British Journal of Cancer (2004) 90, 1382–1385

www.bjcancer.com

Ductal carcinoma *in situ* of the breast, a population-based study of epidemiology and pathology

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Epidemiology

In a population-based series of 2109 women with ductal carcinoma *in situ* (DCIS) diagnosed in 1995–2000 in New South Wales, Australia, incidence increased by an average of 5.5% a year, mostly between 1995 and 1996 and in women 50–69 years of age. This increase paralleled the increases in mammographic screening. BreastScreen NSW, an organised mammographic screening programme, detected 65% of all DCIS. High-grade lesions were 54% of all lesions and were more likely to be 2+ cm in diameter (OR = 2.12, 95%CI 1.46–3.14) than low-grade lesions. In all, 40% of DCIS in women younger than 40 years was 2+ cm in diameter compared with 21% in women 40 years and older. Young age, high grade, mixed architecture and multifocality were significant and independent predictors of 2+ cm DCIS.
British Journal of Cancer (2004) **90,** 1382–1385. doi:10.1038/sj.bjc.6601677 www.bjcancer.com
Published online 24 February 2004

Keywords: DCIS; epidemiology; pathology; population-based

The epidemiology of ductal carcinoma *in situ* (DCIS) has yet to be described adequately. While mammographic screening has undoubtedly caused increasing diagnosis of DCIS (Ernster *et al*, 1996, 2002; Levi *et al*, 1997; Barchielli *et al*, 1999), studies to date have mainly been small (Levi *et al*, 1997; Barchielli *et al*, 1999) or described populations that had no organised screening programme (Choi *et al*, 1996; Ernster *et al*, 1996; Zheng *et al*, 1997). Population-based descriptions of epidemiology and pathology of DCIS in sizeable screened populations are nonexistent.

We describe the epidemiology and pathology of newly diagnosed DCIS in the 2.7 million female population of New South Wales (NSW) Australia in 1995–2000.

MATERIALS AND METHODS

Data

NSW women with a first diagnosis of DCIS in 1995–2000 and notified to the NSW Central Cancer Registry were eligible for the study; those with a previous or simultaneous (same month) diagnosis of invasive breast cancer were excluded. Ductal carcinoma *in situ* 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1993, and by 1997 all but 4% of DCIS cases diagnosed by pathology laboratories were notified to the Cancer Registry (unpublished data).

Two experienced Cancer Registry personnel extracted information on the type of specimen, size, grade, architecture, presence or absence of necrosis and multifocality of DCIS, and clearance and width of the margins from pathology reports (Kricker *et al*, 1999).

The frequency of mammography was obtained from reports of an organised screening programme, BreastScreen NSW (Estoesta *et al*, 2000; Productivity Commission, 2002), which began in 1991 and reached a steady state between 1995 and 2000. The numbers of bilateral mammograms reimbursed by the national health insurance scheme, Medicare, were also available for 1995–99 (http://www.hic.gov.au/providers/health_statistics/statistical_reporting/medicare.htm). These mammograms would include an unknown but not high proportion of mammograms that were primarily diagnostic. BreastScreen and Medicare account for most of the screening mammography in Australia.

Analyses

Incidence rates and 95% confidence intervals (CIs) (Dobson *et al*, 1991) were calculated in 5- (DCIS) or 10-year (mammography) age groups and age-standardised to the World population. The annual percentage changes in rates were estimated in negative binomial models with terms for age group and year of diagnosis.

Cases were allocated to urban or rural areas using BreastScreen's classification (Estoesta *et al*, 2000) and to five socioeconomic (SES) groups (Australian Bureau of Statistics, 1998), and variation among them tested in Poisson regression models.

The heterogeneity of DCIS distributions by size and grade among age groups and type of architecture among years of diagnosis was evaluated by standard χ^2 tests. Age, grade, architecture, multifocality and presence of necrosis were examined as predictors of size (<2 cm, 2+ cm) in logistic regression models that included year of diagnosis; the additional effects of urban or rural residence and SES of the women were also examined.

RESULTS

Incidence

In 1995–2000, 2109 NSW women were notified with DCIS. More than half (54%) were 50–69 years of age, the target age group for

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Received 17 September 2003; revised 15 December 2003; accepted 7 January 2004; published online 24 February 2004

breast cancer screening in NSW, and had the highest incidence (32.3 per 100 000) (Table 1).

Incidence at all ages increased from 1995 (6.8 per 100 000) to 2000 (8.9 per 100 000) (annual average 5.5%, 95% CI 2.5–8.6), mostly between 1996 and 1997 (39% increase) and in women 50–69 years of age (48% increase 1996–1997) (Figure 1). Ductal carcinoma *in situ* rates were higher in 1998–2000 than 1995–1997 in every age group, but did not continue to increase except, perhaps, in women 70+ years of age.

