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Original Article

A Population-Based Observational Study of First-Course Treatment and Survival for Adolescent and Young Adult Females with Breast Cancer

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Purpose: Young age at breast cancer diagnosis is associated with poor survival. However, little is known about factors associated with first-course treatment receipt or survival among adolescent and young adult (AYA) females aged 15–39 years.
Methods: Data regarding 19,906 eligible AYA breast cancers diagnosed in California during 1992–2009 were obtained from the population-based California Cancer Registry. Multivariable logistic regression was used to evaluate clinical and sociodemographic differences in treatment receipt. Multivariable Cox proportional hazards regression was used to examine differences in survival by initial treatment, and by patient and tumor characteristics.
Results: Black and Hispanic AYAs diagnosed with *in situ* or stages I–III breast cancer were more likely than White AYAs to receive breast-conserving surgery (BCS) without radiation; Asian and Hispanic AYAs were more likely than Whites to receive mastectomy. Women in lower socioeconomic status (SES) neighborhoods were more likely to omit radiation after BCS, more likely to receive mastectomy, and less likely to receive chemotherapy, compared to those in higher SES neighborhoods. Among patients with invasive disease, survival improved an average of 5% per year during 1992–2009. AYAs who received BCS with radiation experienced better survival than other surgery/radiation options. Black AYAs had poorer survival than Whites. AYAs who resided in higher SES neighborhoods had better survival.
Conclusions: Treatment receipt among AYAs with breast cancer varied by race/ethnicity and neighborhood SES. Poor survival for Black AYAs and AYAs living in low SES neighborhoods in models adjusted for treatment receipt suggests that factors other than treatment may also be important to disease outcome.

Keywords: breast cancer, treatment, survival, race/ethnicity, socioeconomic status

Breast cancer accounts for 14% of all cancer diagnoses among adolescents and young adults (AYAs) between 15 and 39 years of age and 7% of all breast cancers in the United States occur in AYA females.[1,2] AYA breast cancer has a molecular subtype distribution[3] and etiology[1] distinct from that in older women. In addition, many AYAs experience unique conditions that may affect treatment.[1,4,5] For example, concerns over a burgeoning career, young children, maintenance of fertility, or inadequate insurance coverage may result in omissions, delays, or poor adherence to treatment.[1,4] On the other hand, the possibility of recurrence during an extended survivorship period and fewer comorbid conditions among AYAs may lead them to receive more intense treatment regimens.[1,4,5] The National Cancer Institute (NCI) and the LIVESTRONG Young Adult Alliance have called for research to determine factors that may affect cancer outcomes for AYAs.[6] Understanding factors related to initial treatment and to survival among AYAs with breast cancer is important in addressing this goal.

Little is known about either the receipt of treatment or survival among AYAs diagnosed with breast cancer. Shavers et al. determined that young females who received BCS with radiation had a lower risk of breast cancer death compared to those who received BCS without radiation or mastectomy.[7] The same report also found that African American and Hispanic women less than 35 years of age diagnosed between 1990 and 1998 were less likely to receive radiation after breast-conserving surgery (BCS) relative to Whites.[7] To our knowledge, no reports have addressed chemotherapy receipt specifically among AYAs. To understand better the treatment

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received by AYAs with breast cancer and their survival after breast cancer diagnosis, we analyzed patient, clinical, and hospital data from the large and diverse population-based California Cancer Registry (CCR) from 1992 to 2009.

Methods

Cancer cases

California mandates that cancer cases be reported to the population-based CCR, which participates in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. We obtained information about all female California residents diagnosed with *in situ* or invasive breast cancer (International Classification of Disease for Oncology, 3rd Edition [ICD-O-3] site codes C50.0–50.9) from January 1, 1992, through December 31, 2009, the most recent years of diagnosis for which data on hormone receptor (HR) status are available. For each breast cancer case, we obtained cancer registry information routinely abstracted from the medical record (Table 1): age at diagnosis; American Joint Committee on Cancer (AJCC) stage at diagnosis; tumor size; tumor grade (low [1 or 2], high [3 or 4], or unknown); lymph node involvement; metastases; vital status as of December 31, 2010; and, for the deceased, the underlying cause of death. Vital status and cause of death are routinely determined by the CCR through hospital follow-up and database linkages. Race/ethnicity were collapsed into the categories Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, and other/unknown (hereafter referred to as "White," "Black," "Hispanic," "Asian," and "other/unknown").

