Breast Cancer Research and Treatment
https://doi.org/10.1007/s10549-020-06014-5

EPIDEMIOLOGY

Ductal carcinoma in situ in patients younger than 30 years: differences in adjuvant endocrine therapy and outcomes

Sasha R. Halasz[1] · Thomas O'Keefe[1] · Anne M. Wallace[2] · Sarah L. Blair[2]

Received: 21 September 2020 / Accepted: 3 November 2020

Abstract

Purpose To use the National Cancer Database to assess treatment patterns in very young women with ductal carcinoma in situ (DCIS) given their propensity for higher risk features and increased risk of recurrence.

Methods We used the NCDB to identify female patients who underwent surgery for a first cancer diagnosis of DCIS within three different age groups: ≤30, 31–50, and >50. Demographic information, tumor characteristics, and initial treatment patterns were characterized and compared. Univariable and multivariable logistic regression of individuals with hormone-receptor-positive disease who underwent breast-conserving surgery (BCS) was conducted to assess for group differences in adjuvant endocrine therapy utilization. Survival analysis was conducted via Kaplan-Meier method and Cox regression.

Results We identified 236,832 patients meeting inclusion criteria. Individuals in the youngest group were more likely to be a minority, had better Charlson-Deyo scores, lived further from their treatment facility, and were less often insured. This group also had more unfavorable tumor features and were more likely to undergo bilateral mastectomy. In subgroup analysis of patients with hormone-receptor-positive disease who underwent BCS, the youngest group was significantly less likely to have received endocrine therapy. There was also a trend toward worse overall survival in the youngest group.

Conclusion We report differences in demographics, tumor characteristics, and treatment of very young women with DCIS. Given the known reduction in recurrence with use of adjuvant endocrine therapy, there may be room for increasing therapy rates or otherwise altering guidelines for treatment of young women with hormone-receptor-positive DCIS who undergo BCS.

Keywords DCIS · Young breast cancer · Survival · Endocrine therapy · Radiation therapy

Introduction

Ductal carcinoma in situ (DCIS) is a non-invasive malignant transformation of the breast milk ducts with a 20-year breast cancer-specific mortality reported around 3% [1]. There are ongoing trials attempting to define the appropriate patient selection criteria and cohort in which to consider an active surveillance strategy [2–4]. Until these trials result, current treatment typically includes surgical resection with adjuvant therapy efforts directed at reducing risk of recurrence. Selection of a personalized treatment plan is influenced by tumor characteristics and patient demographics, including patient age [5–7].

Despite the fact that young age is a known risk factor for a second event and development of invasive disease in DCIS, there is a paucity of literature describing treatment patterns and outcomes in young women [8, 9]. Breast cancer is rare at baseline in this age group, and there is controversy regarding appropriate treatment, making this a particularly challenging area of study [10]. Very few studies report breast cancer outcomes on cohorts aged less than age 30, with most including up to at least age 40 [11]. Therefore, the evidence for treating these patients is highly driven by data from women aged 31–40 and may not be reflective of the unique characteristics of even younger patients. This leaves providers who are treating patients ≤30 without specific evidence-based treatment.

This is an invited commentary to article doi: 10.1007/s10549-020-06014-5.

✉ Sarah L. Blair
slblair@health.ucsd.edu

[1] Department of Surgery, University of California San Diego, 9300 Campus Point Drive, #7220, La Jolla, CA 92037, USA

[2] Division of Breast Surgery and The Comprehensive Breast Health Center, University of California San Diego, Mailbox 0819, 3855 Health Sciences Dr, La Jolla, CA 92037, USA

Published online: 12 November 2020

There is an evidence that very young age at diagnosis presents unique challenges in treatment algorithms [12]. Treatment patterns have been shown to differ between age cohorts, including an increasing predilection for contralateral prophylactic mastectomy as the selected surgical option in younger patients, though this is not shown to confer survival benefit [13]. Regarding adjuvant endocrine therapy, there are unique fertility and side effect concerns for younger women that can make initiation and compliance more challenging, but there is evidence that differences in treatment for eligible patients between age cohorts may be due in large part to differences in recommendations by healthcare providers [14, 15].

