Breast Cancer Res Treat (2007) 102:347–356
DOI 10.1007/s10549-006-9337-2

EPIDEMIOLOGY

Are there racial differences in breast cancer treatments and clinical outcomes for women treated at M.D. Anderson Cancer Center?

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Received: 7 July 2006 / Accepted: 7 July 2006 / Published online: 21 September 2006

Abstract
Purpose To determine the influence of race on breast cancer treatment and on recurrence and breast cancer specific death.
Patients and Methods The study population consisted of 6,054 African-American or white women who were diagnosed with breast cancer and received at least one of the treatments including mastectomy or breast conservative surgery, radiation, adjuvant chemotherapy, neo-adjuvant chemotherapy, and adjuvant endocrine therapy at M.D. Anderson Cancer Center between June 1997 and February 2005. The clinical outcomes were disease-free survival and breast-cancer-specific survival. Logistic regression analysis was performed to investigate if race was associated with the selection of each primary treatment while adjusting for tumor characteristics at diagnosis. Cox proportional hazards model was used to determine the effect of race on recurrence-free survival and breast-cancer-specific survival controlling for tumor characteristics, presence of co-morbidity conditions and use of these treatments.
Results The use of any primary treatment for breast cancer was not significantly different by race after adjusting for tumor characteristics and co-morbidity conditions. Although tumor characteristics at diagnosis explained the major differences in clinical outcomes, race remained an independent prognostic factor for breast-cancer-specific survival ($P = 0.002$), and a marginally significant factor for disease-free survival ($P = 0.063$) in multivariate analyses.
Conclusion Equal treatment may not lead to equal clinical outcomes given similar tumor characteristics at diagnosis. To reduce racial differences in breast cancer recurrence and survival, it is important to have a better understanding of differences in tumor biology by race and to promote the use of early detection programs among African-American women.

Keywords Breast cancer · Racial differences · Recurrence · Survival · Treatment

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Introduction

As the most frequently diagnosed cancer and the second leading cause of cancer death among North American women, breast cancer remains a major public health concern. Research literature has shown a disturbing trend of higher breast cancer recurrence rate and greater mortality among African-American women compared with white women. Important risk factors contributing to this racial disparity include, but not restricted to, differences in tumor characteristics at diagnosis, and treatments received afterward.

Shavers and Brown [1] reviewed the literature on racial disparities in cancer treatments and the clinical

outcomes. It has been observed there is a more advanced stage of disease at diagnosis among minorities compared to whites [2–5]. Their conclusions about disparities in treatments and clinical outcomes were mixed: some studies reported statistically significant differences in cancer treatment and survival by race [6–12], while others reported no racial disparities in treatment or in survival [13–17]. Differing conclusions may result from different data sources, heterogeneities in the study populations, and/or different methods of analysis. Most of the studies were limited to data observed before 2000, and some lacked complete tumor biological information at diagnosis.

In this study, we used an up-to-date breast cancer database from one of the largest cancer institutions in the United States. This database includes detailed information on patients' tumor biology and characteristics at diagnosis, their co-morbidity conditions, their treatments related to breast cancer, and times-to-recurrence and death. Our purpose is to describe the influence of race on breast cancer treatment and clinical outcomes, while adjusting for tumor characteristics and co-morbidity conditions at diagnosis.

Patients and methods

Data source

A comprehensive database at the Department of Breast Medical Oncology contains detailed information on patients who have received their primary treatments at M.D. Anderson Cancer Center (MDACC). For this study, we focused on a cohort of women who had been diagnosed with primary breast cancer either at MDACC or elsewhere, and had received their primary treatments at MDACC between June 1997 and February 2005. Following approval by the institutional review board of MDACC, we retrieved the records of 6,422 female patients with breast cancer who had indicated that their race was white or African-American (AA) from the database retrospectively. The identified patients had received at least one of their primary breast cancer therapies at MDACC. We excluded patients who had been treated for recurrent disease only. The total number of patients included in the final analysis was 6,054. The median follow-up time was 40 months (range 0.6–104 months).