HR categories were determined according to estrogen receptor (ER) and progesterone receptor (PR) expression. ER and PR status, extracted from patients' medical records, were recorded as positive, negative, borderline, not tested, not recorded, or unknown.[8] "HR-positive or borderline" was defined as ER- and/or PR-positive or borderline, "HR-negative" as ER- and PR-negative, and "HR-unknown" as ER and PR unknown or not determined. Our analyses are limited to 1992–2009 due to higher completeness of these data in the CCR since 1992.[9–11] We also obtained cancer registry information on first-course treatment modality (chemotherapy, radiation, and surgery). Cases were categorized as having received mastectomy with radiation, mastectomy without radiation, BCS with radiation, BCS without radiation, or no surgery.

Of the 23,656 female breast cancer cases aged 15 to 39 years diagnosed between 1992 and 2009 in California, we excluded those cases with inflammatory carcinoma ($n=630$); mammographic or xerographic diagnosis only, or with no mass or tumor found ($n=121$); autopsy or death certificate only ($n=12$); Paget's disease ($n=27$); surgery and/or radiation therapy unknown or NOS ($n=54$); with breast cancer as a non-first primary ($n=1655$); or with unknown stage ($n=1251$). The resulting study population included 19,906 cases.

Neighborhood and hospital variables

Each cancer case was assigned to a census block group based on home address at diagnosis. Neighborhood socioeconomic status (SES) was measured using a previously described index that incorporates 1990 or 2000 census data on education, occupation, unemployment, household income, and poverty.[12] This index was in turn classified into a quintile based on its distribution across all census block groups in California. As a measure of quality of care, we classified the reporting hospitals according to whether or not they were a National Cancer Institute–designated comprehensive or noncomprehensive cancer center (hereafter collectively referred to as "NCI-designated cancer hospital").

Analyses

Treatment analyses. Multivariate logistic regression was used to evaluate associations of clinical and sociodemographic characteristics with breast cancer treatment. Odds ratios (ORs) and associated 95% confidence intervals (CIs) are presented. The National Comprehensive Cancer Network (NCCN) guidelines do not recommend BCS for stage IV breast cancer or diffuse histology, so treatment analyses were restricted to *in situ* and stages I–III. Thus, we excluded 808 females with stage IV disease and 63 cases with diffuse histology for a final population of 19,035 eligible patients. ORs for the "no surgery" treatment category ($n=672$) are not presented, as this group comprised a very small portion (1.6%) of the study population.

Survival analyses. Cox proportional hazards regression models were used to estimate hazard ratios and associated 95% CIs. For deceased patients, survival time was measured in days from the date of diagnosis to the date of death from any cause for overall survival or to the date of death from breast cancer for breast cancer–specific survival. Patients who died from other causes were censored at the time of death for analyses of breast cancer–specific survival. Patients alive at the study end date (December 31, 2010) were censored at this time or at date of last follow-up (i.e., last known contact). Ninety-two percent of censored patients had a follow-up date (i.e., were verified as being alive) within 2 years of the study end date, somewhat lower than the percentage for women over 40 years of age (97%). After exclusion of 2248 patients with *in situ* (Stage 0) disease, the final population for the survival analyses included 17,658 eligible patients and 4314 deaths.

We assessed the proportional hazards assumption by statistical testing of the correlation between weighted Schoenfeld residuals and logarithmically transformed survival time. No violations of the assumption were observed. Multivariate Cox regression models included all variables significant at $p<0.05$ in unadjusted models. AJCC stage levels I–IV were included as a stratifying variable in the model to account for varying baseline hazards by stage. Analyses were carried out using SAS software v9.3 (SAS Institute Inc., Cary, NC). All p-values reported are two-sided, and those with $p<0.05$ were considered to be statistically significant.

Results

Mastectomy without radiation was the most frequent initial surgery/radiation treatment (37.4%), followed by BCS with radiation (30.6%), mastectomy with radiation (14.5%), BCS without radiation (14.1%), and no surgery (3.4%; Table 1). Most women were of White race/ethnicity (50.9%), with fewer of Hispanic (25.8%), Asian (14.1%), or Black (8.4%) race/ethnicity. AYAs were most often diagnosed with stage II disease (48.2%) and high-grade tumors (52.9%). Most AYAs (65.3%) received chemotherapy. Nearly half (47.8%) resided in the two highest neighborhood SES quintiles, and fewer than 10% received treatment at NCI-designated cancer hospitals.