If discrepancies between endocrine therapy guidelines and actual treatment patterns are indeed mainly provider-driven rather than secondary to patient preference, this suggests either a need to adjust guidelines or improve compliance with best practice. This is especially prudent when it comes to very young women who are at high risk for recurrence and stand to gain greatly from appropriate therapy. Thus, we seek to use a large cancer database to address this understudied group overall and with specific attention to endocrine therapy.

Methods

The present study was conducted using data from the National Cancer Database (NCDB). This database, which is one of the largest clinical cancer registries in the world, represents a joint effort between the American College of Surgeons and the American Cancer Society. It contains de-identified hospital-based patient data from Commission on Cancer's (CoC) accredited programs and includes over 70% of newly diagnosed cancers [16]. This study was conducted in accordance with U.S. Common Rule. The UCSD HRPP/IRB deferred need for approval due to use of public, de-identified data.

Female patients diagnosed with pure DCIS between 2004 and 2016 who underwent surgical intervention with breast conserving surgery or mastectomy were identified using International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) primary location, behavior, and histology codes. Patients were excluded if diagnosis to last contact or death was less than six months. Patients were divided into three age groups for analysis: age ≤ 30, age 31–50, and age > 50. The filtering process is detailed in Table 1.

Table 1 Criteria for inclusion in study

Filter criteria	Number of patients remaining
All cases in breast PUF	*2,696,734*
Females only	*2,672,744*
DCIS	*282,730*
Patients who underwent mastectomy or BCS	*280,745*
Follow-up time of at least six months	*236,832*

The National Cancer Database breast participant user file (PUF) was filtered for female patients with pure ductal carcinoma in situ (DCIS) using location, pathology, histology, and behavior codes. Only patients who underwent surgical therapy with mastectomy or breast conserving surgery (BCS) with a minimum follow-up of at least six months were included

Statistics

Patient-level data for cases meeting inclusion criteria were categorized by age group and demographics were compared for significant group differences via Chi Square or ANOVA. Univariable and multivariable logistic regression was conducted to determine significant variables affecting receipt of endocrine therapy in patients with hormone-receptor-positive (HR+) DCIS who underwent BCS. The NCDB reports hormone-receptor expression as positive, negative, or borderline without additional detail on the intensity of expression. Although "borderline" is no longer a designation, data before this change was reported in this manner. Therefore, the rare cases listed as "borderline" were included as positive as has been done by other investigators using the NCDB [17]. These results were reported using odds ratios (ORs) for which 95% confidence intervals (CIs) were calculated. Survival analysis was conducted using the Kaplan-Meier method with log-rank test. Univariable and multivariable Cox regressions were developed using variables known to affect DCIS outcomes. Cox models were tested for proportional hazards assumption with both graphical and residual-based methods. *P* values were calculated as two sided, and statistical significance was declared for p less than 0.05.

Analysis was performed using IBM SPSS Statistics for Macintosh, Version 26.0 (IBM Corp., Armonk, N.Y., USA) and R (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria) using RStudio (Version 1.1.463) and packages "tidyverse" (Version 1.3.0), "survival" (Version 3.1–7), and "survminer" (Version 0.4.6).

Results

We identified 236,832 patients who met inclusion criteria (Table 1) of whom 652 were age 30 or younger, 58,158 were aged 31–50, and 178,022 were older than age 50. Demographic differences were noted between age groups. By proportion, individuals in the youngest group were more likely to be black (21% vs 12% in older groups), live further from treatment centers (31.5 miles vs 21.0 miles in older groups), and be more likely to be on Medicaid insurance (age ≤ 30 13%, age 31–50 7%, age > 50 4%). Women age 30 or less were more likely to have tumor size >10 mm (53% vs 40% in the older groups). They were also more likely to have high grade tumors (45% vs 36% in the older groups). In terms of treatment, a higher percentage of younger women underwent bilateral mastectomy (37%) rather than unilateral mastectomy (31%) or breast-conserving surgery (BCS) (21%) whereas BCS was the most common surgical extent for the middle and older group (54.6% and 69.2%, respectively) (Table 2).

Among the subgroup of women who underwent BCS for estrogen or progesterone receptor (ER or PR)-positive disease, 32.1% of the youngest age group received ET compared to 56.4–61.6% in the older groups. However, among those who did not receive ET, the reason was reported as due to patient preference only 11.5%, 11.8%, and 12.3% of the time in the youngest, middle, and oldest groups, respectively (Table 3). Age was a significant predictor of initiation of endocrine therapy even when adjusted for confounders ($p < 0.001$). With the youngest age group as a reference, the odds ratio (OR) of receiving endocrine therapy was found to be 2.904 (95% confidence interval [CI] 1.769, 4.766) and 2.927 (95% CI 1.784, 4.803) for the middle and older age groups, respectively (Table 4).