Definitions of outcomes

The primary clinical outcomes of interest were disease-free survival (DFS), the time from diagnosis of breast cancer to disease recurrence or death, whichever occurred first, and breast-cancer-specific survival (BCSS), the time from diagnosis to death due to breast cancer. Patients received one or a combination of following treatments consisted of surgery, including mastectomy or breast-conserving surgery (BCS), radiation, adjuvant chemotherapy, adjuvant endocrine (referring to anti-estrogen or aromatase inhibitor) therapy, and neo-adjuvant chemotherapy.

Demographics, co-morbidity and tumor characteristics at diagnosis

Demographic data included age at diagnosis, and race (AA, white). The information for race was self-reported by the patient. We retrieved data indicating the presence of several common co-morbid conditions, including hypertension, diabetes and heart disease. Tumor characteristics data included the American Joint Committee on cancer tumor stage by TNM (tumor size, node, metastasis) system, nodal status, estrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status, nuclear grade, lymphatic invasion, vascular invasion, and skin involvement. Tumor staging for patients in receipt of neo-adjuvant therapy was based on clinical stage, where the tumor size was measured before surgery. Otherwise, tumor staging was based on pathological staging, where tumor size was measured at surgery.

Statistical models

To assess the relationship between a patient's race, her tumor characteristics and the treatment she received, we used a chi-square test or Fisher's exact test to compare the distributions of tumor characteristics at diagnosis and the treatment by race. We used univariate and multivariate logistic regression models and the estimated odds ratios (OR) to investigate if race was a significant factor in the selection of each primary treatment option while adjusting for covariates. The covariates included in the multivariable logistic analyses included age at diagnosis, tumor characteristics, and co-morbid conditions (diabetes, hypertension and heart disease). We used the Cox proportional hazards model to determine the effect of race on DFS and BCSS, with or without adjusting for the above potential risk factors and major treatments that patients received. We calculated the relative risk (RR) of DFS or BCSS and their 95% confidence intervals (CI) between AA and white patients. All P values are two-sided. We performed the statistical analyses using SAS 9.0.

Results

Demographics and tumor characteristics at diagnosis

Table 1 lists age and tumor characteristics by race. The racial composition of the study cohort was 88% white, and 12% African-American. The mean age at diagnosis for AA women was 52, which was 3 years younger than that of white women at diagnosis ($P < 0.001$). Among patients received neo-adjuvant therapies, AA women tended to have larger tumors than white women, but the difference was not statistically significant. Excluding patients who received neo-adjuvant therapies, the pathologic tumor sizes for whites were significantly smaller than those for AAs (1.71 vs. 2.18 cm; $P < 0.001$). Among invasive cancers, the proportion of stage III/IV disease was larger for AA women than for white women (23% vs. 14%; $P < 0.001$), who had a higher proportion of stage I breast cancer. There was also a statistically significant difference in node-positive breast cancer between AAs and whites.

Breast cancers in AA women were less likely to have ER positive tumors than white women (53% vs. 65%; $P < 0.001$). Similar trend was observed for PR positive tumors by race (45% vs. 54%; $P < 0.001$). The data for HER2 status (measured by fluorescence in situ hybridization, FISH) were available for about 35% of the patients across the race groups. There was no statistically significant difference in the percentages of HER2 gene amplification by race. AA women had a significantly higher proportion of poorly differentiated tumors than white women (63% vs. 47%; $P < 0.001$). There were no statistically significant differences by race for lymphatic invasion, vascular invasion and skin involvement. AA women were more likely than white women to have co-morbid conditions such as diabetes and hypertension.

