

Male Breast Cancer According to Tumor Subtype and Race

A Population-Based Study

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BACKGROUND: Breast cancer occurs rarely in men. To the authors' knowledge, no population-based estimates of the incidence of human epidermal growth factor receptor 2 (HER2)-positive breast cancer or of the distribution of breast cancer subtypes among male breast cancer patients have been published to date. Therefore, the objective of the current study was to explore breast tumor subtype distribution by race/ethnicity among men in the large, ethnically diverse population of California. **METHODS:** This study included men who were diagnosed with invasive breast cancer between 2005 and 2009 with known estrogen receptor (ER) and progesterone receptor (PR) (together, hormone receptor [HR]) status and HER2 status reported to the California Cancer Registry. Among the men with HR-positive tumors, survival probabilities between groups were compared using log-rank tests. **RESULTS:** Six hundred six patients were included. The median age at diagnosis was 68 years. Four hundred ninety-four men (81.5%) had HR-positive tumors (defined as ER-positive and/or PR-positive and HER2-negative). Ninety men (14.9%) had HER2-positive tumors, and 22 (3.6%) had triple receptor-negative (TN) tumors. Among the patients with HR-positive tumors, non-Hispanic black men and Hispanic men were more likely to have PR-negative tumors than non-Hispanic white men. No statistically significant differences in survival were observed according to tumor subtype ($P = .08$). Differences in survival according to race/ethnicity were observed among all patients ($P = .087$) and among those with HR-positive tumors ($P = .0170$), and non-Hispanic black men had poorer outcomes. **CONCLUSIONS:** In this large, representative cohort of men with breast cancer, the distribution of tumor subtypes was different from that reported for women and varied by patient race/ethnicity. Non-Hispanic black men were more likely to have TN tumors and ER-positive/PR-negative tumors than white men. *Cancer* 2013;119:1611-7. © 2013 American Cancer Society.

KEYWORDS: breast cancer, males, race, population-based study, breast cancer subtypes.

INTRODUCTION

Male breast cancer is an uncommon disease and accounts for only 0.6% to 1% of all patients with breast cancer.¹ In 2011, it is estimated that a total of 2140 men will be diagnosed with breast cancer in the United States.² The etiology of male breast cancer is unclear, but hormone levels and testicular abnormalities play a role in the development of this disease. It has been demonstrated that breast cancer susceptibility gene 2 (*BRCA2*) mutations confer a significant risk of breast cancer in men. Other recognized risk factors include radiation exposure, family history of breast cancer, Klinefelter syndrome, and different benign breast conditions.^{3,4}

Previous reports have suggested that cancers of the male breast are more likely than female breast cancers to have a ductal histology and are significantly more likely to express hormone receptors, even after adjustment for tumor stage, grade, and patient age.^{5,6} Early reports suggested equivalent or even higher rates of human epidermal growth factor receptor 2 (HER2) overexpression in male breast cancer versus female breast cancer.^{4,7-9} However, those studies were small and were performed before improved standardization of assay methodology, and they may have overestimated HER2 overexpression.^{3,10}

However, as knowledge about the biology of breast cancer has improved, it has become clear that breast cancers should be classified according to tumor subtype. The categorization of breast cancers into estrogen receptor (ER) and progesterone receptor (PR) (together, hormone receptor)-positive, HER2-positive, and triple receptor-negative (TN) tumors has important implications for the prognosis and management of patients with breast cancer. Among female patients with breast cancer, there are strong racial/ethnic differences in tumor subtype distribution.¹¹ In the current population-based

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study, we explored the distribution of the different breast cancer tumor subtypes according to race/ethnicity among male patients with breast cancer who were identified through the California Cancer Registry (CCR).

MATERIALS AND METHODS

Study Population and Variables

We used data from the CCR, a population-based registry that has collected data from all cancers diagnosed in California since 1988. By state law, all cancer cases are reported to the CCR from hospitals and from any other facility that provides care or therapy to patients with cancer residing in California.¹² It is estimated that CCR case ascertainment is 99% complete.¹³ Information on patients with cancer, including demographic characteristics (age, race/ethnicity), tumor characteristics, and treatment information, was abstracted from the medical record by trained tumor registrars. The CCR has collected data on ER and PR status since 1990 and started collecting HER2 data in 1999; however, for the reporting of HER2 status, uptake was not immediate. Issues associated with the collection and reporting of HER2 status have been described in a previous report.¹⁴ Because HER2 status was more likely to be present in the medical record and, thus, was reported to the CCR for patients who were diagnosed after 2005, we limited our assessment to patients who were diagnosed in that year or later.

