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ORIGINAL ARTICLE

Age at diagnosis predicts local recurrence in women treated with breast-conserving surgery and postoperative radiation therapy for ductal carcinoma *in situ*: a population-based outcomes analysis

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ABSTRACT

Purpose

The main goal of treating ductal carcinoma *in situ* (DCIS) is to prevent the development of invasive breast cancer. Most women are treated with breast-conserving surgery (BCS) and radiotherapy. Age at diagnosis may be a risk factor for recurrence, leading to concerns that additional treatment may be necessary for younger women. We report a population-based study of women with DCIS treated with BCS and radiotherapy and an evaluation of the effect of age on local recurrence (LR).

Methods

All women diagnosed with DCIS in Ontario from 1994 to 2003 were identified. Treatments and outcomes were collected through administrative databases and validated by chart review. Women treated with BCS and radiotherapy were included. Survival analyses were performed to evaluate the effect of age on outcomes.

Results

We identified 5752 cases of DCIS; 1607 women received BCS and radiotherapy. The median follow-up was 10.0 years. The 10-year cumulative LR rate was 27% for women younger than 45 years, 14% for women 45–50 years, and 11% for women more than 50 years of age ($p < 0.0001$). The 10-year cumulative invasive LR rate was 22% for women younger than 45 years, 10% for women 45–50 years, and 7% for women more than 50 years of age ($p < 0.0001$). On multivariate analyses, young age (<45 years) was significantly associated with LR and invasive LR [hazard ratio (HR) for LR: 2.6; 95% confidence interval (CI): 1.9 to 3.7; $p < 0.0001$; HR for invasive LR: 3.0; 95% CI: 2.0 to 4.4; $p < 0.0001$]. An age of 45–50 years was also significantly associated with invasive LR (HR: 1.6; 95% CI: 1.0 to 2.4; $p = 0.04$).

Conclusions

Age at diagnosis is a strong predictor of LR in women with DCIS after treatment with BCS and radiotherapy.

KEY WORDS

Ductal carcinoma *in situ,* age, recurrence, young patients, radiation

1. BACKGROUND

Ductal carcinoma *in situ* (DCIS) is a noninvasive form of breast cancer that is most often diagnosed during mammographic screening. Although DCIS is not life-threatening, up to 20% of women with DCIS can develop invasive breast cancer at 10 years, which is associated with an increased risk of breast cancer mortality[1–6]. The goals of treating DCIS are to maximize breast conservation, optimize cosmesis, and prevent the development of invasive breast cancer. Most women with DCIS are treated with breast-conserving surgery (BCS), followed by whole-breast irradiation. Radiotherapy after BCS has been proved to reduce the rate of local recurrence (both *in situ* and invasive)[7–12]. Randomized and nonrandomized clinical trials report that after BCS and radiation, approximately 12%–15% of women will experience a local recurrence within 10 years, and 5%–10% will develop an invasive local recurrence[7–12].

It is important to identify factors associated with the development of local recurrence and subsequent invasive breast cancer, because women with such factors may be candidates for more extensive therapy. It has been suggested that younger age at diagnosis is a risk factor for local recurrence after treatment for DCIS[7,12–14]. Multivariable analyses from randomized clinical trials suggest that the efficacy of radiation

in preventing local recurrence after BCS may be less in younger women, but data on long-term outcomes (rates of DCIS recurrence and invasive breast cancer) in younger women with DCIS treated with BCS and radiation are limited[5,7,12,15].

Past estimates of outcomes in younger women with DCIS treated with BCS and radiation were derived from subgroup analyses of randomized clinical trials or institutional case series, which may not be representative of outcomes in young women with DCIS from the population at large. No population-based studies of young women treated for DCIS have been published. The long-term rates of recurrence and invasive breast cancer in young women with DCIS treated with BCS and radiation and the independent effect of age at diagnosis therefore remain unclear.

We report the results of a population-based analysis of women with DCIS treated with BCS and radiation with long-term follow-up. The objective of our study was to evaluate long-term outcomes in a population of young women with DCIS treated with BCS and radiation. We describe the rates of local recurrence and of invasive breast cancer and evaluate the independent effect of age at diagnosis as a predictor of subsequent invasive breast cancer.