Table 1. Demographic and Clinical Characteristics of Adolescent and Young Adult Females with *In Situ* and Invasive Breast Cancer by First-Course Surgery and Radiation Treatment, California, 1992–2009

	Total N = *19,906* n *(%)*	*BCS with radiation* n = *6089* n *(%)*	*BCS no radiation* n = *2809* n *(%)*	*Mastectomy with radiation* n = *2886* n *(%)*	*Mastectomy no radiation* n = *7450* n *(%)*	*No surgery* n = *672* n *(%)*
Age at diagnosis (years)						
15–24	261 (1.3)	56 (0.9)	52 (1.9)	43 (1.5)	93 (1.2)	17 (2.5)
25–29	1460 (7.3)	418 (6.9)	193 (6.9)	254 (8.8)	531 (7.1)	64 (9.5)
30–34	5216 (26.2)	1554 (25.5)	719 (25.6)	805 (27.9)	1938 (26.0)	200 (29.8)
35–39	12,969 (65.2)	4061 (66.7)	1845 (65.7)	1784 (61.8)	4888 (65.6)	391 (58.2)
Race/ethnicity						
White	10,139 (50.9)	3376 (55.4)	1392 (49.6)	1382 (47.9)	3723 (50.0)	266 (39.6)
Black	1676 (8.4)	503 (8.3)	275 (9.8)	211 (7.3)	595 (8.0)	92 (13.7)
Hispanic	5133 (25.8)	1374 (22.6)	746 (26.6)	859 (29.8)	1923 (25.8)	231 (34.4)
Asian/Pacific Islander	2801 (14.1)	809 (13.3)	351 (12.5)	419 (14.5)	1148 (15.4)	74 (11.0)
Other/unknown	157 (0.8)	27 (0.4)	45 (1.6)	15 (0.5)	61 (0.8)	9 (1.3)
Year of diagnosis						
1992–1993	2170 (10.9)	668 (11.0)	199 (7.1)	212 (7.3)	1044 (14.0)	47 (7.0)
1994–1995	2195 (11.0)	718 (11.8)	220 (7.8)	253 (8.8)	942 (12.6)	62 (9.2)
1996–1997	2148 (10.8)	715 (11.7)	289 (10.3)	285 (9.9)	806 (10.8)	53 (7.9)
1998–1999	2239 (11.2)	736 (12.1)	327 (11.6)	347 (12.0)	769 (10.3)	60 (8.9)
2000–2001	2355 (11.8)	711 (11.7)	393 (14.0)	382 (13.2)	813 (10.9)	56 (8.3)
2002–2003	2142 (10.8)	658 (10.8)	366 (13.0)	344 (11.9)	699 (9.4)	75 (11.2)
2004–2005	2216 (11.1)	744 (12.2)	299 (10.6)	350 (12.1)	736 (9.9)	87 (12.9)
2006–2007	2184 (11.0)	644 (10.6)	345 (12.3)	344 (11.9)	754 (10.1)	97 (14.4)
2008–2009	2257 (11.3)	495 (8.1)	371 (13.2)	369 (12.8)	887 (11.9)	135 (20.1)
Stage at diagnosis						
In situ	2248 (11.3)	551 (9.0)	628 (22.4)	52 (1.8)	962 (12.9)	55 (8.2)
I	5014 (25.2)	2292 (37.6)	726 (25.8)	163 (5.6)	1799 (24.1)	34 (5.1)
II	9588 (48.2)	2857 (46.9)	1243 (44.3)	1546 (53.6)	3795 (50.9)	147 (21.9)
III	2248 (11.3)	300 (4.9)	126 (4.5)	1003 (34.8)	740 (9.9)	79 (11.8)
IV	808 (4.1)	89 (1.5)	86 (3.1)	122 (4.2)	154 (2.1)	357 (53.1)
Tumor size						
< 2 cm	6980 (35.1)	2921 (48.0)	1183 (42.1)	430 (14.9)	2379 (31.9)	67 (10.0)
2–3.9 cm	7378 (37.1)	2382 (39.1)	1017 (36.2)	1012 (35.1)	2830 (38.0)	137 (20.4)
4 + cm	4025 (20.2)	547 (9.0)	303 (10.8)	1285 (44.5)	1623 (21.8)	267 (39.7)
Microinvasion	322 (1.6)	59 (1.0)	83 (3.0)	17 (0.6)	160 (2.1)	3 (0.4)
Diffuse	90 (0.5)	4 (0.1)	2 (0.1)	34 (1.2)	33 (0.4)	17 (2.5)
Unknown	1111 (5.6)	176 (2.9)	221 (7.9)	108 (3.7)	425 (5.7)	181 (26.9)
Lymph node involvement						
Negative	10,815 (54.3)	3992 (65.6)	1853 (66.0)	544 (18.8)	4229 (56.8)	197 (29.3)
Positive	8684 (43.6)	2053 (33.7)	891 (31.7)	2295 (79.5)	3141 (42.2)	304 (45.2)
Unknown	407 (2.0)	44 (0.7)	65 (2.3)	47 (1.6)	80 (1.1)	171 (25.4)
Metastasis						
Negative	17,692 (88.9)	5656 (92.9)	2301 (81.9)	2749 (95.3)	6696 (89.9)	290 (43.2)
Positive	738 (3.7)	76 (1.2)	81 (2.9)	104 (3.6)	133 (1.8)	344 (51.2)
Unknown	1476 (7.4)	357 (5.9)	427 (15.2)	33 (1.1)	621 (8.3)	38 (5.7)
Tumor grade						
Low	7090 (35.6)	2408 (39.5)	955 (34.0)	904 (31.3)	2633 (35.3)	190 (28.3)
High	10,536 (52.9)	3113 (51.1)	1390 (49.5)	1810 (62.7)	3936 (52.8)	287 (42.7)
Unknown	2280 (11.5)	568 (9.3)	464 (16.5)	172 (6.0)	881 (11.8)	195 (29.0)
Hormone receptor status						
Negative	5234 (26.3)	1711 (28.1)	684 (24.4)	853 (29.6)	1826 (24.5)	160 (23.8)
Positive or borderline	10,627 (53.4)	3426 (56.3)	1255 (44.7)	1727 (59.8)	3951 (53.0)	268 (39.9)
Unknown	4045 (20.3)	952 (15.6)	870 (31.0)	306 (10.6)	1673 (22.5)	244 (36.3)
Chemotherapy						
None	6472 (32.5)	1695 (27.8)	1500 (53.4)	193 (6.7)	2876 (38.6)	208 (31.0)
Given	12,992 (65.3)	4324 (71.0)	1213 (43.2)	2674 (92.7)	4336 (58.2)	445 (66.2)
Unknown	442 (2.2)	70 (1.1)	96 (3.4)	19 (0.7)	238 (3.2)	19 (2.8)

