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Disparities in the Use of Radiation Therapy in Patients with Local-Regionally Advanced Breast Cancer

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Abstract

Background—Radiation therapy (RT) is indicated for the treatment of local-regionally advanced breast cancer (BCa).

Hypothesis—We hypothesized that black and Hispanic patients with local-regionally advanced BCa would receive lower rates of RT than their white counterparts.

Methods—The Surveillance Epidemiology and End Results (SEER) database was used to identify white, black, Hispanic, and Asian patients with invasive BCa and ≥ 10 metastatic lymph nodes diagnosed between 1988 and 2005. Univariate and multivariate logistic regression evaluated the relationship of race/ethnicity with use of RT. Multivariate models stratified for those undergoing mastectomy or lumpectomy.

Results—Entry criteria were met by 12,653 patients. Approximately half of the patients did not receive RT. Most patients were white (72%); the remainder were Hispanic (10.4%), black (10.3%), and Asian (7.3%). On univariate analysis, Hispanics (OR 0.89, 95% CI 0.79–1.00) and blacks (OR 0.79, CI 0.70–0.89) were less likely to receive RT than whites. On multivariate analysis, blacks (OR 0.76, CI 0.67–0.86) and Hispanics (OR 0.80, CI 0.70–0.90) were less likely than whites to receive RT. Disparities persisted for blacks (OR 0.74, CI 0.64–0.85) and Hispanics (OR 0.77, CI 0.67–0.89) who received mastectomy, but not for those who received lumpectomy.

Conclusions—Many patients with local-regionally advanced BCa do not receive RT. Blacks and Hispanics were less likely than whites to receive RT. This disparity was noted predominately in patients who received mastectomy. Future efforts at improving rates of RT are warranted. Efforts at eliminating racial/ethnic disparities should focus on black and Hispanic candidates for post-mastectomy RT.

Keywords

breast cancer; advanced; radiation; disparities; race; ethnicity

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Introduction

Radiation therapy (RT) is indicated for the treatment of local-regionally advanced breast cancer (BCa), regardless of the surgical therapy provided. Current recommendations warrant the use of adjuvant RT for all cases of breast conservation 1, 2. The use of postmastectomy radiation (PMRT) is more controversial. A meta-analysis by The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) demonstrated improved local control with PMRT, but no significant difference in 10-year overall survival 3. Later studies utilizing improved radiation techniques demonstrated that the cardiac-related mortality of PMRT was offset by decreased breast cancer mortality 4. A randomized trial by the Danish Breast Cancer Cooperative Group 5 demonstrated an overall survival advantage with PMRT + adjuvant chemotherapy vs. adjuvant chemotherapy alone (RR 0.71, 95% CI: 0.62–0.82, p<0.001). Similarly, the British Columbia Cancer Agency 6 showed a significant breast cancer specific survival advantage (RR 0.71, p=0.05) and a trend towards improved overall survival (p=0.07) for patients receiving PMRT + chemotherapy vs. chemotherapy alone. This advantage was noted in patients with ≥ 4 positive lymph nodes, but not in those with 1–3 positive lymph nodes (p=0.06)6. Ten years after their review in 1995, the EBCTCG reported results in accordance with the Danish and Canadian groups. Node-positive patients undergoing PMRT had improved breast cancer-specific and overall survival at 15 years 2. On these grounds, PMRT is warranted for patients at high risk for local recurrence, including those with tumors involving the chest wall or ≥ 4 metastatic lymph nodes. Adherence to RT guidelines improves overall and disease-specific survival, and has been used as a surrogate marker of quality BCa care 7.

Racial/ethnic disparities in treatment, including RT, are well-documented for early-stage breast cancer 8–14, but are less clear for local-regionally advanced disease. Based upon racial/ethnic disparities noted in the treatment of other malignancies [14–16], we hypothesized that black and Hispanic patients with American Joint Committee on Cancer (AJCC) stage IIIC (≥ 10 metastatic lymph nodes) BCa would receive lower rates of RT than their white counterparts.