2. METHODS

2.1 Study Cohort

To identify the study population, all breast pathology reports held by the Ontario Cancer Registry (OCR) for tissue removed between January 1, 1994, and December 31, 2003, including reports with codes 174 (invasive breast cancer) or 233 (DCIS) from the *International Classification of Diseases,* 9th revision (ICD-9) or with benign diagnoses were obtained (n = 129,140). The OCR is a population-based registry for the province of Ontario, the largest province in Canada. The OCR collects information on every newly diagnosed case of cancer in the province using multiple data sources. All hospitals and laboratories in Ontario forward copies of all cancer-associated pathology reports to the OCR[16].

We initially reviewed and abstracted all pathology reports held at the OCR and used automated text extraction to identify cases involving a diagnosis of DCIS. We excluded cases with a final diagnosis of invasive breast cancer or benign breast disease (n = 118,905) or DCIS with microinvasion (n = 1447). We found 7282 cases with a final diagnosis of DCIS, and 2953 reports with DCIS and microinvasion. We subsequently linked cases diagnosed as pure DCIS or DCIS and microinvasion with the OCR database to exclude cases with a prior history of any invasive cancer. We excluded 4483 such cases. The provincial cohort included 5752 cases of pure DCIS.

Age at initial diagnosis was determined for each case. Information on the type of presentation (screen-detected vs. clinical symptoms) was not available. Follow-up for each patient was obtained using the Registered Persons Database, which includes demographic information on all residents in Ontario (place of residence, date of death, and date of last medical contact). The study was approved by the Research Ethics Board at Sunnybrook Hospital and the Ontario Cancer Research Ethics Board.

2.2 Treatment

To identify surgical treatment (mastectomy vs. BCS), we used deterministic linkage between the study cohort database and the Canadian Institute for Health Information (CIHI) database. The CIHI database is an administrative database containing information about every patient discharged from an Ontario hospital. It includes patient demographics (age, sex, and postal code), major diagnoses, and procedures (including same-day surgery). The date of definitive diagnosis was the date of histologic confirmation of DCIS. We reviewed all surgical procedures performed within 6 months of the date of definitive diagnosis to determine if the final surgical treatment included BCS or mastectomy. Cases treated with mastectomy and BCS alone were excluded from the study cohort because our objective was to evaluate outcomes in women treated with BCS and radiation. To identify patients treated with breast radiation, we linked the study cohort database with the Ontario Health Insurance Program physician billings database to identify patients seen in consultation by a radiation oncologist within 12 months of definitive diagnosis (thus allowing for the possibilities of multiple surgical procedures and of an extended waiting period before radiotherapy consultation).

All radiation data were obtained by primary chart abstraction. For each case, we abstracted the radiation scheme used (total dose, number of fractions), beam energy (megavolts), and whether additional radiation treatment was delivered to the tumour cavity ("boost" radiation). In 89 cases, the administration of boost radiation was not indicated in the chart, and we therefore performed multivariate analyses categorizing cases with unreported boost both on their own and combined with "no boost" cases. There being no difference in the results, "unreported boost" and "no boost" cases were combined for presentation in this report. All surgical and radiation treatments were validated through primary review of hospital charts[17].

2.3 Pathology

When original slides were available, a centralized pathology review of all diagnostic slides was performed by an expert breast pathologist. Data from the pathology review were included in all analyses involving those cases. In the remaining cases, we abstracted data from the original pathology report using an electronic data mining algorithm[18].

We initially validated the accuracy of the data mining algorithm in a subset of 1000 cases of DCIS by comparing the pathology data extracted electronically to the data obtained by manual data abstraction. The data algorithm achieved more than 95% accuracy for the following features: architectural subtype, nuclear grade, margin status, presence of comedonecrosis, and presence of multifocality. Tumour size and width of the resection margin were not consistently reported during the time interval of this study and were missing from many pathology reports. Those variables were therefore not abstracted. The data elements abstracted from the original pathology report were nuclear grade (low, intermediate, high, unreported), presence of comedonecrosis (present, absent, unreported), multifocality (present, absent, unreported), and margin status (positive, negative, unreported). Margin status was defined as "positive" if tumour cells were identified at the inked resection margin.