The incidence of DCIS was about 25% higher in urban than rural areas of NSW ($P<0.001$) and increased strongly with increasing socio-economic status in Sydney ($P<0.001$, Table 1), but not other areas of the State ($P=0.09$). BreastScreen NSW detected 65% of incident DCIS, with higher proportions in women older than 50 years.

Table 1 Incidence of ductal carcinoma *in situ* of the breast in NSW women in 1995–2000 by age, urban or rural residence and socioeconomic status

	Number	Rate[a]	95% CI
All NSW women	2109	8.6	8.2–9.0
Age group			
20–39	91	1.4	1.1–1.7
40–49	458	17.3	15.7–19.0
50–59	634	31.8	29.4–34.4
60–69	495	32.8	29.9–35.8
70–79	354	28.8	25.8–32.0
80+	77	10.6	8.4–13.3
50–69	1129	32.2	30.4–34.2
70+	431	24.2	21.9–26.7
Urban & rural area			
All areas	2100	8.5	8.2–8.9
Urban	1712	9.0	8.6–9.4
Rural	388	7.1	6.3–7.8
			$P<0.001$[b]
Socioeconomic status (Sydney Statistical Division only)			
All areas	1369	9.2	8.7–9.7
1 lowest	205	7.2	6.2–8.2
2	197	7.5	6.4–8.6
3	226	8.5	7.4–9.8
4	342	10.9	9.7–12.1
5 highest	399	11.2	10.1–12.4
			$P<0.001$[c]

[a]Rates are per 100 000 women age-standardised to the World population. [b]χ^2 test for difference in rates between urban and rural (metro *vs* non-metro) – Poisson regression model. [c]*P*-value for heterogeneity and trend <0.001.

Screening

BreastScreen and Medicare screened 265.1 per 1000 women 40 years of age and older in 1995 and 284.6 in 1999; all the increase was in BreastScreen. BreastScreen screened twice as many women 50–69 years of age (269.2 per 1000) as women 40–49 (122.4) and 70+ years (120.1) (Figure 2); Medicare screening rates in the two younger age groups were nearly equal. There was little difference in the screening rates between urban (189.0 per 1000) and rural (186.6) areas.

The numbers of DCIS detected were strongly correlated with the numbers of women screened by BreastScreen in 1995–2000 ($R=0.83$, $P<0.001$). There was a weaker correlation between Medicare reimbursed mammograms and DCIS not detected by BreastScreen in 1995–1999 ($R=0.64$, $P=0.002$).

Pathology information

Pathology reports were available for all but two cases of DCIS, mainly from excision or re-excision specimens (73%) and mastectomies (24%). Size was reported in 76%, grade in 89% (both in 69%), presence or absence of necrosis in 63%, architecture

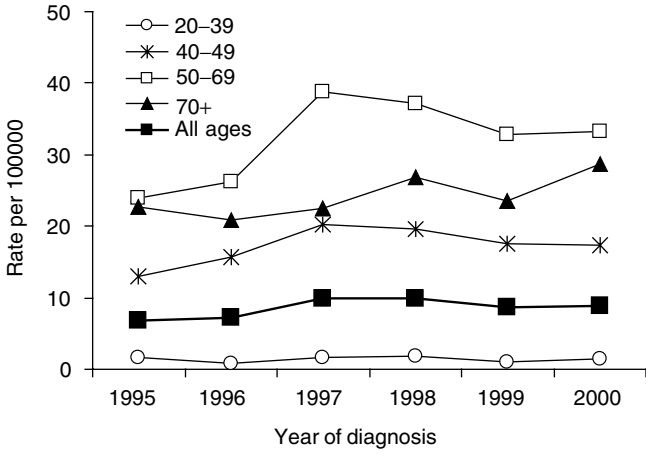

Figure 1 Trends in incidence of DCIS by age group in NSW women from 1995 to 2000. Rates were standardised by 5-year age intervals within broad age groups, using the World standard population.