Methods

The Surveillance Epidemiology and End Results (SEER) database of the National Cancer Institute was used to identify all white, black, Hispanic, and Asian patients with AJCC stage IIIC (≥10 metastatic lymph nodes) invasive ductal carcinoma (IDC), lobular carcinoma (ILC), or mixed ductal/lobular carcinoma (MDLC) of the breast diagnosed between 1988 and 2005. SEER collects cancer incidence and survival data from 17 population-based cancer registries representing 26% of the U.S. population. Current SEER registries consist of: the states of Connecticut, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah; the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, Seattle-Puget Sound, and San Jose-Monterey; and the Alaska Native Tumor Registry, rural Georgia, Greater California, and Los Angeles County. SEER registries routinely collect data on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, and first course of treatment.

Patients were divided according to whether or not RT was given. Patients with distant metastases were excluded. Further exclusions were made if the use of RT was unknown, or if race/ethnicity was other than white, black, Hispanic, Asian. We compared differences among racial/ethnic groups using analysis of variance (ANOVA) for continuous variables and Chi-square testing for categorical variables and proportions.

Univariate logistic regression was used to evaluate the relationship of race/ethnicity with the use of RT using white patients as the referent population. Odds ratios (OR) are reported with associated 95% confidence intervals (CI). Differences were considered significant at $p \leq 0.05$.

Three multivariate logistic regression models were constructed. The first model included all patients. Using RT as the outcome variable, we controlled for race, age, sex, tumor size, estrogen receptor (ER) and progesterone receptor (PR) status, and type of surgery. White patients were the referent population. Because significant interactions were noted between the type of surgery and RT use, two additional multivariate models were constructed that stratified patients based on whether they received lumpectomy or mastectomy. Analyses were conducted using STATA version 10 (StataCorp, College Station, Texas).

Results

Patient Characteristics

Of 15,895 patients with local-regionally advanced BCa identified in the SEER registry, 12,653 met entry criteria. Patient characteristics, tumor factors, and RT status are included in Table 1. Briefly, the mean age of study patients was 57 years (range, 21–97 years). Less than 1% (N=115) of patients were men. Tumor histology was IDC, ILC, or MDLC for 75.3%, 14.5%, and 10.2% of patients, respectively. Approximately half of the patients received RT and half did not. The majority of patients were white (N=9,102; 72%). The remainder were Hispanic (N=1,318; 10.4%), black (N=1,305; 10.3%), and Asian (N=928; 7.3%). Patient characteristics, tumor factors, and RT status according to patient race/ethnicity are included in Table 1.

Univariate Analysis

Only Asians demonstrated an odds of receiving RT that was not significantly different (OR 1.09, 95% CI 0.95–1.24; p=0.23) from whites (Table 2). Both Hispanics (OR 0.89, 95% CI 0.79–1.00; p=0.05) and blacks (OR 0.79, CI 0.70–0.89; p<0.001) were less likely to receive radiation than whites.

Multivariate Analysis

The first multivariate logistic regression model encompassed all patients and is summarized in Table 3A. Briefly, use of RT was more likely in ILC (OR 1.28, CI 1.15–1.43, p<0.001), and among patients receiving lumpectomy as surgical treatment (OR 1.98, CI 1.79–2.18; p<0.001). Conversely, use of RT was less likely with advancing age (OR 0.98, CI 0.98-0.98; p<0.001), ER negative tumors (OR 0.83, CI 0.73–0.94; p=0.003), PR equivocal tumors (OR 0.57, CI 0.33–0.96; p=0.04), and in black (OR 0.76, CI 0.67–0.86; p<0.001) and Hispanic (OR 0.80, CI 0.70–0.90; p<0.001) patients.

The second multivariate logistic regression model stratified for patients who underwent mastectomy. Results are summarized in Table 3B. Once again, use of RT was more likely in patients with ILC (OR 1.28, CI 1.13–1.44; p<0.001). Additionally, patients with increasing tumor size displayed a borderline statistically significant likelihood of receiving RT (OR 1.00, CI 1.00-1.00, P=0.03). A decreased likelihood of receiving RT was seen with advancing age (OR 0.98, CI 0.98-0.98, p<0.001), ER negative tumors (OR 0.74, CI 0.65–0.86, p<0.001), and in black (OR 0.74, CI 0.64–0.85; p<0.001) and Hispanic (OR 0.77, CI 0.67–0.89; p<0.001) patients.

The third multivariate logistic regression model stratified for patients who underwent lumpectomy. Results are summarized in Table 3C. Use of RT was more likely in ER negative tumors (OR 1.32, CI 1.00–1.75; p=0.05). Increasing tumor size was associated with a decreased likelihood of receiving RT (OR 0.99, CI 0.99–1.00; p<0.001). No differences in the receipt of RT were noted based on race/ethnicity in this patient sub-population.