For the current study, all patients with male breast cancer (International Classification of Disease-Oncology [ICD-O-3] codes C50.0-C50.9) who were diagnosed with a first primary invasive breast cancer between 2005 and 2009 were identified ($n = 829$). Patients who were diagnosed on death certificate or autopsy only ($n = 4$) and those who had missing or invalid follow-up data were excluded ($n = 1$); in addition only patients who had complete information on ER, PR, and HER2 status were included, resulting in a total of 606 patients. Patients who were excluded from our study for unknown receptor status did not differ significantly from those who were included with respect to age or race/ethnicity. No differences were observed in the distribution according to disease stage (all $P > .05$); however, patients who were excluded from the study had a higher proportion of unknown stage ($P < .001$). In addition, patients who were diagnosed in 2005 were more likely to be excluded than patients who were diagnosed in subsequent years ($P < .020$).

We used the American Joint Committee on Cancer staging system (sixth edition). Tumor histology was classified as ductal (ICD-O-3 morphology codes 8500, 8501,

8502, 8503, 8504, 8507, 8708, and 8523), lobular (ICD-O-3 morphology codes 8520 and 8521), and papillary/mixed/other (morphology codes 8550, 8260, 8522, and 8524). Breast cancer subtypes were defined as hormone receptor (HR)-positive (ER-positive and/or PR-positive and HER2-negative), HER2-positive (HER2-positive, regardless of ER or PR status), and TN (negative for HER2, ER, and PR). Race/ethnicity was categorized into 4 mutually exclusive groups: non-Hispanic white, non-Hispanic black, Hispanic, and Asian/Pacific Islander (API)/other.

Data Analysis

Descriptive statistics were used to evaluate characteristics of the patient population. Differences between groups were assessed using the chi-square test and the Fisher exact test. For each patient, information on vital status was obtained from the CCR. The CCR regularly updates vital status information through hospital follow-up and linkages with state and national databases and agencies, such as the National Death Index, the Social Security Administration, the Centers for Medicaid and Medicare Services, the Office of Statewide Health Planning and Development, CalVoter, the Indian Health Service, the National Change of Address, the Department of Motor Vehicles, birth certificate linkages, and state vital statistics. Seventy-four percent of our patients had confirmed vital status as of December 31, 2010, and 88% had confirmed vital status within 3 months of that date. Survival was measured in months since diagnosis. Kaplan-Meier analysis was used to calculate the probability of survival. Patients were censored if they were alive as of December 31, 2010. The median follow-up was 33.7 months (range, 2.7-71.9 months). Patients who had complete follow-up did not differ significantly on age, race, stage, tumor subtype, year of diagnosis, or socioeconomic status from patients without current follow-up ($P > .05$; chi-square test).

Survival analysis according to tumor subtype and race/ethnicity was performed, and differences between groups were compared using the log-rank test. A subanalysis of survival by race/ethnicity also was performed limited to patients with HR-positive tumors. A Cox proportional-hazards analysis was performed with race/ethnicity, disease stage, and age included in the model. Tumor subtype had a significant interaction with time and violated the proportional hazards assumption; therefore, the tumor subtype variable was not included in the final model. Statistical analyses were performed using the SAS statistical software package (version 9.3; SAS institute

Inc., Cary, NC) and R (R Foundation for Statistical Computing, Vienna, Austria).

Deidentified data from the CCR were used for all analyses; however, to preserve confidentiality, in all tables, cells with patient numbers <5 were suppressed. The Institutional Review Board (IRB) of the Cancer Prevention Institute of California approved this analysis, and The University of Texas MD Anderson Cancer Center IRB provided an exemption.