(*continued*)

Table 1. (Continued)

	Total N = 19,906 n (%)	BCS with radiation n = 6089 n (%)	BCS no radiation n = 2809 n (%)	Mastectomy with radiation n = 2886 n (%)	Mastectomy no radiation n = 7450 n (%)	No surgery n = 672 n (%)
Neighborhood SES quintile						
Highest	4924 (24.7)	1624 (26.7)	648 (23.1)	669 (23.2)	1866 (25.0)	117 (17.4)
Higher-middle	4603 (23.1)	1557 (25.6)	641 (22.8)	698 (24.2)	1592 (21.4)	115 (17.1)
Middle	4033 (20.3)	1237 (20.3)	573 (20.4)	578 (20.0)	1518 (20.4)	127 (18.9)
Lower-middle	3497 (17.6)	957 (15.7)	525 (18.7)	504 (17.5)	1373 (18.4)	138 (20.5)
Lowest	2849 (14.3)	714 (11.7)	422 (15.0)	437 (15.1)	1101 (14.8)	175 (26.0)
National Cancer Institute–designated hospital						
No	18,394 (92.4)	5604 (92.0)	2612 (93.0)	2655 (92.0)	6936 (93.1)	587 (87.4)
Yes	1512 (7.6)	485 (8.0)	197 (7.0)	231 (8.0)	514 (6.9)	85 (12.6)

BCS, breast-conserving surgery; SES, socioeconomic status.

Treatment receipt according to patient and tumor characteristics

Relative to diagnoses in 1992–1993, AYAs diagnosed after 2000 were more than twice as likely to receive BCS without radiation compared to BCS with radiation (Table 2). Mastectomy receipt remained below 1992–1993 levels until 2008–2009, when it was significantly higher relative to BCS with radiation. Chemotherapy receipt decreased in 2008–2009 compared to 1992–1993.

Relative to Whites, Black AYAs were 25% more likely to have BCS without radiation than BCS with radiation. Hispanic AYAs were 13% more likely than Whites to have BCS without radiation, and 11% more likely to have mastectomy than BCS with radiation. Hispanic AYAs were also 14% more likely to receive chemotherapy compared to Whites. Asian AYAs were more likely than Whites to have mastectomy.

Relative to the highest neighborhood SES quintile, AYAs in the lower-middle and lowest quintiles were 20% and 24% more likely to receive BCS without radiation than BCS with radiation, and 9% and 10% more likely to receive mastectomy respectively. AYAs in the lowest neighborhood SES quintile were also 23% less likely to receive chemotherapy. In addition, women who were HR negative were 22% less likely to receive chemotherapy than those that were HR positive or borderline. AYAs treated at NCI-designated cancer hospitals were 15% less likely to receive mastectomy and 53% more likely to receive chemotherapy.