Treatment patterns

As expected, there were racial differences in the receipt of treatment in the overall comparisons, shown in Table 2, because the comparisons were not adjusted by tumor characteristics at diagnosis, which were different by race. Although the difference in the rate of surgery between AA and white women was not large (97% vs. 99%), it was statistically significant ($P < 0.001$). A further subset analysis showed that there were no statistically significant differences in the proportion of patients undergoing surgery within the subgroups of patients with in situ and stage III/IV tumors. Among patients with stage I/II tumors, slightly more AA women had not undergone surgery (1.9%) compared to white women (0.2%) ($P < 0.001$). Examining the 16 patients with stage I/II tumors who did not receive surgery, we found that a higher percentage of AA than white patients had one (or more than one) of the co-morbid conditions (5/9 vs. 1/7), which prevented the surgery.

Among patients who had undergone surgery, AA women were more likely than white women to have had a mastectomy plus radiation rather than a mastectomy alone (22% vs. 17%; $P = 0.002$). It was not unexpected, because more AA women than white women had tumors of advanced stages at diagnosis. Among patients with stage III/IV tumors, AA women were more likely to have had BCS with radiation than mastectomy (24% vs. 13%; $P = 0.007$).

There were no statistically significant differences in the use of adjuvant chemotherapy by race, either in the overall analysis or the analysis by stage. Among patients treated with adjuvant chemotherapy, more than 40% had received anthracycline-based therapies only, about 44% received both anthracycline- and taxane-based chemotherapy, 10% received taxane-based agents only, and the other 10% received other regimens. No difference was observed in the choice of chemotherapy regimens by race.

Among patients with ER- or PR-positive tumors, AA women were somewhat less likely than white women to have received adjuvant endocrine treatments (71% vs. 78%, $P = 0.001$), especially for patients with stage III/IV tumors (59% vs. 70%, $P = 0.039$). Among patients with both ER- and PR-negative tumors, no statistically significant difference was observed in the receipt of endocrine therapy by race. The use of initial endocrine therapy is also listed by menopausal status, the type of agent and race. Tamoxifen and aromatase inhibitors (AI) were standard agents for endocrine therapies. No statistically significant difference was observed in their use by race. AA women were more likely than white women to have received neo-adjuvant chemotherapy (30% vs. 23%; $P < 0.001$). The differences were not statistically significant by race conditional on disease stage at diagnosis.

Treatment selection is a complicated decision, and depends on tumor characteristics at diagnosis, and the existence of co-morbid conditions. The multivariate analyses (in Table 3) showed that the association between race and any of the individual treatment option was not statistically significant. Among surgery patients, disease stage, nodal status, and tumor size were significantly associated with the choice of mastectomy versus BCS with or without radiation. Although AA patients tended to have BCS (versus mastectomy)