2.4 Outcomes

"Any local recurrence" was defined as detection of DCIS or invasive breast cancer that developed in the same breast 6 months or more after the initial diagnosis of DCIS. To determine any local recurrence, we identified all surgical procedures performed on the same breast (ipsilateral) as the index DCIS lesion 6 months or more after the date of diagnosis through the CIHI database. We abstracted the associated diagnosis (invasive, DCIS, or benign) from the CIHI database. We found that a CIHI diagnosis of benign breast lesion was 98% accurate and a diagnosis coded as either invasive or DCIS was more than 90% accurate. Therefore, to validate local recurrences that were invasive breast cancer, we linked each surgical procedure date to the OCR. Cases with a corresponding ICD diagnostic code of 174 (invasive breast cancer) were accepted as an invasive local recurrence, because the accuracy of ascertainment of invasive cancers by the OCR is more than 95%[16]. Cases in which the corresponding hardcopy pathology report confirmed invasive breast cancer were coded as invasive breast cancer. The remaining cases were coded as DCIS recurrence. Contralateral cancer is defined as DCIS or invasive carcinoma developing in the contralateral breast after a diagnosis of DCIS.

Overall survival was determined using the Registered Persons Database to determine the date of death from any cause. The date of last follow-up of the cohort was March 31, 2010.

2.5 Statistical Analysis

We conducted descriptive analyses for any local recurrence (*in situ,* invasive), invasive local recurrence, breast-cancer specific survival, and overall survival. We examined the effect of age as a continuous variable and as a categorical variable using cut-points previously reported in the literature: less than 45 years, 45–50 years, and more than 50 years of age[8,11,13,14,19]. Actuarial results for any local recurrence, invasive local recurrence, local recurrence-free survival, invasive local recurrence-free survival, and overall survival were calculated by the Kaplan–Meier method. The statistical significance of differences between actuarial curves was tested using the log-rank test. Proportional differences for categorical variables were tested using chi-square tests, and mean differences for continuous variables, by *t*-tests. A p value of 0.05 or less was considered statistically significant. To evaluate the independent effect of age on the outcomes of interest (any local recurrence, invasive local recurrence, and *in situ* local recurrence), univariate and multivariate survival analyses were performed using Cox proportional hazards models once it had been confirmed that the assumptions of the proportional hazards model were not violated.

3. RESULTS

3.1 Population Cohort

Using data from the OCR, we located 1949 patients diagnosed with DCIS without microinvasion from 1994 to 2003 who were treated with BCS and radiation. A pathology review was performed in 1363 of the cases (70%). After the pathology review, 314 cases (16%) were excluded because the diagnosis changed to invasive cancer, lobular carcinoma *in situ,* benign disease, or DCIS with microinvasion. Another 10 cases were excluded because the treatment was mastectomy and not BCS, and 18 cases were excluded because the invasive recurrence was found less than 6 months after the initial diagnosis, leaving 1607 patients in the study cohort. In that group, median age at diagnosis was 56 years (range: 20–85 years), with 195 of the women (12%) being less than 45 years of age at diagnosis, 281 (17%) being 45–50 years, and 1131 (70%) being more than 50 years. Most of the women received a conventional dose–fractionation radiation scheme of 50 Gy in 25 fractions delivered over 5 weeks (n = 969, 60%). The remaining 638 women (40%) received a hypofractionated regimen (40–44 Gy in 16 fractions). Boost radiation was given to 30% of the women (n = 488, Table I).