Discussion

Healthcare disparities exist. In particular, racial/ethnic minority populations have worse access to care and poorer quality of care for a wide range of conditions than their white counterparts [14, 17, 18]. In 2005, the Agency for Healthcare Research and Quality issued the National Healthcare Disparities Report which identified several barriers to quality healthcare encountered by minority populations [19]. Blacks, Hispanics, and Asians had worse access to care for 43% to 88% of indicators and received poorer quality of care for 21% to 53% of indicators relative to whites [19]. The reasons for these disparities are often unknown, but are likely multifactorial [17, 20, 21]. Once identified, these disparities represent interventional opportunities to improve patient treatment and subsequent outcomes.

RT represents a key component in the management of patients with local-regionally advanced BCa. RT is indicated for all patients undergoing breast conservation [1]. Post-mastectomy RT is the current standard for breast cancers with ≥ 4 axillary lymph node metastases [22]. These guidelines were established after compelling randomized clinical trial data indicated improved rates of local-regional control and survival[2, 5, 6, 23]. As such, adherence to RT guidelines in advanced BCa patients is a surrogate marker of quality cancer care. We identified racial/ethnic disparities in the use of RT in advanced BCa patients with ≥10 lymph node metastases.

The racial/ethnic disparities identified on univariate logistic regression persisted on multivariate analysis controlling for potential confounders. Both black and Hispanic patients were less likely to receive RT compared to their white counterparts in the all-inclusive model. We reasoned that patients would be more likely to receive RT if they received lumpectomy as surgical treatment, as RT is a recognized component of breast conservation therapy. Post-mastectomy RT guidelines have been adopted more recently [22]. Significant statistical interactions existed among tumor size, type of surgery received, and use of RT. We therefore constructed two additional logistic regression models stratifying patients according to the type of surgical therapy received (mastectomy vs. lumpectomy). The stratified analysis allowed us to conclude that the most significant racial/ethnic disparities in use of RT occurred among black and Hispanic patients who had undergone mastectomy.

Despite the fact that post-mastectomy RT has been advocated for several decades, it can be argued that a significant proportion of patients included in the present study were diagnosed and treated prior to the advent of current guidelines. To ensure that the year of breast cancer diagnosis was not confounding the rates of RT usage, we performed additional logistic regression analyses inclusive of the years 1998 to 2005 with similar results regarding racial/ethnic disparities (data not shown).

Regardless of the racial/ethnic disparities noted, rates of RT were low for all populations (range, 46% to 54%). The reasons for this are unknown. It is possible that clinicians take a nihilistic approach to AJCC stage IIIC patients, assume that they have occult systemic disease, and eliminate consideration of RT altogether. Access to care is less likely to be the underlying cause, as reported rates of RT are higher for patients with early stage tumors receiving breast conservation. There are situations where the use of RT may be inappropriate, such as in cases of prior radiation exposure, collagen vascular disease, inability to lay flat, or unrelated patient co-morbidities. The SEER database does not allow us to capture these data fields, although it is unlikely that these factors alone could explain the overall low rates of RT seen in our study.

There are several other reasons why patients may not receive RT when indicated, which can be broadly characterized as physician factors, patient factors, and structural factors. Physicians may make different recommendations for treatment based on what they perceive the patient's attitude towards treatment to be. In addition, there is some evidence 24 that physicians believe blacks are less likely to comply with treatment, which may influence their recommendations.

In a study assessing the effect of race and sex on physicians' recommendations for cardiac catheterization by Schulman et al, women and black patients were significantly less likely to be referred for cardiac catheterization than their male and white counterparts respectively 25. Structural barriers such as lack of health insurance, income, transportation issues, language barriers, and family support are just some factors that may affect RT use [14]. Some researchers suggest that socioeconomic status (SES) is more predictive of treatment quality received than race or ethnicity [19, 26, 27]. Poverty, low education level, and lack of health insurance are known to contribute to poorer quality care. As highlighted in the AHRQ National Healthcare Disparities Report, blacks with higher incomes and at least some college education, and Hispanics of all income and education levels, are less likely to have health insurance than their white counterparts 19. Unfortunately, our current analysis did not afford us the opportunity to assess individual patients' SES with certainty. Patients also may refuse recommended treatment as a result of distrust of the medical system or the physician. Although some have shown that minority populations are more likely to refuse invasive procedures [21], studies by Ayanian et al [28] and Canto et al [29] have demonstrated disparities in treatment even after adjusting for patient preferences or eliminating those who refused treatment, respectively. We have attempted to control for potential confounding factors that could influence our ability to detect differences between racial or ethnic groups, but this is admittedly hard to do.