Table 1 Demographic and tumor characteristics by race

Variable	White (n = 5,314)		AA (n = 740)		Total (n = 6,054)		P
	No.	%	No.	%	No.	%	
Age at diagnosis (yrs)							
# of observed	5,314		740		6,054		
Mean ± SD	54.6 ± 12.2		51.8 ± 12.2		54.2 ± 12.2		<0.001
Clinical tumor size (cm)—among patients with neo-adjuvant therapies							
# of observed	1,206		217		1,423		
Mean ± SD	4.29 ± 2.63		4.66 ± 2.91		4.35 ± 2.67		0.085
Pathologic tumor size (cm)—among patients without neo-adjuvant therapies							
# of observed	3,703		462		4,165		
Mean ± SD	1.71 ± 1.42		2.18 ± 2.01		1.77 ± 1.51		<0.001
Tumor stage							
In situ	687	12.9	96	13.0	783	12.9	
Stage I	1,884	35.5	197	26.6	2,081	34.4	
Stage II	1,989	37.4	270	36.5	2,259	37.3	
Stage III/IV	736	13.9	173	23.4	909	15.0	
Unknown	18	0.3	4	0.5	22	0.4	<0.001
Nodal status							
Negative	3,446	64.8	450	60.8	3,896	64.3	
Positive	1,860	35.0	288	38.9	2,148	35.5	
Unknown	8	0.2	2	0.3	10	0.2	0.035
ER status							
Positive	3,454	65.0	391	52.8	3,845	63.5	
Negative	1,233	23.2	255	34.5	1,488	24.6	
Unknown	627	11.8	94	12.7	721	11.9	<0.001
PR status							
Positive	2,884	54.3	329	44.5	3,213	53.1	
Negative	1,774	33.4	312	42.1	2,086	34.4	
Unknown	656	12.3	99	13.4	755	12.5	<0.001
ER/PR status							
ER- or PR-positive	3,690	69.4	432	58.4	4,122	68.1	
ER- and PR-negative	998	18.8	214	28.9	1,212	20.0	
ER- or PR-unknown	626	11.8	94	12.7	720	11.9	<0.001
HER2 status (FISH)							
Negative	1,409	26.5	198	26.8	1,607	26.5	
Positive	411	7.7	60	8.1	471	7.8	
Unknown	3,494	65.8	482	65.1	3,976	65.7	0.809
Nuclear grade							
Well/moderately differentiated	2,690	50.6	253	34.2	2,943	48.6	
Poorly differentiated	2,469	46.5	466	63.0	2,935	48.5	
Unknown	155	2.9	21	2.8	176	2.9	<0.001
Lymphatic invasion							
No	4,286	80.6	569	76.9	4,855	80.2	
Yes	959	18.1	140	18.9	1,099	18.2	
Unknown	69	1.3	31	4.2	100	1.6	0.346
Vascular invasion							
No	4,472	84.2	600	81.1	5,072	83.8	
Yes	768	14.4	109	14.7	877	14.5	
Unknown	74	1.4	31	4.2	105	1.7	0.613
Skin involvement							
No	5,028	94.6	676	91.4	5,704	94.2	
Yes	221	4.2	34	4.6	255	4.2	
Unknown	65	1.2	30	4.0	95	1.6	0.475
Diabetes							
No	5,010	94.3	623	84.2	5,633	93.1	
Yes	304	5.7	117	15.8	421	6.9	<0.001
Hypertension							
No	3,818	71.8	393	53.1	4,211	69.6	
Yes	1,496	28.2	347	46.9	1,843	30.4	<0.001
Heart disease							
No	4,701	88.5	662	89.5	5,363	88.6	
Yes	613	11.5	78	10.5	691	11.4	0.425

Abbreviations: AA – African-American; SD – standard deviation; ER – estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor 2; FISH – fluorescence in situ hybridization