RESULTS

In total, 829 men patients with primary invasive breast cancer were identified between 2005 and 2009. Of these, 606 men (73.2%) had information available on ER, PR, and HER2 status; and their median age at diagnosis was 68 years. The majority of patients were non-Hispanic white (71%; $n = 431$), and 7.4% were non-Hispanic black ($n = 45$), 11.1% were Hispanic ($n = 67$), and 10.4% were API/other/unknown ($n = 63$). Four hundred ninety-four patients (81.5%; 95% confidence interval [CI], 78.4%-84.6%) had HR-positive tumors, 90 patients (14.9%; 95% CI, 12%-17.7%) had HER2-positive tumors, and 22 patients (3.6%; 95% CI, 2.1%-5.1%) had TN tumors. Table 1 lists the patient characteristics according to tumor subtype. There was a statistically significant difference in the distribution of tumor subtypes according to age ($P = .020$), indicating that younger patients were more likely to have HER2-positive tumors. Among non-Hispanic whites, 82.8% of patients (95% CI, 79.3%-86.4%) had HR-positive tumors, 14.6% (95% CI, 11.3%-18%) had HER2-positive tumors, and 2.6% (95% CI, 1.1%-4%) had TN breast cancer. In contrast, among non-Hispanic blacks, 73.3% of patients had HR-positive tumors (95% CI, 60.4%-86.3%), 17.8% had HER2-positive tumors (95% CI, 6.6%-29%), and 8.9% had TN-tumors (95% CI, 0.6%-17.2%); whereas, among Hispanics, 77.6% had HR-positive tumors (95% CI, 67.6%-87.6%), 16.4% had HER2-positive tumors (95% CI, 7.6-27.5%), and 6% had TN tumors (95% CI, 0.3%-11.6%).

HR-positive tumors represented the most common breast cancer subtype in our patient population ($n = 494$); therefore, we evaluated ER and PR status separately. Table 2 indicates the different combinations of ER and PR status among HR-positive patients according to race/ethnicity. We observed that Hispanics and non-Hispanic blacks were more likely to have ER-positive and PR-negative tumors compared with non-Hispanic whites (17.3% [95% CI, 7%-27.6%], 15.2% [95% CI, 2.9%-27.4%], and 4.5% [95% CI, 2.3%-6.6%], respectively; $P < .001$).

Although we had small numbers of patients and deaths for the current study ($n = 117$ events), next, we evaluated whether overall survival varied by tumor subtype. Figure 1 is a Kaplan-Meier curve that suggests worse survival among patients who had TN tumors, although the results from a log-rank-test were not significant ($P = .089$). Figure 2 illustrates significant differences in survival by race/ethnicity among all participants ($n = 606$), indicating that non-Hispanic blacks had the worst outcomes ($P = .008$). The observed differences may be explained by the different distribution of tumor subtype according to race. For that reason, we explored the survival of patients according to each tumor subtype by race/ethnicity. Unfortunately, given the small number of patients, we could not separately examine the influence of HER2-positive tumors and the influence of TN tumors. Figure 3 is a Kaplan Meier survival curve that was calculated according to race/ethnicity for patients with HR-positive tumors ($n = 494$), and it demonstrates significant differences in survival according to race/ethnicity ($P = .017$). Among these patients, non-Hispanic blacks had the worst survival.

After adjusting for disease stage and age and using non-Hispanic whites as a reference category, we observed no significant differences in survival according to race/ethnicity (Hispanics: hazard ratio, 0.78; 95% CI, 0.38-1.58; non-Hispanic blacks: hazard ratio, 1.32; 95% CI, 0.75-2.33; and API/other: hazard ratio, 0.631; 95% CI, 0.27-1.46), suggesting that the effect of race/ethnicity on survival was attenuated by disease stage.

DISCUSSION

To the best of our knowledge, this is the first and largest population-based study evaluating the distribution of tumor subtypes in men with breast cancer. The majority of patients in our study (81.5%) had HR-positive tumors. We observed that a clinically significant proportion of patients had HER2-positive tumors (14.9%), and a low proportion had TN tumors (3.6%).

In a large study that included >60,000 women using data from the CCR, 63.8% of patients had HR-positive tumors, 22.8% had HER2-positive tumors, and 13.4% had TN tumors,¹⁵ suggesting that patients with male breast cancer have lower rates of HER-2-positive and TN tumors than their female counterparts. It has been well described that patients with male breast cancer are more likely than their female counterparts to have HR-positive tumors.^{3,5,6,16} It is estimated that the incidence of ER-positive and PR-positive tumors is 82% and