Survival analyses

Risk of all-cause and breast cancer–specific death for AYAs with breast cancer improved by 5% per year from 1992 to 2009 (Table 3). Relative to BCS with radiation, all other forms of surgery/radiation were associated with a significantly increased risk of death. Receipt of chemotherapy was also associated with an increased risk of death. Relative to Whites, Black AYAs were 47% more likely to die from breast cancer. Having a high-grade or larger-sized tumor, lymph-node involvement, or the presence of metastases were all associated with an increased risk of death. Relative to the highest neighborhood SES quintile, the lower four neighborhood SES quintiles were associated with an increased risk of death. Patients treated at NCI-designated cancer hospitals were 20% less likely to die from breast cancer. Associations did not vary substantially when treatment was removed from the model or when *in situ* cancers were included (data not shown).

Discussion

Treatment receipt according to race/ethnicity

Our study adds to the sparse literature describing first-course treatment receipt and survival among AYAs with breast cancer. Hispanic and Black AYAs were more likely than Whites to omit radiation after BCS. Omission of radiation after BCS by Hispanics and Blacks is well documented in older women, and one study in females less than 35 years of age found lower receipt of radiation after BCS for these groups.[7,13,14] Some studies have suggested that socioeconomic factors mediate these differences in breast cancer treatment by race, but our results indicate race was an independent factor.[15] Treatment disparities in receipt of radiation after BCS are a concern, as omission of radiation after BCS decreases 10- and 15-year overall survival in pooled analyses.[16,17] Omission of radiation by Hispanics and Blacks has been attributed to differences in insurance coverage, nativity (among Hispanics), and patient–physician interaction.[18–21]

Asian and Hispanic AYAs in our study were more likely than Whites to receive mastectomy. Studies involving females of all ages have also reported a greater receipt of mastectomies by Asians and Hispanics compared to Whites.[22] For Asian women of all ages, the receipt of mastectomy varies by ethnic subgroup and nativity, and may be influenced by cross-cultural and language barriers.[23–26] Given the lack of survival difference between BCS and mastectomy in clinical studies, the higher rates of mastectomy among some groups may indicate a treatment disparity in which these women receive more invasive surgeries for disease that could be equally controlled with BCS.[27–29]

Treatment receipt according to neighborhood SES and hospital NCI designation

Our results indicate that AYAs living in lower SES versus higher SES neighborhoods were more likely to omit radiation after BCS, more likely to receive mastectomy, and less likely to receive chemotherapy. Similarly, women treated at NCI-

Table 2. Adjusted[a] Odds Ratios for First-Course Treatment Type Among Adolescent and Young adult Females 15–39 Years of Age with *In Situ* and Stages I–III Breast Cancer[b] by Select Demographic and Tumor Characteristics, California 1992–2009

	Surgery/Radiation[c] (versus BCS with radiation)		*Chemotherapy (versus none)*
	BCS without radiation	*Mastectomy[d]*	*Given*
Age at diagnosis (years)	0.99 (0.97–1.00)	0.99 (0.98–1.00)	**0.97 (0.96–0.99)**
Race/ethnicity			
White	Ref	Ref	Ref
Black	**1.25 (1.05–1.49)**	0.92 (0.81–1.05)	0.98 (0.84–1.13)
Hispanic	**1.13 (1.00–1.28)**	**1.11 (1.01–1.21)**	**1.14 (1.03–1.26)**
Asian/Pacific Islander	0.93 (0.80–1.08)	**1.30 (1.18–1.44)**	0.92 (0.82–1.03)
Other/unknown	**3.33 (2.00–5.55)**	**1.79 (1.13–2.85)**	0.96 (0.61–1.49)
Year of diagnosis			
1992–1993	Ref	Ref	Ref
1994–1995	1.08 (0.85–1.36)	**0.85 (0.74–0.97)**	1.01 (0.86–1.18)
1996–1997	**1.51 (1.20–1.88)**	**0.80 (0.70–0.92)**	1.04 (0.88–1.22)
1998–1999	**1.76 (1.41–2.20)**	**0.77 (0.67–0.88)**	1.02 (0.86–1.19)
2000–2001	**2.27 (1.83–2.82)**	**0.85 (0.74–0.98)**	1.06 (0.90–1.24)
2002–2003	**2.36 (1.90–2.95)**	**0.79 (0.68–0.91)**	1.05 (0.89–1.23)
2004–2005	**1.77 (1.41–2.22)**	**0.66 (0.58–0.77)**	0.95 (0.80–1.12)
2006–2007	**2.40 (1.91–3.00)**	**0.79 (0.69–0.92)**	0.93 (0.79–1.10)
2008–2009	**3.52 (2.80–4.43)**	**1.22 (1.05–1.42)**	**0.75 (0.64–0.88)**
AJCC stage at diagnosis			
In situ	**2.19 (1.86–2.58)**	**1.84 (1.62–2.10)**	**0.01 (0.01–0.02)**
I	Ref	Ref	Ref
II	**1.29 (1.15–1.44)**	**2.16 (2.00–2.34)**	**4.00 (3.69–4.34)**
III	1.09 (0.86–1.38)	**6.68 (5.80–7.68)**	**7.03 (6.02–8.21)**
Tumor grade			
Low	Ref	Ref	Ref
High	1.10 (0.98–1.23)	**1.10 (1.02–1.19)**	**1.58 (1.45–1.72)**
Unknown	**1.53 (1.29–1.81)**	**1.16 (1.02–1.32)**	**0.59 (0.52–0.68)**
Hormone receptor status			
Positive or borderline	Ref	Ref	Ref
Negative	0.95 (0.84–1.07)	**1.18 (1.08–1.28)**	**0.78 (0.71–0.86)**
Unknown	**2.00 (1.71–2.34)**	**1.48 (1.32–1.66)**	**0.32 (0.28–0.37)**
Neighborhood SES quintile			
Highest	Ref	Ref	Ref
Higher-middle	0.99 (0.86–1.13)	**0.88 (0.80–0.97)**	1.04 (0.93–1.16)
Middle	1.09 (0.94–1.26)	0.98 (0.89–1.09)	1.02 (0.91–1.15)
Lower-middle	**1.20 (1.03–1.40)**	1.09 (0.98–1.22)	**0.88 (0.78–0.99)**
Lowest	**1.24 (1.04–1.47)**	1.10 (0.97–1.24)	**0.77 (0.67–0.88)**
National Cancer Institute–designated hospital			
No	Ref	Ref	Ref
Yes	0.90 (0.75–1.07)	**0.85 (0.75–0.97)**	**1.53 (1.30–1.80)**

