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European Journal of Cancer 40 (2004) 2396–2402

European Journal of Cancer

www.ejconline.com

Surgery and outcomes of ductal carcinoma *in situ* of the breast: a population-based study in Australia

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Received 21 April 2004; received in revised form 25 June 2004; accepted 13 July 2004
Available online 18 August 2004

Abstract

We examined surgery and outcome in a population-based series of 2109 women newly diagnosed with ductal carcinoma *in situ* (DCIS) in 1995–2000 in New South Wales (NSW), Australia. The sole data source for the study was pathology records in the NSW Cancer Registry. Most DCIS was treated with breast-conserving surgery (BCS); use of breast conservation increased throughout the 6 years of the study. Women who were younger, had higher grade DCIS or had larger lesions were significantly and independently less likely to have BCS than other women. Eighteen percent of women had lymph nodes removed, most often with mastectomy. The NSW Cancer Registry does not collect information about radiotherapy. Based on cancer registrations alone, 97.7% of women were free of ipsilateral invasive cancer after three years; more women who had mastectomy were cancer-free (100%) than women who had breast-conserving surgery (97.2%; $P = 0.05$).

Keywords: Ductal carcinoma *in situ*; Breast-conserving surgery; Mastectomy; Trends; Epidemiology; Recurrence

1. Introduction

Ductal carcinoma *in situ* (DCIS) in 1995–2000 in New South Wales (NSW) has increased with increasing screening mammography [1]. DCIS detected by mammographic screening differs from that observed before screening: it presents as a mammographic abnormality, unlike the palpable mass of pre-screening lesions, it may convey smaller risks of recurrence or death and its nature, treatment options, and outcome are not readily explicable to women [2–4].

Breast conservation, the recommended management for early invasive breast cancer, has been recommended for DCIS too [5], but there is less consensus about which women with DCIS can be appropriately treated with breast conservation [6] and whether adjuvant radiotherapy is needed or not [7].

Present evidence indicates that a diagnosis of DCIS is associated with an increased risk of subsequent invasive breast cancer [6]. Currently, prognosis is mainly predicted by grade, although guidance about long-term prognosis is limited [8] and population-based reports of eventual death from breast cancer in women with DCIS are scarce [4]. The key, current issue is whether the incidence of invasive breast cancer is reduced by early detection of DCIS. Information is needed on the proportion of women in sizeable screened populations who experience recurrence of DCIS, that is, further ipsilateral DCIS or invasive breast cancer after apparently successful treatment, after sufficiently long periods of follow-up.

We present information on surgical management alone in 2109 women notified with newly diagnosed DCIS in NSW, Australia in 1995–2000. The NSW

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doi:10.1016/j.ejca.2004.07.008

Cancer Registry does not collect information on radiotherapy. We also briefly examined outcome.

2. Patients and methods

NSW women who were first diagnosed with DCIS in 1995–2000 and notified to the NSW Central Cancer Registry were eligible for this study. Notification of cancer to the Registry is legally required of all pathology laboratories, hospitals and radiotherapy facilities in NSW, which has a population of 6.5 million, 74% of whom live in Sydney and two adjacent, but much smaller, coastal cities. Women were excluded if they had a previous or simultaneous (same month) diagnosis of invasive breast cancer, or if there was microinvasive disease which the NSW Cancer Registry codes as invasive breast cancer. DCIS has been notifiable in NSW since 1993 and by 1997 all but 4% of DCIS cases diagnosed by pathology laboratories were notified to the Cancer Registry (data not shown).

Pathology reports in the Cancer Registry were collated for each woman and two experienced Cancer Registry personnel extracted information on DCIS: the type of specimen; size, grade, architecture, presence or absence of necrosis, and multifocality; and clearance and width of the margins [9]. The epidemiology and pathology of DCIS in 1995–2000 in this population have been described previously [1]. With specific relevance to this report, we extracted information on the type of surgery and the number and status of lymph nodes removed at the time of excision of DCIS.

The type or types of specimen recorded for each woman were used to classify the most extensive surgical procedure as breast-conserving surgery only, mastectomy after initial breast conservation or mastectomy only (together referred to as mastectomy). No treatment type was recorded when the only report available was from a core biopsy. A re-excision specimen that fell short of mastectomy was taken to indicate breast conservation. Cancer Registry records for 1995–1997 were linked to the corresponding hospital records in the NSW Inpatient Statistics Collection (http://www.health.nsw.gov.au/im/ims/isc/) and the surgical procedure codes in this collection compared with those inferred from pathology reports. The two sources agreed on mastectomy in 94.2% of cases in which it was inferred from the pathology reports and on breast-conserving surgery in 97.5% (data not shown).