Kaplan-Meier analysis demonstrated worse overall survival in the youngest age group compared to the middle age group (log-rank p value = 0.004, Fig. 1) which became non-significant after multivariable Cox regression analysis (HR 1.27, CI 0.60–2.71, $p = 0.53$) (Table 5). The >50 age group was not included in overall survival analysis due to high chance of confounding with survival variables outside the scope of this study making it a poor surrogate of disease-specific survival in this age group. Variables associated with significant changes in overall survival included black race and receipt of radiation therapy in the 30–50 age group. In a subgroup analysis of patients undergoing BCS, receipt of endocrine therapy was associated with improved overall survival (HR 0.72, CI 0.54–0.96, $p = 0.02$, Table 6).

Discussion

Here, we examined the effect of young age at diagnosis of DCIS on patient and disease-related factors, treatment patterns, and outcomes, while accounting for known confounding factors, by using a large national database. Among our findings, the youngest age group included a higher proportion of minorities and tended to live further from treatment centers. Not unexpectedly, they also tended to have less comorbidities and be uninsured or on Medicaid insurance compared to the older cohorts. Overall more unfavorable tumor characteristics in this group may be due to genetic predisposition or the fact that this group is generally below the age for formal breast cancer screening which leads to more advanced presentation [10]. These same reasons may also contribute to the higher proportion of the youngest age group who chose to undergo bilateral mastectomy rather than BCS observed in our study.

For women with hormone-receptor-positive DCIS who wish to undergo BCS, endocrine therapy is recommended to reduce recurrence and new occurrences [18]. However, in support of previous literature in young women, we find in the present study that at least a third of patients who meet these criteria may not be receiving ET [19]. This is especially true in the youngest age cohort where 67.9% of patients meeting these criteria did not receive ET. Interestingly, although this age group likely has unique concerns regarding fertility and side effects, patient preference to forgo ET was only 11.5% which was a similar and in fact smaller percent than in other age groups. This suggests that there is potential for an increased proportion of younger patients to receive this therapy and better physician education is needed to make sure it is offered when appropriate.

The benefit of ET is reported to be due to reduced recurrence rather than improvement in survival. We detected a possible trend toward worse survival in the youngest age group which was the group least likely to receive ET, as well as a significant association with improvement in overall

Table 2 Patient demographics

	Age ≤ 30	Age 31–50	Age > 50	Naive *p* value
Total Number				
	652	58,158	178,022	
Race				< 0.001
White	433 (66.4)	45,643 (78.5)	146,036 (82.0)	
Black	137 (21.0)	7302 (12.6)	21,909 (12.3)	
Other	68 (10.4)	4469 (7.7)	8507 (4.8)	
Unknown	14 (2.1)	744 (1.3)	1570 (0.9)	
Ethnicity				< 0.001
Non-Hispanic	552 (84.7)	51,022 (87.7)	161,211 (90.6)	
Hispanic	68 (10.4)	4184 (7.2)	7966 (4.5)	
Unknown	32 (4.9)	2952 (5.1)	8845 (5.0)	
Charlson-Deyo Score				< 0.001
0	625 (95.9)	53,750 (92.4)	148,239 (83.3)	
1	27 (4.1) *collapsed due to cell <10	3912 (6.7)	24,369 (13.7)	
2		385 (0.7)	4340 (2.4)	
3+		111 (0.2)	1074 (0.6)	
Average Distance to Treatment Center (miles)				0.010
	31.5	21.0	21.0	
Type of Insurance				< 0.001
Private	510 (78.2)	49,472 (85.1)	88,433 (49.7)	
Medicare/Gov	17 (2.6)	2292 (3.9)	78,176 (43.9)	
Medicaid	83 (12.7)	3985 (6.9)	6653 (3.7)	
None	29 (4.4)	1377 (2.4)	2055 (1.2)	
Unknown	13 (2.0)	1032 (1.8)	2705 (1.5)	
ER status				< 0.001
Positive	466 (71.5)	45,031 (77.4)	129,808 (72.9)	
Negative	103 (15.8)	5692 (9.8)	26,810 (15.1)	
Unknown	83 (12.7)	7435 (12.8)	21,404 (12.0)	
PR status				< 0.001
Positive	399 (61.2)	390,186 (67.4)	106,732 (60.0)	
Negative	138 (21.2)	8750 (15.0)	41,307 (23.2)	
Unknown	115 (17.6)	10,222 (17.6)	29,983 (16.8)	
Tumor grade				< 0.001
High	292 (44.8)	21,222 (36.5)	63,158 (35.5)	
Intermediate	167 (25.6)	20,427 (35.1)	58,805 (33.0)	
Low	63 (9.7)	5871 (10.1)	22,757 (12.8)	
NA	130 (19.9)	10,638 (18.3)	33,302 (18.7)	
Tumor size				< 0.001
<10 mm	136 (20.9)	18,092 (31.1)	59,853 (33.6)	
> = 10 mm	348 (53.4)	23,439 (40.3)	70,442 (39.6)	
Unknown	168 (25.8)	16,627 (28.6)	47,727 (26.8)	
Margin Status				< 0.001
Negative	615 (94.3)	55,450 (95.3)	170,764 (95.9)	
Positive	37 (5.7) *collapsed due to cell <10	2009 (3.5)	5495 (3.1)	
Unknown		699 (1.2)	1763 (1.0)	
Surgery				< 0.001
Partial Mastectomy	137 (21.0)	31,747 (54.6)	123,178 (69.2)	
Unilateral Mastectomy	202 (31.0)	11,527 (19.8)	31,503 (17.7)	
Bilateral Mastectomy	241 (37.0)	11,135 (19.1)	13,293 (7.5)	

