0) | 74 (4.1) | 60 (3.6) | 58 (3.3) | 77 (3.9) | 57 (2.7) | 88 (4.2) | 60 (2.9) | 730 (4.1) |
| No axillary surgery | 526 (34.5) | 523 (35.3) | 676 (36.9) | 601 (33.6) | 607 (36.3) | 649 (36.1) | 714 (35.6) | 677 (31.5) | 711 (31.9) | 673 (32.3) | 2196 (12.3) |
| **Number in brackets: percentage of women with DCIS who have had the procedure. ALND, axillary lymph node dissection; BCS, breast conserving surgery; DCIS, ductal carcinoma in situ; SNB, sentinel node biopsy.** | | | | | | | | | | | |

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reflect current practice, the BQA does not record these biological markers, and this will be important in the future.

Given that these cases represent pure DCIS, and DCIS would not be expected to have metastasized to the axillary nodes, SNB use seems high. However, this may have been done to obviate the need for a separate axillary procedure, for example, where there is risk of underestimation of invasive disease at core-needle biopsy, or where a subsequent axillary surgery may not be feasible, for example, BCS with synchronous oncoplastic procedure. In the previous study looking at the treatment trends in Australia and New Zealand, 6.5% had a SNB alone, and 23.3% underwent some form of axillary procedure.14 In our study, the proportion of women who had SNB is much higher compared to the previous study; however, the number of women who had axillary dissection has decreased. High rates of SNB use for women with pure DCIS have also been found in other countries, (54% in Denmark, 64% in Turkey) and similarly the appropriateness of its use has been questioned.24,25

The use of SNB for DCIS treatment may have been appropriate for some patients; we note that current guidelines for the management of women with pure DCIS specify reasons for considering SNB for DCIS as planned mastectomy, or when the risk of finding an invasive component at excision surgery is estimated to be high (extensive high-grade DCIS, palpable tumor/mass forming DCIS, and/or microinvasion is suspected in biopsy).22,23,26,27 In our study, 44.9% of women presenting with a high-grade DCIS as well as 53.3% of women presenting with a DCIS tumor greater than 20 mm, had a SNB. In these cases, where the risk of finding invasive disease is expected to be higher, a SNB might be an appropriate management. Yet 19.6% of low-grade, 29.8% of intermediate-grade, and 23.2% of DCIS cases with a tumor size less than 20 mm had SNB. The appropriateness of conducting a SNB in these latter cases is unclear (Table 3).

The benefit of a SNB during the initial surgery is that the woman will not require a second surgical procedure, if an invasive component is found in the excised tissue. In our study, 18.0% of the women who had a BCS also had a SNB which may represent overtreatment of a condition which often does not progress, thus causing unnecessary intervention with potential harm. Even though complications following SNB seem to be rare, ranging between 0.1% and 8.6% of women affected, they include axillary wound infection, axillary seroma, axillary hematoma, axillary paresthesia, decreased upper extremity motion, and lymphedema.28 The prevalence of SNB use among women when it is not indicated should be monitored so guidelines and practice better align.

### Strengths and limitations

The large sample size and long timeframe makes our study well powered to detect changes in practice. Even though this database represents the largest record of DCIS management in Australia and New Zealand, the capture rate of 60% of self-reporting breast surgeons who are members of specialist society is a limitation. The practice of surgeons not submitting cases for audit through the BQA may differ.

Consensus management guidelines may lag behind contemporary practice or even fail to make an impact on current therapeutics. This overview is an important assessment of the state of DCIS treatment in Australia and New Zealand. Perhaps, as it largely reflects the work of a group of sub-specialists committed to audit, it may present “best practice,” acknowledging a potential selection bias toward better outcomes.

### Implications for practice and research

There remains a need for education and promulgation of practice guidelines as, even among subspecialist surgeons committed to quality assurance and best practice, there may be over-treatment. Over-diagnosis is a risk in this condition and there remains a need to inform treating specialists about the opportunities to deescalate

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management. The path to de-escalation is difficult, as often overtreatment is preferred in the absence of evidence to contrary. Currently, only 0.4% of women with DCIS in Australia and New Zealand do not undergo surgery; this rate may be influenced in the future by the results of the ongoing trials.

Biological markers and gene profiling of DCIS pathology will increasingly inform decisions about management. The inclusion of biological markers in the BQA or future registry should be encouraged.

The management of DCIS has been essentially stable for 10 years. There have been modest increases in the use of reconstruction and adjuvant therapy. This relative stability may be in part because DCIS is a condition where practice changing evidence requires long-term follow-up. Audits of surgical activity, such as the BQA, are a useful tool to promote self-assessment against best-practice. However, we would advocate for a formal bi-national registry to link existing databases and assess a range of DCIS therapy for efficacy, cost–benefit, and patient satisfaction.

Conclusion

The management of women with DCIS does not seem to have changed markedly during the past decade, but the potential for less invasive treatments should be investigated. Clearer guidelines are required into the appropriateness of SNBs in women with pure DCIS. Further investigation of compliance of treatment with guidelines for management of DCIS is recommended both in Australia, New Zealand, and internationally.

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Author contributions

Sofia Omling: Formal analysis; investigation; writing-original draft. Alexandra Barratt: Conceptualization; funding acquisition; methodology; supervision; writing-review & editing. Nehmat Houssami: Methodology; supervision; writing-review & editing. Sophia Zackrisson: Supervision; validation; writing-review & editing. Kevin McGeechan: Formal analysis; methodology; software; writing-review & editing. Gemma Jacklyn: Conceptualization; data curation; supervision. David Walters: Resources; validation; writing-review & editing. Rachel Farber: Formal analysis; investigation; methodology; supervision; validation; writing-review & editing.

Conflict of interest

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Table S1. Surgical procedures by SNB, open biopsy, re-excision and radiotherapy.
Table S2. Adjuvant treatments over 10 years in women with DCIS.