Note: $p<0.05$ indicated in bold.
[a]Adjusted for all variables in table.
[b]Models include 19,035 patients.
[c]Odds ratios for the "no surgery" treatment category are not presented as this group comprised a very small portion ($n=313$, 1.6%) of the study population.
[d]Including mastectomy with radiation and mastectomy without radiation.
AJCC, American Joint Committee on Cancer; BCS, breast-conserving surgery; Ref, reference; SES, socioeconomic status.

designated cancer hospitals were less likely to receive mastectomy and more likely to receive chemotherapy. Earlier studies have linked greater hospital volume or metropolitan location to BCS use in women of all ages.[30,31] Likewise, while studies considering treatment according to SES are scarce, studies of Medicaid-enrolled women of all ages have shown that significant portions of these women did not receive radiation after BCS or failed to complete radiation therapy.[14,32] Additionally, socioeconomic factors like rural residence, lower income, and lower educational attainment have been associated with greater mastectomy use and nonstandard or lower-dose chemotherapy regimens among women of all ages.[33–35] These results underscore the need to target low-SES groups for treatment adherence and support, as these women are also more likely to be diagnosed with triple-negative breast cancer—an aggressive subtype with poor prognosis that is negative for HR and human epidermal growth factor receptor 2 (HER2) and is not currently amenable to targeted

Table 3. Risk of Death[a] From any Cause or From Breast Cancer for Adolescent and Young Adult Females 15 to 39 Years of Age with Invasive Breast Cancer,[b] California, 1992–2009