3.2 Outcomes

After a median follow-up of 10.0 years, 209 women treated with BCS and radiotherapy (13%) experienced a local recurrence (*in situ* or invasive). The risk of local recurrence increased with lower age at diagnosis. The effect of age on the risk of local recurrence and invasive recurrence was continuous. For each year of increase in age, local recurrence decreased 4%

TABLE I Patient and tumour characteristics by age of the patient at diagnosis

Variable	*Patient group [n (%)]*				p *Value*
	Whole cohort	*<45 Years*	*45–50 Years*	*>50 Years*	
Patients	1607	195	281	1131	—
Nuclear grade					
High	591 (36.8)	74 (37.9)	112 (39.9)	405 (35.8)	0.31
Moderate	671 (41.8)	87 (44.6)	114 (40.6)	470 (41.6)	
Low	95 (5.9)	9 (4.6)	10 (3.6)	76 (6.7)	
Unreported	250 (15.6)	25 (12.8)	45 (16.0)	180 (15.9)	
Necrosis					
Present	948 (59.0)	114 (58.5)	175 (62.3)	659 (58.3)	0.45
Absent	374 (23.3)	52 (26.7)	58 (20.6)	264 (23.3)	
Unreported	285 (17.7)	29 (14.9)	48 (17.1)	208 (18.4)	
Multifocality					
Present	343 (21.3)	33 (16.9)	69 (24.6)	241 (21.3)	0.12
Absent	981 (61.0)	117 (60.0)	165 (58.7)	699 (61.8)	
Unreported	283 (17.6)	45 (23.1)	47 (16.7)	191 (16.9)	
Subtype					
Solid	1,073 (66.8)	137 (70.3)	184 (65.5)	752 (66.5)	0.94
Cribriform	332 (20.7)	36 (18.5)	65 (23.1)	231 (20.4)	
Micropapillary	21 (1.3)	2 (1.0)	3 (1.1)	16 (1.4)	
Other	50 (3.1)	6 (3.1)	9 (3.2)	35 (3.1)	
Unreported	131 (8.2)	14 (7.2)	20 (7.1)	97 (8.6)	
Margin status					
Negative	1,001 (62.3)	121 (62.1)	170 (60.5)	710 (62.8)	0.56
Positive	256 (15.9)	27 (13.8)	53 (18.9)	176 (15.6)	
Unreported	350 (21.8)	47 (24.1)	58 (20.6)	245 (21.7)	
Radiation scheme					
Conventional	827 (51.5)	107 (54.9)	150 (53.4)	570 (50.4)	0.01
Conventional+boost	142 (8.8)	15 (7.7)	31 (11.0)	96 (8.5)	
Hypofractionation	292 (18.2)	23 (11.8)	36 (12.8)	233 (20.6)	
Hypofractionation+boost	346 (21.5)	50 (25.6)	64 (22.8)	232 (20.5)	
Boost radiation					
Yes	488 (30.4)	65 (33.3)	95 (33.8)	328 (29.0)	0.18
No	1,119 (69.6)	130 (66.7)	186 (66.2)	803 (71.0)	
Year of diagnosis					
1994–1996	38 (19.5)	59 (21.0)	248 (21.9)	345 (21.5)	0.36
1997–1999	78 (40.0)	106 (37.7)	378 (33.4)	562 (35.0)	
2000–2003	79 (40.5)	116 (41.3)	505 (44.7)	700 (43.6)	

[hazard ratio (HR): 0.96; 95% confidence interval (CI): 0.95 to 0.98; $p < 0.0001$], and invasive local recurrence decreased 5% (HR: 0.95; 95% CI: 0.94 to 0.97; $p < 0.0001$; Figure 1). The 10-year cumulative rates of any local recurrence were 27% among women less than 45 years of age at diagnosis, 14% among women 45–50 years, and 11% among women more than 50 years (log-rank $p < 0.0001$, Table II).

The rate of invasive local recurrence decreased progressively with increasing age: 22% for the group less than 45 years of age at diagnosis, 10% for those 45–50 years, and 7% for those more than 50 years ($p < 0.0001$, Figure 2). The cumulative incidence rates for DCIS recurrence were 6% among women less than 45 years of age, 4% among those 45–50 years, and 3% among those more than 50 years (log-rank $p = 0.17$). We observed no significant difference in the 10-year rates of contralateral breast cancer by age, which ranged between 5% and 6% (Table II).