The number of lymph nodes removed at the time of excision of DCIS was recorded and in this study was the indicator of axillary surgery.

Cases were allocated to urban or rural areas using the classification system of the mammographic screening programme, BreastScreen NSW [10], and to 5 socioeconomic groups using a published index constructed from 1996 Census data on distributions of income, education, unemployment, occupation, non-English speaking background and indigenous origin of households in local government areas [11]. We examined predictors of surgical management (breast-conserving surgery only, mastectomy) of DCIS by fitting logistic regression models of age, year of diagnosis, grade, size, architecture, and presence of necrosis. For predictors of axillary surgery, we also included type of surgical management. Odds Ratios (ORs) for each variable and 95% Confidence Intervals (CIs) were adjusted for age group and year of diagnosis. For each outcome, variables with ORs significant at $P < 0.001$ were included in a single prediction model; the best predictors were identified by eliminating variables stepwise.

To estimate survival free of ipsilateral invasive cancer, we followed Cancer Registry records and flagged women with DCIS in 1995–1997 who had a diagnosis of invasive breast cancer up to the end of 2000. Completeness of ascertainment of invasive breast cancer in these women would be high since a very high proportion of breast cancer cases are recorded by the NSW Cancer Registry [12], including cases who move to other Australian States and have been traced through the National Cancer Statistics Clearing House [13]. Any diagnosis of invasive breast cancer three months or more after the index diagnosis of DCIS was regarded as a terminating event. Three-year rates of survival free of invasive cancer were calculated using the Kaplan–Meier method for all women and in categories of age, year of diagnosis, surgical treatment, surgical margin, and DCIS size, grade, architecture, and necrosis. Heterogeneity between groups was tested for each stratification variable by log-rank tests.

3. Results

In 1995–2000, 2109 NSW women were notified to the NSW Cancer Registry with DCIS, more than half ($n = 1129$, 54%) of whom were in the target age group for mammographic screening in NSW, 50–69 years [1]. Information on surgical management was available in pathology reports for 2075 of the 2109 women: most ($n = 1480$, 71%) had breast-conserving surgery. The proportion having breast-conserving surgery increased from 65% in 1995–1997 to 76% in 1998–2000 (Table 1). Fewer women aged 20–39 years (49%) than women aged 40 years and older (72%) had breast-conserving surgery (P for heterogeneity among 4 categories of age <0.001). Of the 29% of women who had a mastectomy, 13% had it as their primary procedure and 15% had it following an initial excision biopsy. Most (75%) of the cases had no DCIS at the surgical margin when a statement on margins was made in the report. More than half (59%) of the cases with a clear margin also had a

Table 1
Surgical management of women with DCIS in NSW in 1995–2000

	1995–97		1998–2000		1995–2000	
	n	(%)	*n*	(%)	*n*	(%)
Surgery						
Mastectomy	327	(34.6)	268	(23.7)	595	(28.7)
Breast-conserving surgery only	617	(65.4)	863	(76.3)	1480	(71.3)
Total	944	(100.0)	1131	(100.0)	2075[a]	(100.0)
Lymph nodes removed						
Yes	179	(18.9)	207	(17.8)	386	(18.3)
No	768	(81.1)	955	(82.2)	1723	(81.7)
Total	947	(100.0)	1162	(100.0)	2109	(100.0)
Excision margin						
Free of DCIS	593	(77.6)	672	(73.4)	1265	(75.3)
Involved	171	(22.4)	244	(26.6)	415	(24.7)
Total	764	(100.0)	916	(100.0)	1680	(100.0)
Not mentioned	183		246		429	
Margin measurement						
⩽2 mm	148	(49.3)	168	(38.2)	316	(42.7)
>2 mm	152	(50.7)	272	(61.8)	424	(57.3)
Total	300	(100.0)	440	(100.0)	740[b]	(100.0)

DCIS, ductal carcinoma *in situ*; NSW, New South Wales.
[a] Excludes 34 women for whom information on surgical management was not available.
[b] Excludes 525 women stated to have clear margins, but without a measurement of the margin.

measurement, of whom just over half (57%), or 34% of all women with clear margins, had a margin of more than 2 mm (Table 1).