	Deaths, all causes		*Deaths, breast-cancer specific*	
	Number of deaths	*Hazard ratio (95% CI)*	*Number of deaths*	*Hazard ratio (95% CI)*
Age at diagnosis (years)[c]	4314 (100%)	0.99 (0.98–1.00)	3764 (100%)	0.99 (0.98–1.00)
Year of diagnosis (years)[c]	4314 (100%)	**0.96 (0.95–0.96)**	3764 (100%)	**0.95 (0.94–0.95)**
Race/ethnicity				
White	2094 (48.5%)	1.00 (ref)	1830 (48.6%)	1.00 (ref)
Black	560 (13.0%)	**1.45 (1.31–1.61)**	493 (13.1%)	**1.47 (1.32–1.64)**
Hispanic	1181 (27.4%)	1.00 (0.93–1.09)	1027 (27.3%)	1.02 (0.93–1.11)
Asian/Pacific Islander	470 (10.9%)	0.96 (0.87–1.07)	407 (10.8%)	0.96 (0.86–1.07)
Other/unknown	9 (0.2%)	0.47 (0.21–1.05)	7 (0.2%)	**0.37 (0.14–0.99)**
First-course surgical/radiation treatment				
BCS with radiation	990 (22.9%)	1.00 (ref)	856 (22.7%)	1.00 (ref)
BCS without radiation	425 (9.9%)	**1.22 (1.08–1.37)**	363 (9.6%)	**1.21 (1.07–1.38)**
Mastectomy radiation	956 (22.2%)	**1.35 (1.23–1.49)**	862 (22.9%)	**1.36 (1.22–1.51)**
Mastectomy without radiation	1593 (36.9%)	**1.25 (1.15–1.36)**	1387 (36.8%)	**1.25 (1.14–1.37)**
No surgery	350 (8.1%)	**2.17 (1.82–2.60)**	296 (7.9%)	**2.04 (1.69–2.48)**
Chemotherapy				
No	665 (15.4%)	1.00 (ref)	528 (14.0%)	1.00 (ref)
Yes	3556 (82.4%)	**1.27 (1.16–1.39)**	3158 (83.9%)	**1.36 (1.22–1.50)**
Unknown	93 (2.2%)	1.02 (0.81–1.28)	78 (2.1%)	1.05 (0.82–1.35)
Tumor grade				
Low	1129 (26.2%)	1.00 (ref)	982 (26.1%)	1.00 (ref)
High	2772 (64.3%)	**1.46 (1.36–1.57)**	2446 (65.0%)	**1.47 (1.36–1.58)**
Unknown	413 (9.6%)	1.07 (0.94–1.22)	336 (8.9%)	1.00 (0.87–1.15)
Tumor size (cm)[c]	4314 (100%)	**1.02 (1.01–1.03)**	3764 (100%)	**1.02 (1.01–1.03)**
Lymph node involvement				
Negative	1112 (25.8%)	1.00 (ref)	902 (24.0%)	1.00 (ref)
Positive	2928 (67.9%)	**1.93 (1.75–2.12)**	2623 (69.7%)	**2.02 (1.83–2.24)**
Unknown	274 (6.4%)	**2.30 (1.92–2.74)**	239 (6.3%)	**2.42 (2.00–2.92)**
Metastasis				
Negative	3788 (87.8%)	1.00 (ref)	3295 (87.5%)	1.00 (ref)
Positive	517 (12.0%)	**1.91 (1.31–2.78)**	461 (12.2%)	**2.07 (1.40–3.07)**
Unknown	9 (0.2%)	2.28 (0.82–6.34)	8 (0.2%)	2.73 (0.98–7.65)
Neighborhood SES quintile				
Highest	830 (19.2%)	1.00 (ref)	731 (19.4%)	1.00 (ref)
Higher-middle	922 (21.4%)	**1.13 (1.03–1.25)**	817 (21.7%)	**1.14 (1.03–1.26)**
Middle	918 (21.3%)	**1.22 (1.10–1.35)**	795 (21.1%)	**1.19 (1.07–1.33)**
Lower-middle	860 (19.9%)	**1.36 (1.23–1.51)**	761 (20.2%)	**1.36 (1.22–1.52)**
Lowest	784 (18.2%)	**1.37 (1.23–1.53)**	660 (17.5%)	**1.29 (1.14–1.45)**
National Cancer Institute–designated hospital				
No	4025 (93.3%)	1.00 (ref)	3526 (93.7%)	1.00 (ref)
Yes	289 (6.7%)	**0.86 (0.76–0.98)**	238 (6.3%)	**0.80 (0.70–0.92)**

Note: $p < 0.05$ indicated in bold.
[a]Cox models were adjusted for all variables in the table; AJCC stage levels I–IV were included as a stratifying variable.
[b]Models include 17,658 eligible patients.
[c]Age at diagnosis, year of diagnosis, and tumor size are presented as continuous variables. Relevant units are presented in parentheses.
AJCC, American Joint Committee on Cancer; BCS, breast-conserving surgery; CI, confidence interval; ref, reference; SES, socioeconomic status.

therapy.[36,37] In this study, we were unable to account for breast cancer subtype in our models, as pre-2005 data on HER2 are not considered sufficiently robust.[3]

Changes in treatment receipt over time

Compared to BCS with radiation, we found that receipt of BCS without radiation increased steadily after 1996 and doubled by 2000. Increases in BCS without radiation have also been observed among women of all ages in recent years.[38] Nevertheless, this result is surprising, since the importance of radiation after BCS is well accepted.[16,17] Increasing receipt of BCS without radiation over time may be driven by concerns over long-term effects of chest irradiation in young women.[39,40] On the other hand, it is also likely that radiation receipt is underascertained by the registry, particularly with increasing use of neoadjuvant therapies that may result in underreport of adjuvant radiation occurring later in the treatment process.[41]

Compared to BCS with radiation, mastectomy receipt increased in the final years of the study period. In this same period, chemotherapy receipt decreased. Two recent studies also noted increasing mastectomy rates among early-stage breast cancer diagnoses;[42,43] one found this trend to be driven, in part, by women less than 50 years of age.[42] Recent decreases in chemotherapy have not been reported previously. Once additional years of data are available, future analyses will determine whether these recent changes in treatment receipt constitute the beginning of a trend.