TABLE 1. Patient Characteristics According to Tumor Subtype

Characteristic	Total No.	Tumor Subtype: No. of Patients (%)			P
		HR-Positive	HER2-Positive	Triple Negative	
All patients	606	494 (81.5)	90 (14.9)	22 (3.6)	
Age at diagnosis, y					.0204
<50	60	40 (66.7)	17 (28.3)	<5 (5) ^a	
50-69	268	223 (83.2)	38 (14.2)	7 (2.6)	
≥70	278	231 (83.1)	35 (12.6)	12 (4.3)	
Race					.2274
Non-Hispanic white	431	357 (82.8)	63 (14.6)	11 (2.6)	
Non-Hispanic black	45	33 (73.3)	8 (17.8)	<5 (8.9) ^a	
Hispanic	67	52 (77.6)	11 (16.4)	<5 (6) ^a	
API/other/unknown	63	52 (82.5)	8 (12.7)	<5 (4.8) ^a	
Year of diagnosis					0.213
2005	87	66 (75.9)	17 (19.5)	<5 (4.6) ^a	
2006	133	102 (76.7)	22 (16.5)	9 (6.8)	
2007	114	94 (82.5)	16 (14)	<5 (3.5) ^a	
2008	133	110 (82.7)	20 (15)	<5 (2.3) ^a	
2009	139	122 (87.8)	15 (10.8)	<5 (1.4) ^a	
Socioeconomic status quintile					.4822
1	70	57 (81.4)	8 (11.4)	5 (7.1)	
2	97	77 (79.4)	19 (19.6)	<5 (1)	
3	125	101 (80.8)	19 (15.2)	5 (4)	
4	119	95 (79.8)	19 (16)	5 (4.2)	
5	195	164 (84.1)	25 (12.8)	6 (3.1)	
Tumor histology					.6915
Ductal	513	419 (81.7)	77 (15)	17 (3.3)	
Lobular	11	9 (81.8)	<5 (18.2) ^a	0 (0)	
Papillary/mixed/other	82	66 (80.5)	11 (13.4)	5 (6.1)	
Grade					< .0001
1	83	71 (85.5)	9 (10.8)	<5 (3.6) ^a	
2	315	271 (86)	42 (13.3)	<5 (0.6) ^a	
3/4	183	133 (72.7)	34 (18.6)	16 (8.7)	
Unknown	25	19 (76)	5 (20)	<5 (4) ^a	
Stage at diagnosis					.2277
I	195	167 (85.6)	21 (10.8)	7 (3.6)	
II	248	203 (81.9)	36 (14.5)	9 (3.6)	
III	101	80 (79.2)	18 (17.8)	<5 (3) ^a	
IV/unknown	62	44 (71)	15 (24.2)	<5 (4.8) ^a	
Surgery					.0002
No surgery	32	22 (68.8)	8 (25)	<5 (6.3) ^a	
Mastectomy	495	413 (83.4)	73 (14.7)	9 (1.8)	
Breast conservation	79	59 (74.7)	9 (11.4)	11 (13.9)	
Radiation therapy					.6657
No/unknown	441	356 (80.7)	69 (15.6)	16 (3.6)	
Yes	165	138 (83.6)	21 (12.7)	6 (3.6)	
Vital status as of December 31, 2010					.0770
Dead	117	89 (76.1)	20 (17.1)	8 (6.8)	
Alive	489	405 (82.8)	70 (14.3)	14 (2.9)	

Abbreviations: API, Asian/Pacific Islander; HER2, human epidermal growth factor receptor 2; HR, hormone (estrogen and progesterone) receptor.

^a Cell counts <5 have been suppressed to protect patient confidentiality.

TABLE 2. Tumor Receptor Status Combinations According to Race for Hormone Receptor-Positive and HER2-Negative Patients^a

HR Status	Total No.	Race: No. of Patients (%)			
		Non-Hispanic White	Non-Hispanic Black	Hispanic	API/Other/Unknown
ER+/PR+	456	336 (94.1)	27 (81.8)	42 (80.8)	51 (98.1)
ER+/PR-	31	16 (4.5)	5 (15.2)	9 (17.3)	<5 (1.9) ^b
ER-/PR+	7	5 (1.4)	<5 (3) ^b	<5 (1.9) ^b	0 (0)
All patients	494	357 (100)	33 (100)	52 (100)	52 (100)

Abbreviations: -, negative; +, positive; Asian/Pacific Islander; ER, estrogen receptor; HR, hormone receptor; PR, progesterone receptor.

^a P < .001

^b Cell counts <5 have been suppressed to protect patient confidentiality.