Table 2 (continued)

	Age ≤ 30	Age 31–50	Age > 50	Naive *p* value
Mastectomy Type Unspecified	72 (11.0)	3749 (6.4)	10,048 (5.6)	
Radiation				< 0.001
Yes	95 (14.6)	25,195 (43.3)	87,256 (49.0)	
No	557 (85.4)* collapsed due to cell <10	32,307 (55.6)	88,829 (49.9)	
Unknown		656 (1.1)	1937 (1.1)	
Endocrine				< 0.001
Yes	118 (18.1)	20,714 (35.6)	64,595 (36.3)	
No	489 (75.0)	33,045 (56.8)	102,174 (57.4)	
Unknown	45 (6.9)	4399 (7.6)	11,253 (6.3)	

Patient demographics, tumor characteristics, and treatment broken down by age cohort

Table 3 Rates of endocrine therapy by age group

	ET (%)	No ET (Patient declined) (%)	No ET (Other reason or unknown) (%)
Age ≤ 30	32.1	11.5	56.4
Age 31–50	61.6	11.8	26.6
Age > 50	56.4	12.3	31.3

Percentage of individuals by age group in the hormone-receptor-positive breast-conserving surgery subgroup, who received endocrine therapy (ET), were reported as declining endocrine therapy, or did not get endocrine therapy for another reason

survival in the BCS subgroup aged <50 who received ET, but are cautious in interpreting these findings as this survival benefit is not disease specific. Although these findings should not be directly interpreted, they suggest that analysis of these parameters as they relate to breast cancer-specific survival may be revealing especially given evidence that mortality is higher for younger individuals with breast cancer [20, 21].

Limitations include much smaller sample size for the youngest age group compared to other groups, especially in subgroup analysis. This is likely why such young age groups are rarely reported on and it is why we relied on the use of a large national database to draw meaningful conclusions. Additionally, although the ability to determine which proportion of these patients declined ET is useful, the reason for which the patient declined is not reported. There is also limited detail as to other reasons why an individual did or did not receive endocrine therapy, and there is no information on attrition rates. We postulate that the rate of ET use in the youngest age group is actually smaller than reported in our study given the high attrition rates reported in the literature [22]. Therefore, their rates of endocrine therapy use may be overestimated in our study. Finally, the database used in this study reports overall survival but not disease-specific survival or recurrence data making it impossible for us to report on these more specific outcomes as they relate to hormonal therapy.