Table 2 Treatment patterns by race and stage

Treatment pattern	All stage		*P*	In situ		*P*	Stage I/II		*P*	Stage III/IV		*P*
	White (n = 5,314) %	AA (n = 740) %		White (n = 687) %	AA (n = 96) %		White (n = 3,873) %	AA (n = 467) %		White (n = 736) %	AA (n = 173) %	
Surgery												
Surgery	99.2	97.3		99.9	100.0		99.8	98.1		95.2	93.6	
No surgery	0.8	2.7	<0.001	0.1	0.0	1.000	0.2	1.9	<0.001	4.8	6.4	0.387
Among surgery patients	n = 5,268	n = 720		n = 686	n = 96		n = 3,863	n = 458		n = 701	n = 162	
BCS alone	6.2	6.7		16.8	15.6		4.7	5.9		3.4	1.8	
BCS + radiation	42.1	41.8		39.6	43.8		47.9	48.0		13.4	24.1	
Mastectomy alone	34.5	29.2		42.6	40.6		36.4	32.1		16.3	14.2	
Mastectomy + radiation	17.2	22.3	0.002	1.0	0.0	0.689	11.0	14.0	0.096	66.9	59.9	0.007
Adjuvant chemotherapy												
Yes	37.4	39.5		0.2	1.0		43.3	46.9		41.2	41.0	
No	62.6	60.5	0.286	99.8	99.0	0.230	56.7	53.1	0.139	58.8	59.0	0.975
Regimens used for adj. chemotherapy	n = 1,989	n = 292					n = 1,675	n = 219		n = 303	n = 71	
Anthracycline-based	40.2	41.1		–	–		44.1	46.6		18.8	23.9	
Taxane-based	9.8	8.2		–	–		7.6	6.8		21.5	12.7	
Anthracycline & taxane-based	44.5	43.2		–	–		44.3	41.1		46.2	49.3	
Other regimens	5.5	7.5	0.465	–	–		4.0	5.5	0.592	13.5	14.1	0.371
Adjuvant endocrine therapy												
ER- or PR-positive	n = 3,690	n = 432		n = 211	n = 39		n = 2,974	n = 299		n = 494	n = 92	
Yes	78.1	71.1		43.1	56.4		81.9	77.3		69.6	58.7	
No	21.9	28.9	0.001	56.9	43.6	0.126	18.1	22.7	0.047	30.4	41.3	0.039
ER- and PR-negative	n = 998	n = 214		n = 45	n = 5		n = 724	n = 134		n = 227	n = 73	
Yes	4.9	7.0		8.9	0.0		5.5	8.2		2.2	5.5	
No	95.1	93.0	0.213	91.1	100.0	1.000	94.5	91.8	0.227	97.8	94.5	0.228
ER- or PR-unknown	n = 626	n = 94		n = 431	n = 52		n = 175	n = 34		n = 15	n = 8	
Yes	29.2	35.1		27.2	30.8		36.0	41.2		20.0	37.5	
No	70.8	64.9	0.247	72.8	69.2	0.581	64.0	58.8	0.567	80.0	62.5	0.621
Initial agents used for endocrine therapy												
Pre-menopausal women	n = 998	n = 132		n = 65	n = 14		n = 795	n = 93		n = 134	n = 25	
Tamoxifen	87.6	90.2		98.5	85.8		88.1	90.3		79.1	92.0	
Aromatase inhibitors	10.9	6.8		1.5	7.1		10.4	6.5		18.7	8.0	
Other agents	1.5	3.0	0.167	0.0	7.1	0.079	1.5	3.2	0.244	2.2	0.0	0.343
Post-menopausal women	n = 2,100	n = 220		n = 147	n = 24		n = 1,734	n = 161		n = 215	n = 35	
Tamoxifen	62.1	59.1		85.7	75.0		61.2	56.5		52.6	60.0	
Aromatase inhibitors	34.8	38.2		5.5	8.3		35.9	42.2		46.0	40.0	
Other agents	3.1	2.7	0.595	8.8	16.7	0.295	2.9	1.3	0.167	1.4	0.0	0.736
Neo-adjuvant chemotherapy	*n = 5,314*	*n = 740*		*n = 693*	*n = 98*		*n = 3,873*	*n = 467*		*n = 736*	*n = 173*	
Yes	23.1	29.7		0.0	0.0		19.3	21.6		64.5	68.2	

Table 2 continued

Treatment pattern	All stage		*P*	In situ		*P*	Stage I/II		*P*	Stage III/IV		*P*
	White (n = 5,314) %	AA (n = 740) %		White (n = 687) %	AA (n = 96) %		White (n = 3,873) %	AA (n = 467) %		White (n = 736) %	AA (n = 173) %	
No	76.9	70.3	<0.001	100.0	100.0	N/A	80.7	78.4	0.239	35.5	31.8	0.362
Regimens for neo-adj. chemotherapy	n = 1,228	n = 220					n = 749	n = 101		n = 475	n = 118	
Anthracycline-based	24.9	19.1		–	–		28.6	23.8		18.7	15.3	
Taxane-based	5.9	9.1		–	–		6.0	11.9		5. 5	6.8	
Anthracycline & taxane-based	68.9	71.4		–	–		65.2	64.3		75.4	77.1	
Other regimens	0.3	0.4	0.095	–	–		0.3	0.0	0.143	0.4	0.8	0.570

Abbreviations: AA – African-American; BCS – breast-conserving surgery; ER – estrogen receptor; PR – progesterone receptor