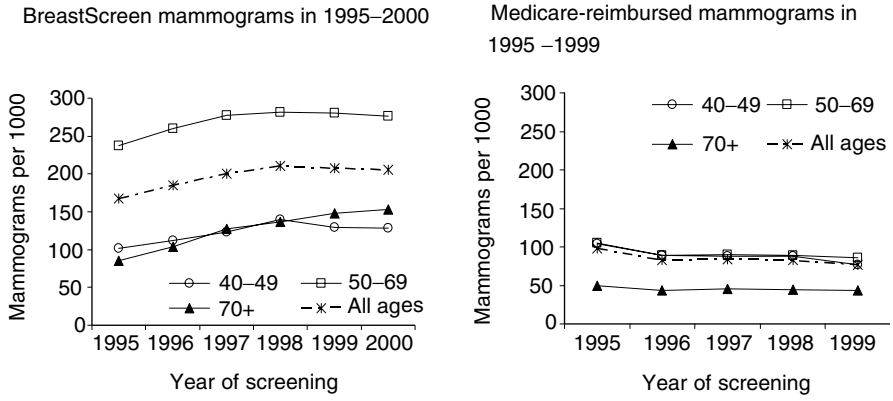

Figure 2 Mammogram rates in NSW women by age group – age-standardised in 10-year age groups to the World population.

in 82% and clearance of the margins in 80%; 37% had all these items. The width of margins was reported in only 41%. All these items except the width of margins were appreciably more complete in 1998–2000 than in 1995–97.

More than half (54%) the DCIS diagnosed in 1995–2000 were high grade and 39% were 2 cm or larger (Table 2). More DCIS were high grade at 20–39 and 50–69 years (57%) than at other ages (50%) ($P = 0.02$) and a higher proportion were 2+ cm at 20–39 (53%) than 40 years and older (38%) ($P = 0.01$). Size, however, was not stated for more DCIS at 20–39 years (34%) than other ages (24%).

Most (65%) of the DCIS were described as cribriform or solid, or a mixture in which these two types predominated. Fewer were identified as comedocarcinoma (10%) in 1998–2000 than in 1995–1997 (26%) and more as a mixture of types (45% compared with 23%; P for difference between the two periods <0.001). High-grade DCIS were distributed across all types (mixed 32%, comedocarcinoma 27%, other specific types 21%, no specific type 20%). Most of the 2+ cm DCIS were mixed (45%) or other specific types (27%) and few were comedocarcinoma (18%) or no specific type (9%).

Age, grade, architecture and multifocality were significant independent predictors of DCIS 2+ cm in size in a logistic regression model (Table 3). Two-fold higher odds of having 2+ cm DCIS appeared to lie with a young age (20–39 years), with high grade and with multifocal lesions. The excess risks of 2+ cm DCIS also lay with mixed types of architecture (OR 1.5) compared to comedocarcinoma and diagnosis in 1996 (OR 1.7), while a report that did not mention necrosis was associated with lower odds (OR 0.7) of a larger DCIS. Otherwise, there was no evident trend across these variables. Neither place of residence (urban or rural) nor SES was significantly predictive of 2+ cm DCIS or appreciably affected the above odds ratios when added to the model.

DISCUSSION

The main strengths of this study are its population base, detail and recency. Population-based registration of DCIS in NSW began 2 years before the first year of our study, and the study's first year coincided with that of complete population coverage by BreastScreen. Its main weakness is lack of linkage between the data sources (BreastScreen, Medicare and the Cancer Registry), without which we cannot fully describe the contribution of screening to the occurrence and outcomes of DCIS.

Table 2 Number, percent and rate of DCIS by grade and size in NSW in 1995–2000

	Number	%	Rate[a]	95% CI
Grade				
Low	313	16.7	1.2	(1.1–1.4)
Intermediate	542	29.0	2.2	(2.0–2.4)
High	1015	54.3	4.2	(3.9–4.5)
Total	1870	100.0	8.6	(8.2–9.0)
Unknown	239		0.9	(0.8–1.1)
Size				
0–0.9 cm	505	31.5	2.1	(1.9–2.3)
1–1.9 cm	480	30.0	2.0	(1.8–2.2)
2–2.9 cm	278	17.4	1.1	(1.0–1.3)
3+cm	339	21.2	1.4	(1.2–1.5)
Total	1602	100.0	8.6	(8.2–9.0)
Unknown	507		2.0	(1.9–2.2)

[a]Rates are per 100 000 women age-standardised to the World population.