More than half (54%) the DCIS in 1995–2000 were high grade and 39% were 2 cm or larger [1]. A smaller percentage of DCIS were reported as low grade in 1998–2000 (15%) than 1995–1997 (19%; $P = 0.03$) and more DCIS were larger, 3+ cm in diameter, in 1998–2000 (23%) than in 1995–1997 (18%; $P = 0.05$). More DCIS were high grade in women aged 20–39 years and 50–69 years (57%) than those aged at other ages (50%) ($P = 0.02$) and a higher proportion were 2+ cm in women aged 20–39 years (53%) than those aged 40 years and older (38%) ($P = 0.01$).

Year of diagnosis, age, size and grade were strong and independent predictors of breast-conserving surgery (Table 2). In a multivariate model, the odds of breast-conserving surgery rose to just over 4-fold between 1995 and 2000 (OR = 4.05, 95% CI 2.73–6.01), and was least likely in the youngest women (20–39 years; OR = 0.44, 95% CI 0.27–0.72), and where high grade lesions (OR = 0.58, 95% CI 0.42–0.80 where low grade was the reference) (Table 2). There was a striking trend towards less breast conservation with increasing tumour size to 3+ cm (OR = 0.14, 95% CI 0.10–0.19 where the reference was tumours <1 cm). When socioeconomic status was added to the model, it showed inconsistent and opposite effects: women in the low socioeconomic status areas of Sydney were less likely (OR = 0.78, 95% CI 0.60–1.00) and in low socioeconomic status areas elsewhere more likely (OR = 1.29, 95% CI 0.96–1.72) to have breast-conserving surgery than high socioeconomic status areas in Sydney. However, place of residence (urban or rural) was not significantly predictive of treatment with breast-conserving surgery when added to the model.

Removal of lymph nodes was recorded in pathology reports for 386 women (18% of the total); none had cancer in the nodes. It was much more common with mastectomy (51%) than with breast conservation (6%) (Table 3). Year of diagnosis and tumour size were important independent predictors of axillary surgery in addition to type of surgery. There was an approximate 2-fold higher odds of lymph node removal in 1997 and later than in 1995–96 (Table 3). As size increased from <1cm, the odds of lymph node removal increased nearly 4-fold with increasing size to 3+ cm (OR = 3.76, 95% CI 2.36–5.97). Neither place of residence (urban or rural) nor socioeconomic status was significantly predictive of lymph node removal or appreciably affected the above odds ratios when added to the model.

3.1. Risk of subsequent, ipsilateral invasive breast cancer

We followed up in the Cancer Registry 945 women diagnosed with DCIS in 1995–97 for a median of 4.3 years (range 4–6 years) to the end of 2000. Forty-two (4.4%) had subsequent invasive breast cancer: 25 ipsilateral, 11 contralateral, 4 bilateral and 2 of unknown laterality. The overall 3-year survival free of ipsilateral

Table 2
Association of breast-conserving surgery with year of diagnosis, age, size and grade in NSW women in 1995–2000[a]

	Breast-conserving surgery	Mastectomy	OR[b]	95% CI	*P*-value
Year					
1995	155	113	1		
1996	170	112	1.27	(0.87–1.84)	
1997	292	102	2.6	(1.80–3.76)	
1998	293	102	2.57	(1.77–3.72)	
1999	271	86	3.2	(2.17–4.72)	
2000	299	80	40.05	(2.73–6.01)	<0.0001
Age (years)					
20–39	43	44	0.44	(0.27–0.72)	
40–49	319	137	0.87	(0.67–1.13)	
50–69	806	300	1		
70+	312	114	1.03	(0.78–1.35)	0.008
Size (cm)					
0–0.9	434	69	1		
1–1.9	392	88	0.73	(0.51–1.04)	
2–2.9	198	80	0.4	(0.27–0.58)	
3+	159	180	0.14	(0.10–0.19)	
Missing	297	178	0.28	(0.21–0.39)	<0.0001
Grade					
Low	239	66	1		
Medium	397	133	0.79	(0.55–1.13)	
High	665	338	0.58	(0.42–0.80)	
Missing	179	58	1.39	(0.89–2.16)	<0.0001

OR, Odds Ratio; 95% CI, 95% Confidence Interval.
[a] Excludes 34 women for whom details of surgical treatment could not be inferred from pathology reports.
[b] ORs adjusted for all other variables in the Table; the best predictors were identified by eliminating variables stepwise from a model containing all variables with ORs significant at $P < 0.001$ when adjusted for age group and year of diagnosis.

invasive cancer was 97.7% (95% CI 96.7–98.7). There was marginally significant heterogeneity in ipsilateral invasive-free survival between categories of surgery type: 100.0% of those who had mastectomy were estimated to be free of ipsilateral invasive cancer at three years compared with 97.2% (95% CI 96.1–98.4) of those who had breast-conserving surgery ($P = 0.05$). No other variable about the woman (age), her surgery (year, surgical margin) or the DCIS (size, grade, architecture, necrosis) had a significant association with recurrence-free survival in these data. In women who had breast conservation, there was evidence of a fall with year of diagnosis in the proportion free of ipsilateral invasive cancer three years after diagnosis: 1995 – 99.4%, 1996 – 97.1%, 1997 – 96.0%, $P = 0.05$.