Table 3 Unadjusted and adjusted odds ratios on treatment patterns by race

Treatment pattern	Race (unadjusted)		Race (adjusted)		Risk factors in multivariate logistic models
	OR (95% CI)	*P*	OR (95% CI)	*P*	
Mastectomy versus BCS	1.00 (0.85–1.16)	0.950	0.87 (0.73–1.03)	0.105	Stage, nodal status, tumor size
BCS + radiation versus BCS alone	0.92 (0.67–1.28)	0.663	1.08 (0.75–1.60)	0.657	Stage, grade, age, diabetes
Mast. + radiation versus mast. alone	1.54 (1.23–1.92)	<0.001	1.20 (0.90–1.60)	0.219	Stage, nodal status, grade, age, heart disease
Mast. all or BCS + radiation versus BCS alone	0.93 (0.68–1.27)	0.633	0.97 (0.68–1.39)	0.887	Stage, nodal status, grade, age, diabetes
Adjuvant chemotherapy (yes versus no)	1.09 (0.93–1.28)	0.286	0.94 (0.78–1.13)	0.488	Stage, nodal status, age, grade
Neo-adjuvant chemotherapy (yes versus no)	1.41 (1.19–1.67)	<0.001	0.96 (0.78–1.18)	0.708	Stage, nodal status, age, heart disease
Adjuvant endocrine therapy (yes versus no)	0.65 (0.56–0.76)	<0.001	0.89 (0.71–1.12)	0.331	Stage, nodal status, grade, age, ER/PR, menopausal status, diabetes

Note: White is baseline group

Abbreviations: AA – African-American; BCS – breast-conserving surgery; ER – estrogen receptor; PR – progesterone receptor

more frequently than did whites (OR, 0.87; 95% CI, 0.73–1.03), the difference was not statistically significant after adjusting for tumor characteristics. There was no statistically significant difference in the regression model between AA and white women in receiving BCS plus radiation versus BCS only (OR, 1.08; 95% CI, 0.75–1.60), whereas tumor stage, grade, age, and presence of diabetes were significant factors determining the use of adjuvant radiation after BCS.

Multivariate analyses showed little difference in the receipt of adjuvant chemotherapy by race (OR, 0.94; 95% CI, 0.78–1.13), and neo-adjuvant chemotherapy by race (OR, 0.96; 95% CI, 0.78–1.18) after controlling for tumor characteristics at diagnosis and co-morbid conditions. As expected, whether a patient had received adjuvant endocrine therapy was associated with ER, PR and menopause status. Race was not an independent variable in the model for endocrine therapy after adjusting for the above factors (OR, 0.89; 95% CI, 0.71–1.12).

Clinical outcomes

Among the 6,054 patients in the cohort, 674 events (recurrence or death) and 350 breast-cancer-specific deaths had been observed over the median follow-up of 40 months. Without adjusting for other factors, disease-free survival distributions differed by race. AA women had a significantly increased relative risk of recurrence (or death) compared to that of white women (RR, 2.04; 95% CI, 1.69–2.47; $P < 0.001$) in the model without adjusting for the covariates. In a Cox proportional-hazards model (model 2 of Table 4), the effect of race was attenuated with a marginally significant effect (RR, 1.24; 95% CI, 0.99–1.56; $P = 0.063$), whereas DFS was statistically associated with tumor

Table 4 Cox proportional hazards regression models of DFS

Variable	Relative risk (95% confidence interval)	
	Model 1 (unadjusted)	Model 2 (adjusted for tumor characteristics and major treatments)
Race		
White	1.00	1.00
AA	2.04 (1.69–2.47)	1.24 (0.99–1.56)
Tumor stage		
In situ or stage I	–	1.00
Stage II	–	1.81 (1.33–2.45)
Stage III/IV	–	3.24 (2.31–4.55)
Nodal status		
Negative	–	1.00
Positive	–	1.62 (1.28–2.06)
Nuclear grade		
Well/moderately differentiated	–	1.00
Poorly differentiated	–	1.53 (1.23–1.89)
ER/PR status		
ER- or PR-positive	–	1.00
ER- and PR-negative	–	1.39 (1.10–1.76)
Lymphatic invasion		
No	–	1.00
Yes	–	1.73 (1.44–2.08)
Surgery and radiation		
BCS alone	–	1.00
BCS + radiation	–	0.38 (0.26–0.54)
Mastectomy alone	–	0.43 (0.30–0.61)
Mastectomy + with radiation	–	0.58 (0.41–0.83)
No surgery	–	1.11 (0.53–2.33)
Adjuvant chemotherapy		
Yes	–	1.00
No	–	1.24 (1.03–1.49)
Adjuvant endocrine therapy		
Yes	–	1.00
No	–	1.78 (1.41–2.25)
# of total patients	6,054	5,131
# of events	674	553
P-value for race	<0.001	0.063