The effect of age on the development of local recurrence remained significant among women treated with boost radiation. Among those who received boost radiation ($n = 488$), the cumulative local recurrence rate was 30% for those less than

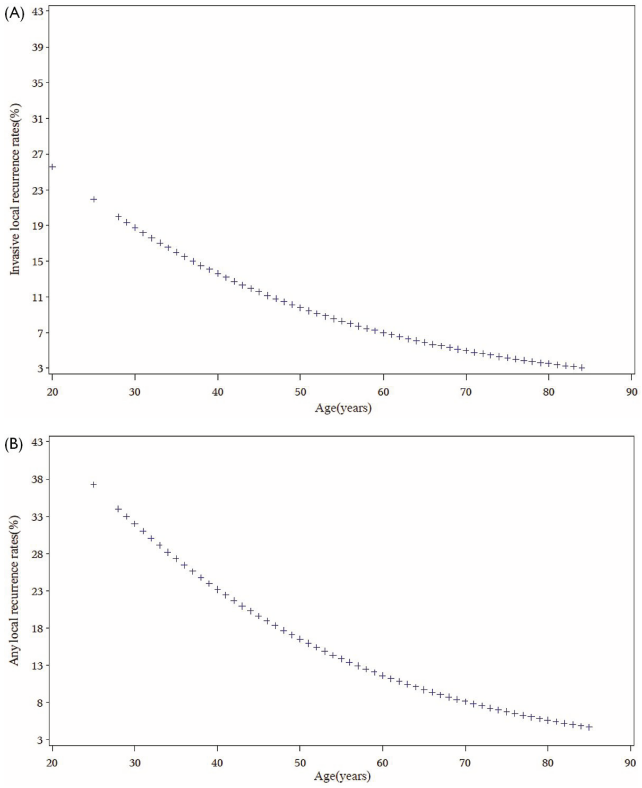

FIGURE 1 *Effect of age as continuous variable on (A) invasive local recurrence and (B) local recurrence of any kind.*

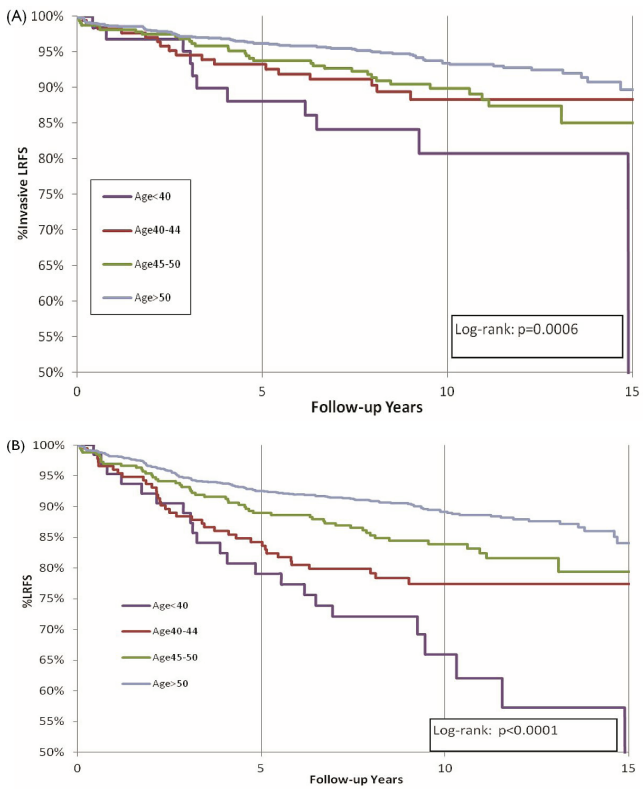

FIGURE 2 *Local recurrence-free survival (LRFS) by age at diagnosis. (A) Invasive local recurrence. (B) Local recurrence of any kind.*

TABLE II Outcomes in women with ductal carcinoma *in situ* (DCIS) treated with breast-conserving surgery and radiation, by age at diagnosis