We chose to examine only BCa patients with ≥ 10 lymph node metastases, rather than specifically those with ≥ 4 lymph node metastases to obtain a more uniform, homogeneous population. The prognosis for patients with AJCC stage IIIC BCa has been almost uniformly reported as poor. The racial/ethnic disparities noted with respect to receipt of RT raise the question of whether such treatment differences result in survival disparities. We intentionally chose not to examine potential differences in overall survival in the present study, so that we could better focus on treatment differences as a surrogate marker of disparities in quality of care.

We utilized use of RT as a single surrogate marker of quality cancer care, but there are certainly others [30]. Rates of breast reconstruction, and adherence to hormonal or systemic therapy guidelines are all potential surrogate markers of quality cancer care[11, 30], but these data fields are either limited or unavailable in the SEER database. While failure to adhere to RT use guidelines is not an absolute indicator of inferior care of an individual patient, such patterns across a large population of patients provides vital information that improvement is needed.

Conclusions

In this select population of patients with AJCC stage IIIC BCa, a significant proportion of patients did not receive indicated RT. Blacks and Hispanics were less likely than whites to receive RT. This disparity, however, was demonstrated primarily in patients who received mastectomy. Future efforts at improving rates of RT are warranted. Specifically, efforts at eliminating racial/ethnic disparities should focus on improving rates of post-mastectomy RT in black and Hispanic populations.

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Table 1

Patient characteristics, tumor factors, and treatment received for the according to race/ethnicity.

Variable		White	Black	Hispanic	Asian	Totals	P value
Mean Age (years)		58.5	54.5	51.8	54	57	<0.001*
Sex							<0.001**
	Female (%)	9,022 (99.1)	1,279 (98)	1,312 (99.5)	925 (99.7)	12,538 (99.1)	
	Male (%)	80 (0.9)	26 (2)	6 (0.5)	3 (0.3)	115 (0.9)	
Mean tumor size (mm)		39.1	42.5	39.7	42.3	39.7	<0.001*
Histology							<0.001**
	Ductal (%)	6,587 (72.4)	1,098 (84.1)	1,059 (80.4)	779 (83.9)	9,523 (75.3)	
	Lobular (%)	1,536 (16.9)	106 (8.1)	131 (9.9)	60 (6.5)	1,833 (14.5)	
	Mixed (%)	979 (10.8)	101 (7.8)	128 (9.7)	89 (9.6)	1,297 (10.2)	
ER							<0.001**
	Positive (%)	4,734 (52)	552 (42.3)	637 (48.3)	462 (49.8)	6,385 (50.5)	
	Negative (%)	1,764 (19.4)	350 (26.8)	292 (22.2)	252 (27.2)	2,658 (21)	
	Equivocal (%)	60 (0.6)	10 (0.8)	5 (0.4)	8 (0.8)	83 (0.6)	
	Unknown (%)	2,544 (28)	393 (30.1)	384 (29.1)	206 (22.2)	3,527 (27.9)	
PR							<0.001**
	Positive (%)	3,851 (42.3)	426 (32.6)	532 (40.4)	408 (44)	5,217 (41.2)	
	Negative (%)	2,524 (27.7)	439 (33.7)	375 (28.4)	304 (32.7)	3,642 (28.8)	
	Equivocal (%)	74 (0.8)	14 (1.1)	7 (0.5)	3 (0.3)	98 (0.8)	
	Unknown (%)	2,653 (29.2)	426 (32.6)	404 (30.7)	213 (23)	3,696 (29.2)	
Surgery							0.04**
	Mastectomy (%)	7,413 (81.4)	1,048 (80.3)	1,039 (78.8)	775 (83.5)	10,275 (81.2)	
	Lumpectomy (%)	1,666 (18.3)	251 (19.2)	276 (21)	148 (16)	2,341 (18.5)	

Variable		White	Black	Hispanic	Asian	Totals	P value
	Unknown (%)	23 (0.3)	6 (0.5)	3 (0.2)	5 (0.5)	37 (0.3)	
Radiation							0.001**
	Yes (%)	4,695 (51.6)	597 (45.8)	641 (48.6)	498 (53.7)	6,431 (50.8)	
	No (%)	4,407 (48.4)	708 (54.2)	677 (51.4)	430 (46.3)	6,222 (49.2)	
Total		9102 (72.0)	1305 (10.3)	1318 (10.4)	928 (7.3)		

* ANOVA

** Chi-square

Table 2

Univariate regression models of radiation use according to race/ethnicity.