Abbreviations: DFS – Disease-free survival; AA – African-American; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery

stage, nodal status, nuclear grade, ER and PR status, and lymphatic invasion. No surgery and BCS alone were associated with an elevated risk of recurrence or death compared with BCS combined with radiation, or mastectomy with or without radiation. Model 2 also indicated extra benefits from chemotherapy and endocrine therapy, in delaying recurrence and death.

AA women had worse BCSS than white women in an unadjusted analysis (RR, 2.48; 95% CI, 1.94–3.19; $P < 0.001$). In multivariate analyses, presented in Model 2 of Table 5, AA women had an attenuated but still significantly increased hazard of death from breast cancer compared to white women after adjusting for stage, nodal status, grade, ER and PR status, lymphatic invasion, and primary treatments received (RR, 1.57; 95% CI, 1.18–2.10; $P = 0.002$). Similar to DFS, more aggressive surgical treatment than BCS alone (or no surgery), and additional adjuvant therapies increased the survival of patients with breast cancer.

Discussion

M.D. Anderson Cancer Center has one of the largest multidisciplinary breast centers in the United States. Compared to the studies based on single hospitals or cancer centers, our study used the most recently available data, and had a largest cohort size [10–12, 16, 18, 19]. Our analyses indicate that the use of primary treatments for breast cancer is not significantly different by race after adjusting for tumor characteristics and other risk factors. The result is fairly consistent with the observation by Giordano et al. [20] that the overall guideline concordance rates for primary treatments are high, especially for patients younger than 75 years. The multivariate survival models that included primary treatments and known tumor characteristics at diagnosis showed that the difference in DFS by race was marginally significant, but attenuated compared to the differences without adjusting for the factors. However,

Table 5 Cox proportional hazards regression models of BCSS

Variable	Relative risk (95% confidence interval)	
	Model 1 (unadjusted)	Model 2 (adjusted for tumor characteristics and major treatments)
Race		
White	1.00	1.00
AA	2.48 (1.94–3.19)	1.57 (1.18–2.10)
Tumor stage		
In situ or stage I	–	1.00
Stage II	–	4.29 (2.56–7.17)
Stage III/IV	–	8.36 (4.87–14.35)
Nodal status		
Negative	–	1.00
Positive	–	1.57 (1.16–2.13)
Nuclear grade		
Well/moderately differentiated	–	1.00
Poorly differentiated	–	1.95 (1.41–2.70)
ER/PR status		
ER- or PR-positive	–	1.00
ER- and PR-negative	–	1.27 (0.93–1.72)
Lymphatic invasion		
No	–	1.00
Yes	–	1.64 (1.29–2.10)
Surgery and radiation		
BCS alone	–	1.00
BCS + radiation	–	0.45 (0.28–0.73)
Mastectomy alone	–	0.51 (0.32–0.81)
Mastectomy + with radiation	–	0.61 (0.38–0.97)
No surgery	–	1.16 (0.48–2.76)
Adjuvant chemotherapy		
Yes	–	1.00
No	–	1.75 (1.36–2.26)
Adjuvant endocrine therapy		
Yes	–	1.00
No	–	2.43 (1.76–3.36)
# of total patients	6,054	5,131
# of events	350	294
P-value for race	<0.001	0.002

Abbreviations: BCSS – Breast-cancer-specific survival; AA – African-American; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery

race was still an independent significant prognostic factor for BCSS after adjusting for the other factors. This observation suggests that unknown or unmeasured factors other than the treatment received and tumor characteristics at diagnosis attribute to the residual racial difference in breast cancer death and recurrence.