Variable	*Patient group*				p *Value*
	Whole cohort (n=1607)	*<45 Years (n=195)*	*45–50 Years (n=281)*	*>50 Years (n=1131)*	
Local recurrence [*n* (%)]					
Any	209 (13)	48 (25)	42 (15)	119 (11)	<0.0001
Invasive	148 (9)	36 (18)	31 (11)	81 (7)	<0.0001
DCIS	61 (4)	12 (6)	11 (4)	38 (3)	0.17
Local recurrence-free survival (%)					
Actuarial					
5-Year	91	84	90	93	<0.0001
10-Year	87	73	86	89	
Invasive					
5-Year	95	88	94	96	<0.0001
10-Year	90	78	90	93	
DCIS					
5-Year	96	95	96	97	0.13
10-Year	96	94	96	97	
Contralateral breast cancer–free survival (%)					
5-Year	97	98	99	97	0.82
10-Year	95	94	95	94	
Overall survival (%)					
5-Year	97	98	97	97	0.002
10-Year	91	91	95	89	

45 years of age at diagnosis, 12% for those 45–50 years, and 9% for those more than 50 years (log-rank $p = 0.0001$). Among individuals who did not receive boost radiation, the local recurrence rate was 25% among those less than 45 years of age, 15% among those 45–50 years, and 11% among those more than 50 years (log-rank $p = 0.0003$; Figure 3).

We performed multivariate analyses to evaluate the effect of age at diagnosis and other independent prognostic variables on the development of any local recurrence, invasive local recurrence, and DCIS local recurrence after BCS and radiotherapy. On multivariate analyses, age less than 45 years (HR: 2.6; 95% CI: 1.9 to 3.7; $p < 0.0001$) and positive or unreported margin status (HR: 1.5; 95% CI: 1.1 to 2.0; $p = 0.01$) were significantly associated with the development of local recurrence (Table III).

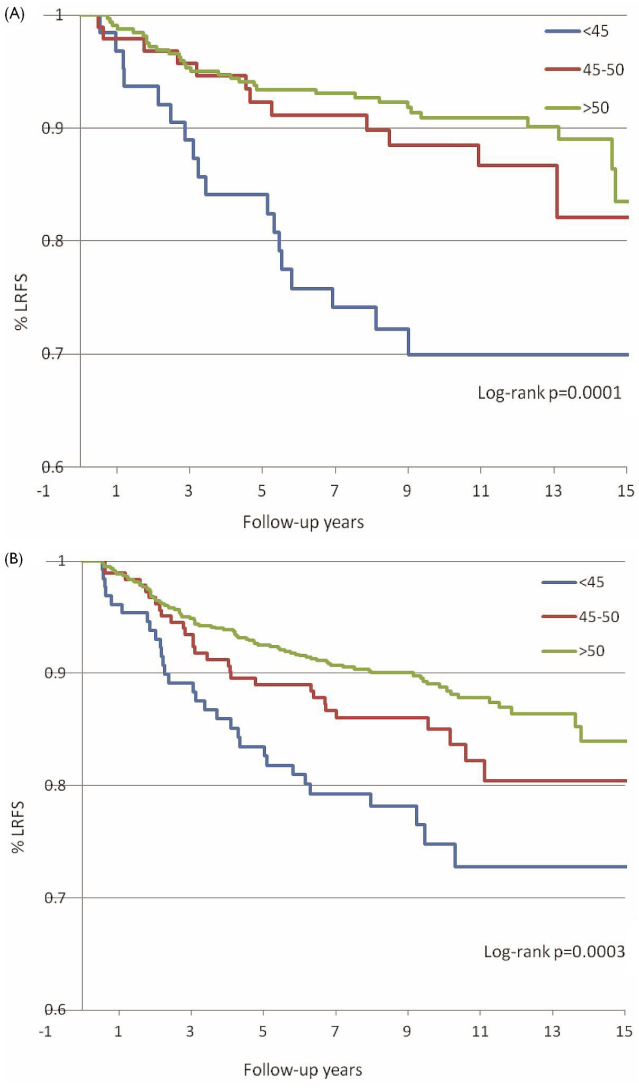

FIGURE 3 *Local recurrence-free survival (LRFS) by age at diagnosis in women who (A) received and (B) did not receive boost radiation.*