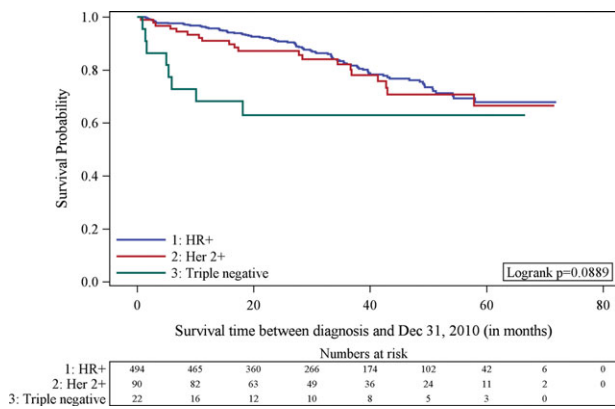


Figure 1. Kaplan-Meier curves illustrate the probability of survival among men with breast cancer according to tumor subtype ($n = 606$). Hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2) and triple negative.

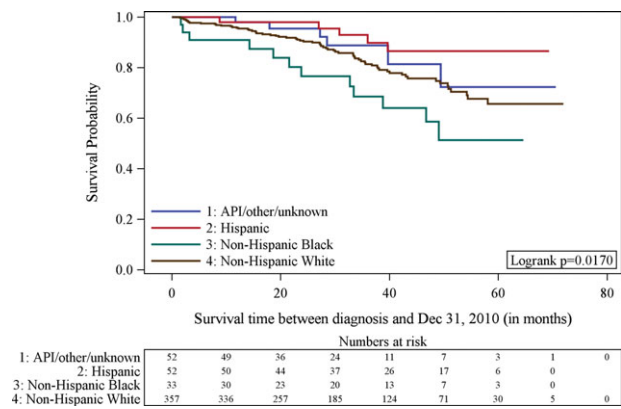


Figure 3. Kaplan-Meier curves illustrate the probably of survival among men with breast cancer according to race/ethnicity for those with (hormone receptor)-positive tumors ($n = 494$). API indicates Asian/Pacific Islander.

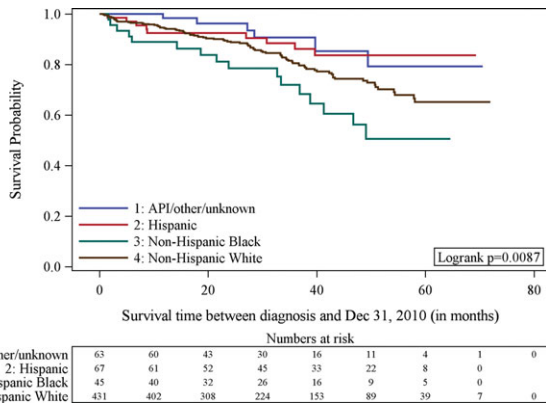


Figure 2. Kaplan-Meier curves illustrate the probably of survival among men with breast cancer according to race/ethnicity. API indicates Asian/Pacific Islander ($n = 606$).

75%, respectively, among men and 69% and 52%, respectively, among women.⁴

However, data in the literature on HER2 overexpression are inconsistent: Earlier studies reported similar or higher rates of HER2 overexpression between men and women,^{3,4,7-9} and pooled data suggest a 35% rate of overexpression in men. In a study published by Bloom et al,¹⁰ 58 male breast cancer specimens were evaluated. Those authors identified HER2 overexpression in only 1 specimen (1.7%), and amplification was not observed. It is noteworthy that their study included a subset of patients ($n = 26$) who had tumors that were considered HER2-overexpressed tumors in a previous report,⁹ and none of those patients had overexpression identified at the time of re-evaluation. The small number of patients and the differences in the techniques used to determine HER2 status

may underlie the previously overestimated rates of HER2 expression among men with breast cancer.³

In our study, 14.9% of tumors were categorized as HER2-positive. Our results are similar to the 17% rate reported by Muir and colleagues¹⁶ and the 15% rate of HER2 amplification described by the European Institute of Oncology¹⁷; however, those were small studies that included only 59 patients and 27 patients, respectively. The rate of TN tumors among men with breast cancer is not clearly described, and the frequency of such tumors largely remains unknown. We observed a 3.8% rate of TN tumors, which was substantially lower than the rates reported in female patients. In a recent study, Arslan et al described a 5.9% rate of TN tumors among patients in a Turkish population of men with breast cancer ($n = 118$).¹⁸

Among women with breast cancer, the categorization of breast tumors into different subtypes has important prognostic implications. After adjusting for clinical and demographic characteristics, women with HR-positive tumors have better outcomes than those with HER2-positive tumors and TN tumors. It is not clear whether breast cancer subtypes are associated with the same prognostic factors among men with breast cancer. A Mayo Clinic study reported no association between HER2 overexpression and survival in univariate analysis among a cohort of 76 men with breast cancer.⁸ More recently, Arslan et al observed a statistically nonsignificant difference in 5-year overall survival among 118 men who had HER2-positive tumors compared with men who had HER2 normal-expressing tumors (85 months vs 144 months; $P = .30$).¹⁸ In our study, we observed that men who had TN tumors tended to have worse survival

compared with those who had HR-positive or HER2-positive tumors; however, this difference did not reach statistical significance ($P = .088$).