4. Discussion

Most DCIS was treated with breast-conserving surgery and its use increased throughout the 6 years of the study. Younger women, and women with higher grade and larger lesions, were significantly and independently less likely to have breast-conserving surgery than other women. The proportion of women free of ipsilateral invasive cancer after three years was 97.7%. It was higher, 100%, in women with mastectomy than women with breast-conserving surgery, 97.2% ($P = 0.05$).

The rate of breast-conserving surgery in NSW in 1998–2000 (76%) was substantially higher than that reported from earlier periods in Australia, 62% in 1995 [14] and 65% (all *in situ* breast cancer) in 1988–1992 [15], and the United States of America (USA), 51% in 1992 in the US Surveillance, Epidemiology and End Results (SEER) registries [16] and 62% in California in 1988–95 [17], but similar to Geneva, 78%, in 1995–99 [18] and SEER registries, 72%, in 1999 [19]. These figures suggest a continuation of the upwards trend in breast conservation observed in the US National Cancer Data Base from 1985 to 1993 [20]. Although there was little consensus about the management of DCIS in Australia in 1995, the increasing uptake of breast conservation in NSW followed the release in 1995 of Australian guidelines on treatment of early invasive breast cancer recommending breast conservation [21]. Australian guidelines for DCIS in 2003 support breast-conserving surgery as the preferred treatment choice when lesion size allows for good cosmetic results [22].

Consistent with their larger lesions, the youngest women in our study had breast conservation least often of all age groups. The increased breast conservation rates

Table 3
Association of axillary surgery with year of diagnosis, age, size, grade and type of surgery in NSW women in 1995–2000[a]

	Axillary surgery		OR[b]	95% CI	*P*-value
	Yes	No			
Year					
1995	48	220	1		
1996	52	230	1.09	(0.66–1.81)	
1997	79	315	2.21	(1.35–3.60)	
1998	72	323	1.81	(1.10–2.97)	
1999	72	285	2.26	(1.36–3.77)	
2000	63	316	1.77	(1.06–2.97)	0.0023
Age (years)					
20–39	26	61	0.95	(0.53–1.69)	
40–49	80	376	0.78	(0.56–1.10)	
50–69	208	898	1		
70+	72	354	0.83	(0.58–1.18)	0.49
Size (cm)					
0–0.9	36	467	1		
1–1.9	62	418	1.78	(1.10–2.87)	
2–2.9	51	227	1.91	(1.14–3.20)	
3+	136	203	3.76	(2.36–5.97)	
Missing	101	374	1.99	(1.26–3.14)	<0.0001
Grade					
Low	43	262	1		
Medium	87	443	0.92	(0.57–1.48)	
High	223	780	1.05	(0.68–1.61)	
Missing	33	204	1.01	(0.56–1.83)	0.89
Surgery type					
Breast-conserving surgery only	83	1397	1		
Mastectomy	303	292	16.59	(12.33–22.32)	<0.0001

[a] Excludes 34 women for whom details of surgical treatment could not be inferred from pathology reports.
[b] ORs adjusted for all other variables in the Table; the best predictors were identified by eliminating variables stepwise from a model containing all variables with ORs significant at $P < 0.001$ when adjusted for age group and year of diagnosis.

for smaller and lower grade DCIS, both in NSW and nationally [14], were consistent with results from the US National Cancer Data Base, US SEER registries and the Geneva Cancer Registry [18–20]. Socioeconomic status of residential areas in our study was inconsistently associated with likelihood of breast conservation, although breast conservation increased with increasing socioeconomic status in the US National Cancer Data Base series [20]. Somewhat surprisingly, likelihood of breast conservation did not vary overall between urban and rural areas in NSW, although breast conservation for invasive breast cancer was much less likely in rural than urban areas, possibly because of less easy access to radiotherapy [23]. Substantial geographical variation in mastectomy for *in situ* breast cancer, unrelated to lesion size or patient characteristics,was reported among US SEER registries in 1983–88 [24], and again in 1992–1999, although not examined by patient characteristics [19]. Given our negative or equivocal findings with respect to socioeconomic status and rural or urban residence, it may be that medical practice variation, as suggested in the US studies, is the main determinant of unexplained variations between areas in NSW.