Age less than 45 years (HR: 3.0; 95% CI: 2.0 to 4.4; $p < 0.0001$) and 45–50 years at diagnosis (HR: 1.6; 5% CI: 1.0 to 2.4; $p = 0.04$), positive or unreported margin status (HR: 1.6; 95% CI: 1.1 to 2.2; $p = 0.01$), and unreported nuclear grade (HR: 0.6; 95% CI: 0.3 to 0.95; $p = 0.04$) were associated with the development of invasive local recurrence after treatment with BCS and radiotherapy (Table IV). On multivariate analysis, age less than 45 years (HR: 1.9; 95% CI: 1.0 to 3.7; $p = 0.05$) and 45–50 years at diagnosis (HR: 1.1; 95% CI: 0.6 to 2.1; $p = 0.79$) and high nuclear grade (HR: 2.8; 95% CI: 1.6 to 5.0; $p = 0.0005$) were associated with the development of DCIS recurrence (Table V).

4. DISCUSSION

We report long-term outcomes in a large, diverse population of women diagnosed with DCIS and treated with BCS and radiation. Among those women, we found that young age at diagnosis is the strongest predictor of local recurrence, invasive local recurrence, and *in situ* local recurrence. Our results demonstrate that the effect of age on recurrence and invasive local recurrence is continuous. For women under 45 years of age at diagnosis, the 10-year local recurrence-free survival and invasive local recurrence-free survival after BCS and radiation were 73% and 78% respectively.

Our study corroborates a recent analysis of two large randomized trials, the National Surgical Adjuvant Breast and Bowel Project B-17 and B-24 trials,

TABLE III Factors associated with any local recurrence: univariate and multivariate analysis, adjusted for year of diagnosis

Variable	*Multivariate analysis*		p *Value*
	HR	*95% CL*	
Age			
<45 Years	2.6	1.9, 3.7	<0.0001
45–50 Years	1.4	0.98, 2.0	0.06
>50 Years	Reference		
Multifocality			
Present	1.4	0.99, 1.9	0.06
Absent	Reference		
Unreported	1.2	0.84, 1.7	0.32
Margin status			
Positive or unreported	1.5	1.1, 2.0	0.01
Negative	Reference		
Nuclear grade			
High	1.2	0.9, 1.7	0.14
Moderate or low	Reference		
Unreported	0.7	0.5, 1.1	0.15
Boost			
Yes	0.8	0.6, 1.1	0.12
No	Reference		

HR = hazard ratio; CL = confidence limits.

TABLE IV Factors associated with invasive local recurrence: multivariate analysis adjusted for year of diagnosis

Variable	*Multivariate analysis*		p *Value*
	HR	*95% CL*	
Age			
<45 Years	3.0	2.0, 4.4	<0.0001
45–50 Years	2.4	1.6, 1.0	0.04
>50 Years	Reference		
Multifocality			
Present	1.3	0.9, 2.0	0.16
Absent	Reference		
Unreported	1.1	0.7, 1.7	0.77
Margin status			
Positive or unreported	1.6	1.1, 2.2	0.01
Negative	Reference		
Nuclear grade			
High	0.9	0.6, 1.3	0.56
Moderate or low	Reference		
Unreported	0.6	0.3, 0.95	0.04
Boost			
Yes	0.7	0.5, 1.1	0.11
No	Reference		

HR = hazard ratio; CL = confidence limits.

TABLE V Factors associated with ductal carcinoma *in situ* local recurrence: multivariate analysis adjusted for year of diagnosis

Variable	*Multivariate analysis*		p *Value*
	HR	*95% CL*	
Age			
<45 Years	1.9	1.0, 3.7	0.05
45–50 Years	1.1	0.6, 2.1	0.79
>50 Years	Reference		
Multifocality			
Present	1.5	0.8, 2.8	0.18
Absent	Reference		
Unreported	1.6	0.8, 3.1	0.16
Margin status			
Positive or unreported	1.2	0.7, 2.1	0.47
Negative	Reference		
Nuclear grade			
High	2.8	1.6, 5.0	0.0005
Moderate or low	Reference		
Unreported	1.5	0.6, 3.7	0.39
Boost			
Yes	0.9	0.5, 1.6	0.75
No	Reference		

HR = hazard ratio; CL = confidence limits.

which demonstrated that women less than 45 years of age experienced higher invasive local recurrence even after controlling for other factors including tumour size, presence of comedonecrosis, and clinical presentation[5]. Half the women enrolled in B-17 did not receive radiotherapy. The strength of that study is that it included a large and diverse population of more than 1600 women with DCIS treated with BCS and radiotherapy in the province of Ontario.