Table 3 Association of 2+ cm DCIS with year of diagnosis, age, size, grade, necrosis and multifocality in NSW women in 1995–2000

	<2 cm	2+ cm	OR	(95% CI)	P-value
Year of diagnosis					
1995	112	46	1		
1996	120	89	1.66	(1.05–2.64)	
1997	190	106	1.19	(0.76–1.86)	
1998	209	105	0.74	(0.47–1.18)	
1999	159	129	1.25	(0.78–1.98)	
2000	184	135	1.05	(0.66–1.67)	0.002
Age group					
20–39	28	32	1.87	(1.07–3.27)	
40–49	210	132	1.07	(0.82–1.40)	
50–69	556	316	1		
70+	180	130	1.39	(1.05–1.84)	0.03
Grade					
Low	156	58	1		
Medium	275	147	1.27	(0.86–1.87)	
High	442	365	2.14	(1.46–3.14)	
Not given	101	40	1.3	(0.78–2.17)	<0.0001
Necrosis					
Present	538	411	1		
Absent	72	45	0.94	(0.61–1.46)	
Not given	364	154	0.65	(0.49–0.86)	0.006
Architecture					
Comedocarcinoma	163	112	1		
Mixed types[a]	309	278	1.46	(1.05–2.04)	
Other specified types[b]	326	166	0.89	(0.63–1.26)	
Type unspecified	176	54	0.49	(0.32–0.73)	<0.0001
Multifocal					
No	737	377	1		
Yes	237	233	1.92	(1.52–2.43)	<0.0001

[a]Mixed types: cribriform with solid or papillary architecture or both (64% of mixed types); comedocarcinoma and other type (18%); other (18%). [b]Other specified types: cribriform (41%), solid (40%), micropapillary (13%) and intracystic papillary carcinoma *in situ* (6%).

Other countries have observed increasing incidence of DCIS, sometimes three- to four-fold, with increasing mammographic screening (Ernster *et al*, 1996; Levi *et al*, 1997; Zheng *et al*, 1997; Barchielli *et al*, 1999; Blanks *et al*, 2000). This increase has stopped in NSW and we would expect further increases only with growth in BreastScreen participation beyond 53–54% in 1998–2000 (Estoesta *et al*, 2000; Productivity Commission, 2002) or resurgence in mammographic screening reimbursed by Medicare.

We observed a higher proportion of high-grade lesions (54%) than in Sweden (43%) and Switzerland (46%) in the early 1990s, but similar to that, 55%, in an Australia-wide sample survey (Levi *et al*, 1997; Wärnberg *et al*, 1999; Shugg *et al*, 2002). This apparent difference between Australia and these European countries may be real and due to the extent of high-grade disease, or caused by differences in the reporting of grade. It could reflect, too, differences in mammography rates since high-grade DCIS is said to show abnormal mammographic features more frequently than low grade (Evans *et al*, 2001).

We found that age, high-grade lesions, mixed architecture and multifocality significantly and independently predicted DCIS larger than 2 cm diameter. That women 20–39 years of age were more likely to have 2+ cm diameter DCIS (average 28 mm in multivariate models in this study) than older women (average 18 mm) is probably due to their lower mammography rate. That high-grade lesions were larger probably reflects a correlation with higher growth rate (1.8 mm per year low grade, 4.2 mm

intermediate and 7.1 mm high grade; Thomson *et al*, 2001), particularly since they may also be more readily detectable mammographically (Evans *et al*, 2001). The Van Nuys prognostic index has shown a parallel increase of size with grade although patients treated with mastectomy, and thus probably the larger lesions, were excluded (Silverstein, 2003). Another series showed a step down from 20 mm diameter poorly differentiated DCIS to 15 mm for all other grades (Solin *et al*, 1991). Our study appears to give the first population-based estimates: the average size increased steadily from 16 mm for low grade to 20 mm for intermediate and 27 mm for high-grade DCIS in the multivariate models of Table 3. Variation in growth rate might also underlie the significant, independent association of architecture with tumour size.

The pathology reports from 1998 to 2000 reported DCIS substantially more completely than did earlier Australian reports (Kricker *et al*, 1999; Giles *et al*, 2001; Shugg *et al*, 2002). The Australian Cancer Network addressed pathology reporting of DCIS with extensive consultation among pathologists in the mid-1990s and published recommendations in 1997 (Australian Cancer Network Working Party, 1997) and 2001 (Australian Cancer Network Working Party, 2001). Their adoption by pathologists may explain the more complete reporting we observed.

Increasing incidence of DCIS is an outcome of mammographic screening for breast cancer. The high proportion of high-grade lesions we have observed suggests that its detection could contribute to reducing breast cancer mortality. If it does not, the high frequency of DCIS in association with screening may be source of unnecessary morbidity and cost. More research is needed into the costs and benefits of detection of DCIS in breast cancer screening.

ACKNOWLEDGEMENTS

The National Breast Cancer Centre, Sydney, Australia funded this study. Incidence data on DCIS in 1995–2000 were supplied by the NSW Central Cancer Registry, which is managed and operated by The Cancer Council NSW under contract to the NSW Health Department.

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