As the proportion having breast-conserving surgery has risen, the proportion having lymph node dissection with DCIS has fallen in the US National Cancer Data Base series, the US SEER registries [19], and in parts of Australia [14,15]. In our series 18% had nodes removed in 1995 and the proportion changed little up to 2000; in the SEER registries, axillary dissection fell from 34% in 1992 to 15% in 1999 [19]. However, when we took account of the trend towards increasing BCS, the odds of node removal increased nearly 2-fold, mainly due to a rise in the proportion of mastectomies in which nodes were removed (from 40% in 1995 to 55% in 2000) and the lack of any fall in the proportion of BCS with node removal (approximately 6% in each year). An overall prevalence of 16% was reported for axillary surgery in DCIS detected by BreastScreen Victoria in 1995–1998 and in 62% of cases, was judged to be unnecessary (i.e., went beyond sampling with removal of the axillary tail at mastectomy): based on small numbers, prevalence

may have fallen in 1998 [25]. The NSW rate of node removal at mastectomy (54%) was higher than in the USA (42%), where the high number of nodes removed was regarded as an indicator of true axillary dissection and not inadvertant axillary lymph node removal [19]. A substantial number of women in NSW too had multiple nodes removed (26% had 5–10, 39% had 11 or more). The 2003 Australian guidelines for the management of DCIS recommend that axillary surgery should be discouraged.

We found that 3.1% of women with DCIS diagnosed in 1995–97 had subsequent ipsilateral invasive breast cancer diagnosed after a median of 4.3 years of follow-up. All except one of these cancers occurred in women treated by breast-conserving surgery ($P = 0.05$). In this study, we were unable to record whether women had received radiotherapy since the NSW Cancer Registry does not receive this information. An increase in the use of radiotherapy in Australia from 1990 to 2000 has been suggested and may be partly due to its increasing use with breast conservation for DCIS [26]. In addition, there was a marginally significant trend towards a lower three year probability of survival free from ipsilateral invasive breast cancer with each year from 1995 to 1997 ($P = 0.05$). In a study of 709 US women with DCIS, treated by breast-conserving surgery in 1980–1992, the probability of an ipsilateral invasive cancer was 8% within 5 years of treatment (or 1.65% a year) and 18% within 10 years (or 1.96% a year) [6]. The corresponding figures from our study were approximately half that of the US study, 2.6% in 3 years or 0.87% a year.

That the risk of invasive cancer after treatment of DCIS may be falling with time is suggested by a 50% fall in the risk of subsequent invasive breast cancer between 1980–82 and 1989–92 in Swedish Cancer Registry data [27]. Kerlikowske and colleagues [7] have shown that the risk of invasive breast cancer was higher in women whose initial DCIS was high grade and was detected by palpation *vs* mammography.

It is not surprising, perhaps, that the risk of ipsilateral invasive breast cancer would be higher in women treated with breast-conserving surgery than women treated with mastectomy, as our study suggests. However, contrary to the longer term trends referred to above, the risk in those treated with breast conservation may have increased in the three, successive one-year cohorts of women. This increase correlates with increasing use of breast-conserving surgery and, probably, a relaxation of the indications for mastectomy. These trends should be watched carefully.

Aspects of our results highlight the fundamental dilemma of screen-detected DCIS. Is it an important contributor to the benefit of breast cancer screening in reducing breast cancer mortality or is it an unwanted finding that cannot be ignored, but should be managed with the least possible trauma to women [28]? Our data show an increasing trend towards breast conservation as a sensible response towards minimising the trauma associated with a diagnosis of DCIS. On the other hand, the incidence of axillary surgery in women with DCIS appears to be continuing at a stable level overall and increasing in those who have mastectomy; some have judged a majority of these axillary procedures to be unnecessary. In the background though is the suggestion of a concern in our data that risk of ipsilateral invasive cancer may have increased recently with the trend to use more breast-conserving surgery. Observational studies such as this can provide information on the trends and raise questions about treatment, but are weak tools for answering questions about what is the best treatment. For these questions, randomised controlled trials are necessary.

Conflict of interest statement

None declared.

Acknowledgements

The National Breast Cancer Centre, Sydney, Australia funded this study; Mr. Chris Goumas analysed the data.

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