Young age at diagnosis and positive or unreported resection margins were significantly associated with an increased risk of local recurrence and invasive local recurrence after treatment with BCS and radiotherapy for DCIS. The risk of local recurrence increased progressively with decreasing age at diagnosis after adjusting for the effect of nuclear grade and boost radiation. At 10 years, the rates of local recurrence after BCS and radiotherapy were 11% for women more than 50 years of age at diagnosis, 15% for those 45–50 years, and 25% for those less than 45 years.

We found that the increased risk of local recurrence associated with younger age was present regardless of the use of boost radiation to the tumour cavity. Excluding women with positive resection margins, the 10-year local recurrence-free survival rates among women who did and did not receive boost radiation were, respectively, 70% and 75% for women less than 45 years of age at diagnosis, 88% and 85% for those 45–50 years, and 91% and 89% for those more than 50 years. Although our study included 1607 women diagnosed over a 10-year period, only 65 of the women less than 45 years of age were treated with boost radiation because boost radiation was not commonly used during the period of our study. In a previous study, we had found no significant effect of boost radiation, but our ability to evaluate the effect of boost radiation on the outcomes of young women with DCIS is limited[18]. The benefit of boost radiation in young women (<45 years of age) was reported in the Rare Cancer Network study[19]. In that report, the 10-year local relapse-free survival was 86% in women treated with boost radiotherapy and 72% in women treated with breast radiotherapy without boost. The results of our study and the Rare Cancer Network study demonstrate that the 10-year rate of local recurrence in young women with DCIS treated with BCS and radiotherapy ranges from 14% to 27%. We could not evaluate the effect of tamoxifen because, during the study period, few women in the cohort received tamoxifen. Further research is needed to determine the optimal dose–fractionation regimen and the effect of tamoxifen in further reducing the risk of local recurrence in young women.

The reasons why younger women have higher rates of local recurrence and invasive recurrence are unknown. We did not identify any differences in the pathologic features of DCIS (such as high grade, presence of necrosis, or resection margin status) in younger women. A previous study noted that, compared with

women diagnosed between 40 and 70 years of age, younger women with DCIS (<40 years) were more likely to be diagnosed with multicentric disease (29.3% vs. 17.7%)[20]. It is also possible that younger women are more likely to present with clinical symptoms (for example, a palpable lump) or more likely to have dense breasts or a family history of breast cancer, which have been shown to be associated with an increased risk of recurrence[21–25]. It has also been hypothesized that the efficacy of radiotherapy may be less in younger women[11]. A study by Holmberg *et al.*[15] reported that radiotherapy had a small benefit with respect to cancer recurrence in women less than 50 years of age, but that a large degree of protection was seen in women more than 60 years. The differential benefit could not be explained by differences in lesion size, completeness of excision, multifocality, or mode of detection, a finding which suggests that the age effect may be to some extent attributable to responsivity to radiotherapy and not solely to an intrinsically higher recurrence risk in young women. That suggestion of differential response might be resolved if studies were to be undertaken in cohorts of women who did and did not receive radiotherapy; however, the latter studies are few in number. Further research is needed to determine the reasons that younger women have a higher risk of recurrence. In this regard, several studies of gene expression profiling are underway.

5. CONCLUSIONS

Young age at diagnosis and positive surgical resection margins are significantly associated with an increased risk of local recurrence after BCS and radiotherapy for DCIS. The results of our study do not suggest that breast-conserving therapy is contraindicated in younger women for DCIS; rather, the findings can be used to guide clinicians in their treatment decisions for women with DCIS—such as ensuring complete clearance of the disease with negative resection margins. Further research is needed to understand the underlying biologic reasons that younger women have higher rates of recurrence and to explore ways to improve outcomes of women with DCIS.

6. ACKNOWLEDGMENTS

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7. CONFLICT OF INTEREST DISCLOSURES

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