Race/ethnicity	OR	95% CI	P value
White	***	***	***
Black	0.79	0.70–0.89	<0.001
Hispanic	0.89	0.79–1.00	0.05
Asian	1.09	0.95–1.24	0.23

Table 3

Multivariate logistic regression model for A) the study population as a whole; B) patients receiving mastectomy; and C) patients receiving lumpectomy.

A. Whole Study Population (N=12,653)				
Variable		**OR**	**CI**	**P value**
Age		0.98	0.98-0.98	<0.001
Sex	Female	***	***	***
	Male	1.20	0.81–1.77	0.37
Tumor size		1.00	1.00-1.00	0.17
Histology	Ductal	***	***	***
	Lobular	1.28	1.15–1.43	<0.001
	Mixed	1.07	0.94–1.21	0.30
ER	Positive	***	***	***
	Negative	0.83	0.73–0.94	0.003
	Equivocal	0.63	0.39–1.01	0.06
	Unknown	1.07	0.79–1.45	0.66
PR	Positive	***	***	***
	Negative	1.09	0.70–1.71	0.70
	Equivocal	0.57	0.33–0.96	0.04
	Unknown	0.99	0.64–1.54	0.97
Surgery	Mastectomy	***	***	***
	Lumpectomy	1.98	1.79–2.18	<0.001
	Unknown	0.56	0.27–1.16	0.12
Race/ethnicity	White	***	***	***
	Black	0.76	0.67–0.86	<0.001
	Hispanic	0.80	0.70–0.90	<0.001
	Asian	1.02	0.89–1.18	0.76
B. Patients Receiving Mastectomy (N=10,275)				
Variable		**OR**	**CI**	**P value**
Age		0.98	0.98-0.98	<0.001
Sex	Female	***	***	***
	Male	1.26	0.85–1.88	0.26
Tumor size		1.00	1.00-1.00	0.03
Histology	Ductal	***	***	***
	Lobular	1.28	1.13–1.44	<0.001

A. Whole Study Population (N=12,653)				
Variable		**OR**	**CI**	**P value**
	Mixed	1.11	0.97–1.27	0.15
ER	Positive	***	***	***
	Negative	0.74	0.65–0.86	<0.001
	Equivocal	0.64	0.37–1.09	0.10
	Unknown	0.94	0.67–1.32	0.72
PR	Positive	***	***	***
	Negative	1.07	0.64–1.79	0.80
	Equivocal	0.55	0.30–1.02	0.06
	Unknown	0.89	0.54–1.49	0.67
Race/ethnicity	White	***	***	***
	Black	0.74	0.64–0.85	<0.001
	Hispanic	0.77	0.67–0.89	<0.001
	Asian	1.00	0.86–1.18	0.96
C. Patients Receiving Lumpectomy (N=2,341)				
Variable		**OR**	**CI**	**P value**
Age		1.00	1.00–1.01	0.27
Sex	Female	***	***	***
	Male	0.46	0.06–3.32	0.45
Tumor size		0.99	0.99–1.00	<0.001
Histology	Ductal	***	***	***
	Lobular	1.32	0.97–1.81	0.08
	Mixed	0.88	0.66–1.18	0.40
ER	Positive	***	***	***
	Negative	1.32	1.00–1.75	0.05
	Equivocal	0.76	0.26–2.23	0.62
	Unknown	1.94	0.99–3.81	0.06
PR	Positive	***	***	***
	Negative	0.97	0.38–2.48	0.95
	Equivocal	0.52	0.17–1.61	0.26
	Unknown	1.30	0.51–3.32	0.58
Race/ethnicity	White	***	***	***
	Black	0.87	0.65–1.15	0.33
	Hispanic	0.93	0.71–1.23	0.62
	Asian	1.12	0.78–1.61	0.55