Future study is needed to further investigate reasons for lower endocrine therapy rates in the youngest age group and should include longer term follow-up of their treatment course. Additionally, it would be beneficial to study this age group in terms of how receipt of endocrine therapy or not relates to rates of recurrence and disease-specific survival. If outcomes are negatively impacted by this treatment disparity, providers could consider dose adjustment to improve side-effect profile and compliance [23]. Overall, our study finds that age ≤ 30 is associated with lower use of ET, and this lower rate does not seem to be related to patient preference. This suggests that there is an alternative explanation for lack of ET initiation in this very young age group that should be explored.

Table 4 Univariable and multivariable analysis of predictors of receiving endocrine therapy if ER/PR+/borderline and BCS

Covariate	ET (n = 53,411)	No ET (n = 39,344)	Unadjusted OR[a] (95% CI)	Unadjusted P value[b]	Adjusted OR (95% CI)	Adjusted P value
Age						
<30	25 (32.1)	53 (67.9)	1 (reference)	< 0.001	1 (reference)	< 0.001
31–50	12,788 (61.6)	7969 (38.4)	3.404 (2.113, 5.478)		2.904 (1.769, 4.766)	
>50	40,598 (56.4)	31,322 (43.6)	2.748 (1.708, 4.422)		2.927 (1.784, 4.803)	
Race						
White	42,792 (57.3)	31,877 (42.7)	1 (reference)	< 0.001	1 (reference)	< 0.001
Black	7312 (59.9)	4899 (40.1)	1.112 (1.069, 1.156)		1.117 (1.072, 1.164)	
Other	2819 (56.7)	2150 (43.3)	0.977 (0.922, 1.035)		0.957 (0.900, 1.017)	
Unknown	488 (53.9)	418 (46.1)	0.870 (0.763, 0.992)		0.985 (0.853, 1.137)	
Ethnicity						
Non-Hispanic	48,194 (57.6)	35,542 (42.4)	1 (reference)	0.004	1 (reference)	0.001
Hispanic	2952 (59.4)	2019 (40.6)	1.151 (1.058, 1.252)		1.182 (1.080, 1.293)	
Unknown	2265 (56.0)	1783 (44.0)	1.067 (1.002, 1.137)		1.110 (1.036, 1.189)	
Charlson-Deyo Score						
0	45,854 (57.9)	33,372 (42.1)	1 (reference)	< 0.001	1 (reference)	0.169
1	6338 (56.4)	4905 (43.6)	0.940 (0.904, 0.979)		1.009 (0.967, 1.053)	
2	993 (54.7)	824 (45.3)	0.877(0.799, 0.963)		1.036 (0.939, 1.144)	
3+	226 (48.2)	243 (51.8)	0.677 (0.564, 0.812)		0.816 (0.674, 0.989)	
Distance to Treatment Center	17.1	19.1	1.000 (0.999, 1.000)	< 0.001	1.000 (1.000, 1.000)	0.091
Type of Insurance						
Private	32,454 (61.5)	20,342 (38.5)	1 (reference)	<0.001	1 (reference)	< 0.001
Medicare/Government	16,780 (50.8)	16,264 (49.2)	0.647 (0.629, 0.665)		0.747 (0.724, 0.771)	
Medicaid	2639 (62.0)	1616 (38.0)	1.024(0.960, 1.092)		1.016 (0.949, 1.087)	
None	847 (62.3)	512 (37.7)	1.037 (0.928, 1.159)		1.058 (0.942, 1.189)	
Unknown	691 (53.1)	610 (46.9)	0.710 (0.636, 0.793)		0.782 (0.696, 0.878)	
Grade						
Low	8265 (54.4)	6939 (45.6)	1 (reference)	< 0.001	1 (reference)	0.444
Intermediate	21,488 (57.5)	15,877 (42.5)	1.136 (1.094, 1.180)		1.000 (0.961, 1.041)	
High	14,677 (60.3)	9650 (39.7)	1.277 (1.226, 1.330)		0.992 (0.950, 1.037)	
Unknown	8981 (56.6)	6878 (43.4)	1.096 (1.048, 1.146)		0.969 (0.924, 1.016)	
Tumor Size						
<10 mm	21,549 (57.2)	16,095 (42.8)	1 (reference)	0.145	1 (reference)	< 0.001
>= 10 mm	18,634 (58.0)	13,504 (42.0)	1.031 (1.000, 1.062)		0.937, 0.907, 0.967)	
Unknown	13,228 (57.6)	9745 (42.4)	1.014 (0.981, 1.048)		0.979 (0.945, 1.014)	
Margin Status						
Negative	51,484 (57.9)	37,373 (42.1)	1 (reference)	< 0.001	1 (reference)	< 0.001
Positive	1542 (49.2)	1594 (50.8)	0.702 (0.654, 0.702)		0.761 (0.705, 0.820)	
Unknown	385 (50.5)	377 (49.5)	0.741 (0.643, 0.855)		0.817 (0.703, 0.950)	
Radiation						
Yes	44,593 (66.2)	22,749 (33.8)	1 (reference)	< 0.001	1 (reference)	< 0.001
No	8707 (34.7)	16,396 (65.3)	0.271 (0.263, 0.279)		0.280 (0.272, 0.289)	
Unknown	111 (35.8)	199 (64.2)	0.285 (0.225, 0.359)		0.298 (0.236, 0.377)	