The literature about differences in the utilization of treatments based on racial designation has been inconsistent. Several studies found racial differences in breast cancer treatment, especially in the receipt of BCS with or without radiation [6, 8, 9, 13, 21, 22], whereas others found few differences in treatments after adjusting for tumor characteristics [16, 17, 19, 23, 24]. Population-based studies are more likely to identify differences in treatment by race compared to the studies based on single hospitals. For population-based studies that often cover multiple regions and hospitals, the variations in patterns of treatment can be a result of the unequal access to care due to variations in socio-economic status. Our multivariate models showed no statistically significant difference in the utilization of BCS versus mastectomy, as well as BCS plus adjuvant radiation versus BCS alone by race. This observation is similar to that of Du and Simon [16] based on the Karmanos Cancer Institute experience and that of Bradley et al. [13] based on the Surveillance Epidemiology and End Results database, but opposite to that of Simon et al [25].

Although the current literature about racial disparity in clinical outcomes has been mixed, there has been a consistent trend showing that AA women have had a somewhat worse clinical prognosis even after adjusting for tumor characteristics at diagnosis and treatment received. In fact, whether the effect of race is ''statistically significant'' essentially depends on the sample size of a study. It is more important to examine and compare the magnitude of the effect of race among these studies. In our analyses, AA women had a 24% increased risk of recurrence or death and 57% increased risk of breast-cancer-death compared to those of white women in Model 2 of Tables 4 and 5. Interestingly, our estimated effects of race are quite consistent with those in the models adjusted for tumor characteristics and/or treatment in other studies, which had the estimated increased risk of recurrence (or death) ranged from 20% to 43% [6–8, 10, 14, 16]. The anomaly for the magnitude of the effect of race among these studies is well within the expected random uncertainty.

First among several limitations to our study is a lack of longer follow-up for this cohort of patients with an overall 11% recurrence (or death) and 5% breast-cancer-specific death. Second, conclusions from this study are based on the data from a single Comprehensive Cancer Center and may not be extrapolated to the general population. However, the advantage of using data from one large cancer center is that we can focus on differentiating the biological characteristics of the tumor and treatment patterns by race, and identifying the causes for survival disparities by race. In this setting, all patients treated at M.D. Anderson should have had access to the same quality of care. The third limitation is the lack of precise information from the database on patients' screening histories and the method of detection of breast cancer, which may provide insight into, and explain some of the remaining differences in the clinical outcomes. Finally, clinical and pathology staging may be somewhat incomparable for neo-adjuvant and non-neo-adjuvant patients.

In summary, there were no major differences in the patterns of care and predictors of the treatment for breast cancer by race at M.D. Anderson Cancer Center. Although tumor characteristics at diagnosis explained the substantial differences in clinical outcomes and were the most important risk factors, race remained an independent prognostic factor for breast-cancer-specific survival, and a marginally significant factor for disease-free survival. The potential factors related to the clinical outcomes may include additional unknown or unmeasured tumor biological characteristics associated with the natural history of breast cancer, but differing by race, such as ER and PR status. Other potential differences by race may be explained by the use of screening mammography and clinical breast examination in early detection programs. The method of detection has been found to be an independent prognostic factor in predicting BCSS in addition to tumor characteristics at diagnosis [26].

Our findings do not imply that equal treatment leads to equal clinical outcomes given similar disease. To reduce racial differences in breast cancer recurrence and survival, it may not be sufficient to provide equal treatment after diagnosis to all women. Rather, achieving a better understanding of differences in tumor biology by race and promoting the use of early detection programs among AA women will hopefully minimize this health disparity [27].

Acknowledgements The authors would like to thank Mr. Limin Hsu for his data management support. This research was supported by Research Grant, CA-79466 from National Cancer Institute and by a grant from the National Comprehensive Cancer Network to fund in part Breast Cancer Medical System database of M.D. Anderson Cancer Center.

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