Survival according to treatment

We found a 5% improvement in survival each year of the study period. BCS with radiation was associated with better survival than other initial treatment regimens, similar to prior results in females under 35 years of age and in females under the age of 50 with early-stage disease.[7,44] However, these findings contrast with large randomized trials that found equivalent survival between mastectomy and BCS with radiation in women of all ages with early-stage disease, and seem at odds with the lower local-recurrence rates in young women receiving mastectomy compared to BCS.[27,45–47] It is possible that females with poorer prognoses at diagnosis may be more likely to choose mastectomy, biasing our results despite adjustment for available prognostic factors.[48] The association of chemotherapy with worse outcomes may also be a result of such a bias. Some studies attempt to account for potential treatment bias with propensity analyses and instrumental variable analyses, but these methods have not been shown to reduce bias more than multivariable regression analyses.[49]

Survival according to race/ethnicity

Black AYAs in our study had poorer survival after adjustment for neighborhood SES and treatment receipt. This result echoes findings of a meta-analysis concluding the African American race to be associated with worse breast cancer–specific survival in women of all ages, independent of area measures of SES.[50] A SEER-Medicaid analysis including women of all ages, however, did not find race/ethnicity to be significantly associated with breast cancer survival after controlling for treatment receipt.[51] Compared to Whites, studies have found that Blacks diagnosed with breast cancer have a much higher proportion of triple-negative breast cancer, which may contribute to survival estimates.[3,52]

Compared to Whites, we found no differences in survival for Hispanic or Asian AYAs. A previous SEER study in females under 35 years of age diagnosed from 1990 to 1998, on the other hand, found marginally poorer survival for Hispanic women compared to White women in models adjusted for treatment and other prognostic indicators.[7] Survival of Hispanic populations (compared to Whites) likely depends on the population being studied, as reports in women of all ages are mixed and results differ by nativity.[18,53–55] In addition, foreign-born nativity is associated with poorer breast cancer survival among Asian populations, suggesting that nativity is important to consider in future AYA studies.[56]

Survival according to neighborhood SES and hospital NCI designation

AYAs with breast cancer who resided in low SES neighborhoods at the time of diagnosis had worse survival. This association was independent of patients' race/ethnicity and treatment receipt. Others have shown indicators of individual-level SES to be independent predictors of poor prognosis among women of all ages with breast cancer.[57,58] Furthermore, we have previously shown that neighborhood SES is also associated with worse survival among Hispanic and Japanese women of all ages with breast cancer, further suggesting that SES is an independent predictor of survival.[53,56] AYAs treated at NCI-designated cancer hospitals had better survival. NCI designation has been shown to associate with better postsurgical outcomes among cancer patients, but associations with long-term survival have been less clear.[59–61]

Study limitations

Under-ascertainment of radiation by the cancer registry is a potential limitation of this study based on a recent report,[41] although an earlier report concluded that SEER and Medicare data were well correlated (94% for breast cancer) for radiation receipt in older women.[62] Under-ascertainment of radiation receipt may have led to our observation that females diagnosed at AJCC stage levels II–III were more likely to omit radiation after BCS.[41] A greater frequency of under-ascertainment among women with low income and under-insurance may suggest that radiation receipt is underreported for females in our study with low neighborhood SES.[41] Others have also observed that patients of non-White race or low SES are more likely to delay radiation therapy, potentially causing underreport of this mode of treatment.[63] As with other studies using registry data, our study is also subject to the potential misclassification of race/ethnicity. However, we have previously found the level of agreement between the CCR data and self-reported race/ethnicity to be excellent for Whites and Blacks and intermediate for Hispanics and Asians.[64,65]

Conclusions

Treatment receipt among AYAs with breast cancer varied by race/ethnicity, neighborhood SES, and hospital NCI designation. We found that both Hispanic and Black AYAs were less likely to receive radiation after BCS, and that Asians and Hispanics were more likely to receive mastectomy relative to Whites. AYAs living in lower SES neighborhoods were less likely to receive radiation after BCS, more likely to receive mastectomy, and less likely to receive chemotherapy. Survival improved for AYAs over the study period, but differences were found by race/ethnicity and neighborhood SES, with poorer survival for Blacks compared to Whites and for those in lower SES neighborhoods, suggesting that issues in addition to treatment and available prognostic factors contribute to these observations.

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Disclaimer

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Author Disclosure Statement

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