Univariable and multivariable binary logistic regression of predictors of receipt of endocrine therapy (ET) for subgroup of individuals with hormone-receptor (estrogen or progesterone receptor)-positive disease who underwent breast-conserving surgery. Unadjusted and adjusted odds ratios (OR) are reported

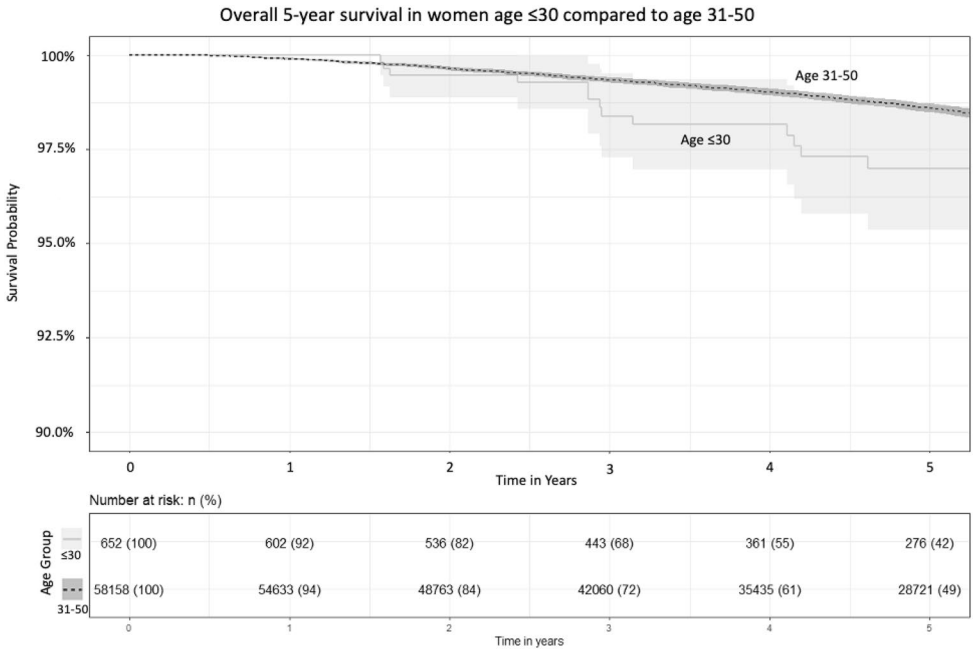

Fig. 1 Kaplan Meier curve of overall five-year survival in age ≤30 compared to age 31–50. Log-rank test $p = 0.004$

Table 5 Overall survival analysis

	Age ≤ 30			Age 30–50		
	HR	95% CI	p value	HR	95% CI	p value
Age						
	1.27	0.60–2.71	0.53	Reference		
Race						
White	Reference			Reference	–	–
Black	2.72	0.52–14.18	0.24	1.80	1.41–2.29	< 0.0001
Other	$2.27 \cdot 10^{-8}$	0.00–N/A	0.999	0.71	0.47–1.08	0.11
Grade						
High	Reference			Reference		
Intermediate	1.38	0.26–7.35	0.71	1.11	0.90–1.36	0.34
Low	$1.10 \cdot 10^{-8}$	0–N/A	0.99	0.86	0.61–1.23	0.41
Size (mm)						
≤20	Reference			Reference		
20–50	0.51	0.05–5.12	0.56	1.05	0.82–1.33	0.71
>50	1.03	0.14–7.53	0.98	1.01	0.69–1.47	0.97
Endocrine Receptor						
Positive	Reference			Reference		
Negative	1.58	0.26–9.56	0.62	1.27	0.96–1.67	0.09
Endocrine Therapy						
No	Reference			Reference		
Yes	0.34	0.04–45.60	0.35	0.86	0.69–1.07	0.17
Radiation Therapy						
No	Reference			Reference		
Yes	3.13	0.11–89.08	0.50	0.74	0.55–0.99	0.04
Surgery						
Breast Conserving	Reference			Reference		
Mastectomy	1.48	0.05–45.60	0.82	0.89	0.67–1.19	0.43

Multivariable regression for overall survival for patients ≤30 and patients aged 31–50. Hazard ratio (HR) with 95% confidence intervals (CI) are reported

Table 6 Subgroup analyses for patients undergoing breast-conserving surgery

	HR	95% CI	p value
Age			
31–50	Reference	–	–
≤30	2.03	0.50–8.21	0.32
Race			
White	Reference	–	–
Black	1.90	1.39–2.60	< 0.0001
Other	0.59	1.39–2.60	0.09
Grade			
High	Reference	–	–
Intermediate	1.10	0.83–1.46	0.50
Low	0.70	0.44–1.12	0.13
Size (mm)			
≤20	Reference	–	–
20–50	1.32	0.95–1.84	0.09
>50	1.00	0.44–2.27	1.00
ER			
Positive	Reference	–	–
Negative	1.31	0.89–1.92	0.17
ET			
No	Reference	–	–
Yes	0.72	0.55–0.96	0.02
RT			
No	Reference	–	–
Yes	0.72	0.54–0.98	0.04

Multivariable regression for overall survival for breast-conserving surgery subgroup patients younger than age 50. Hazard ratio (HR) and 95% confidence intervals (CI) are reported

Funding This study was funded by the National Cancer Institute of the National Institutes of Health under Award Number T32CA121938 and the Academic Senate of UC San Diego. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data Use The National Cancer Database (NCDB) is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The CoC's NCDB and the hospitals participating in the CoC NCDB are the source of the de-identified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Compliance with ethical standards

Conflict of interest Sasha Halasz declares that she has no conflict of interest. Thomas O'Keefe declares that he has no conflict of interest. Anne Wallace declares that she has no conflict of interest. SLB has a family member with an equity interest in Viewpoint Medical, Inc., a company that has no benefit from the research results.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors. The UCSD HRPP/IRB deferred need for approval due to use of public, de-identified data.

References

1. Narod SA, Iqbal J, Giannakeas V et al (2015) Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol 1:888–896. https://doi.org/10.1001/jamaoncol.2015.2510
2. Jones CE, Richman J, Jackson BE et al (2018) Treatment patterns for ductal carcinoma in situ with close or positive mastectomy margins. J Surg Res 231:36–42. https://doi.org/10.1016/j.jss.2018.05.007
3. Sagara Y, Freedman RA, Wong SM et al (2017) Trends in adjuvant therapies after breast-conserving surgery for hormone receptor-positive ductal carcinoma in situ: findings from the National Cancer Database, 2004–2013. Breast Cancer Res Treat 166:583–592. https://doi.org/10.1007/s10549-017-4436-9
4. Van Bockstal MR, Agahozo MC, Koppert LB, van Deurzen CHM (2020) A retrospective alternative for active surveillance trials for ductal carcinoma in situ of the breast. Int J Cancer 146:1189–1197. https://doi.org/10.1002/ijc.32362
5. Nguyen TT, Hoskin TL, Day CN et al (2017) Factors influencing use of hormone therapy for ductal carcinoma in situ: a National Cancer Database Study. Ann Surg Oncol 24:2989–2998. https://doi.org/10.1245/s10434-017-5930-3
6. Nassar H, Sharafaldeen B, Visvanathan K, Visscher D (2009) Ductal carcinoma in situ in African American versus Caucasian American women: analysis of clinicopathologic features and outcome. Cancer 115:3181–3188. https://doi.org/10.1002/cncr.24376
7. Ward EP, Unkart JT, Bryant A et al (2017) Influence of distance to hospital and insurance status on the rates of contralateral prophylactic mastectomy, a National Cancer Data Base study. Ann Surg Oncol 24:3038–3047. https://doi.org/10.1245/s10434-017-5985-1
8. Cronin PA, Olcese C, Patil S et al (2016) Impact of age on risk of recurrence of ductal carcinoma in situ: outcomes of 2996 women treated with breast-conserving surgery over 30 years. Ann Surg Oncol 23:2816–2824. https://doi.org/10.1245/s10434-016-5249-5
9. Vicini FA, Kestin LL, Goldstein NS et al (2000) Impact of young age on outcome in patients with ductal carcinoma-in-situ treated with breast-conserving therapy. J Clin Oncol Off J Am Soc Clin Oncol 18:296–306. https://doi.org/10.1200/JCO.2000.18.2.296
10. Alvarado R, Lari SA, Roses RE et al (2012) Biology, treatment, and outcome in very young and older women with DCIS. Ann Surg Oncol 19. https://doi.org/10.1245/s10434-012-2413-4
11. Xiong Q, Valero V, Kau V et al (2001) Female patients with breast carcinoma age 30 years and younger have a poor prognosis. Cancer 92:2523–2528. https://doi.org/10.1002/1097-0142(20011115)92:10<2523::AID-CNCR1603>3.0.CO;2-6
12. Francis PA (2011) Optimal adjuvant therapy for very young breast cancer patients. Breast 20:297–302. https://doi.org/10.1016/j.breast.2011.05.002
13. Park HL, Chang J, Lal G et al (2018) Trends in treatment patterns and clinical outcomes in young women diagnosed with ductal carcinoma in situ. Clin Breast Cancer 18:e179–e185. https://doi.org/10.1016/j.clbc.2017.08.001
14. Llarena NC, Estevez SL, Tucker SL, Jeruss JS (2015) Impact of fertility concerns on Tamoxifen initiation and persistence. J Natl Cancer Inst 107. https://doi.org/10.1093/jnci/djv202
15. Voci A, Bandera B, Ho E et al (2018) Variations in cancer care for adolescents and young adults (AYAs) with ductal carcinoma in situ. Breast J 24:555–560. https://doi.org/10.1111/tbj.12999

16. Boffa DJ, Rosen JE, Mallin K et al (2017) Using the national cancer database for outcomes research: a review. JAMA Oncol 3:1722–1728. https://doi.org/10.1001/jamaoncol.2016.6905
17. Parsons BM, Landercasper J, Smith AL et al (2016) 21-gene recurrence score decreases receipt of chemotherapy in ER+ early-stage breast cancer: an analysis of the NCDB 2010–2013. Breast Cancer Res Treat 159:315–326. https://doi.org/10.1007/s10549-016-3926-5
18. Allred DC, Anderson SJ, Paik S et al (2012) Adjuvant tamoxifen reduces subsequent breast cancer in women with estrogen receptor-positive ductal carcinoma in situ: a study based on NSABP protocol B-24. J Clin Oncol Off J Am Soc Clin Oncol 30:1268–1273. https://doi.org/10.1200/JCO.2010.34.0141
19. Kauffmann RM, Goldstein L, Marcinkowski E et al (2016) Predictors of Antiestrogen recommendation in women with Estrogen receptor-positive ductal carcinoma in situ. J Natl Compr Cancer Netw 14:1081–1090. https://doi.org/10.6004/jnccn.2016.0118
20. Gnerlich JL, Deshpande AD, Jeffe DB et al (2009) Elevated breast cancer mortality in young women (<40 years) compared with older women is attributed to poorer survival in early stage disease. J Am Coll Surg 208:341–347. https://doi.org/10.1016/j.jamcollsurg.2008.12.001
21. Fredholm H, Eaker S, Frisell J et al (2009) Breast cancer in young women: poor survival despite intensive treatment. PLoS One 4. https://doi.org/10.1371/journal.pone.0007695
22. Virnig BA, Torchia MT, Jarosek SL et al (2011) Use of endocrine therapy following diagnosis of ductal carcinoma in situ or early invasive breast cancer: data points # 14, Data points publication series. Agency for Healthcare Research and Quality (US), Rockville
23. DeCensi A, Puntoni M, Guerrieri-Gonzaga A et al (2019) Randomized placebo controlled trial of low-dose Tamoxifen to prevent local and contralateral recurrence in breast intraepithelial Neoplasia. J Clin Oncol 37:1629–1637. https://doi.org/10.1200/JCO.18.01779