It is important to point out that our patient population included men who received treatment after the approval of trastuzumab-based chemotherapy; therefore, it is possible that our patients with HER2-positive tumors received this treatment, likely improving their outcomes compared with patients who had TN tumors. Our results suggest that, among men with breast cancer, tumor subtype does hold prognostic significance. However, the small number of patients with TN and HER2-positive tumors, the short follow-up, and our inability to perform any multivariable analysis adjusting for clinically relevant characteristics warrant careful interpretation.

Among women with breast cancer, clear racial/ethnic differences exist in the distribution of tumor subtypes.^{11,15} Non-Hispanic black women have higher rates of TN or basal-like tumors and are less likely to have ER-positive and PR-positive tumors. In our study, a similar pattern appeared to be present among men with breast cancer, although this difference was not statistically significant ($P = .227$). The high frequency of tumors associated with a poor prognosis is a theory promulgated to explain, at least in part, the poor outcomes observed in non-Hispanic black women compared with women from other ethnic/racial groups. Among women with breast cancer who have HR-positive tumors, worse outcomes have been reported in non-Hispanic blacks compared with non-Hispanic whites.^{19,20} In our study, among men with breast cancer who had HR-positive tumors ($n = 494$), non-Hispanic black men had worse survival compared with men from other racial/ethnic groups ($P = .017$).

When we separately explored the distribution of PR status among men who had ER-positive tumors, significant differences were observed ($P < .001$). Only 4.25% of non-Hispanic white men had PR-negative tumors compared with 15.26% of non-Hispanic black men and 17.3% of Hispanic men. In a large study from the CCR evaluating 1796 men with breast cancer from 1988 to 2000,²¹ a similar observation was described. Among men who had breast cancer with known PR status ($n = 862$), non-Hispanic whites, Hispanics, and Asians had PR-positive tumors (81%, 90%, and 79.6%, respectively) more frequently than non-Hispanic blacks (64.1%). We consider this an important observation that may help explain the poor outcomes observed among non-Hispanic black men. In women with breast cancer, ER-positive/PR-negative tumors have been associated with tamoxifen resistance and a more aggressive phenotype compared

with ER-positive/PR-positive tumors.²²⁻²⁴ Women aged >60 years who had ER-positive/PR-negative tumors reportedly had worse outcomes compared with those in the same age category who had ER-positive/PR-positive tumors.²⁵

In an exploratory analysis aimed to eliminate the potential effect of ER-positive/PR-negative tumors by limiting the survival analysis according to race/ethnicity exclusively to those men who had ER-positive/PR-positive tumors. Non-Hispanic blacks had worse survival ($P = .023$). Unfortunately, this does not help explain the clinical behavior of tumors in Hispanic patients who, despite also having high rates of ER-positive/PR-negative tumors, had better survival compared with non-Hispanic blacks.

Our study had several important limitations. Despite including one of the largest and most diverse populations of men with breast cancer in the United States, the overall number of patients with HER2-positive and TN tumors was small. Also, our necessarily short follow-up and the small number of events limited our statistical analyses, and we were not able to build a multivariate model to evaluate outcomes according to tumor subtype. Limitations inherent to population-based studies, such as potential errors in reporting or differences in laboratory techniques to assign tumor marker status, could not be quantified. In addition, data on biomarker status (ER, PR, and HER2) were obtained from the CCR but originated in different local pathology laboratories; therefore, no information on quality control was available, and no central biomarker review was possible. Also, the categories that we used in this study to categorize tumor subtypes were derived exclusively from data on ER, PR, and HER2 status, and no information was available on molecular profiles. Our cohort included only patients with known ER, PR, and HER2 status. The patients who were included in our study had characteristics similar to those of the patients who were excluded; however, the patients who were excluded were more likely to be diagnosed in 2005. A sensitivity analysis (data not shown) that included patients who were diagnosed from 2006 to 2009 ($n = 519$) produced similar results.

To our knowledge, this is the first population-based study reporting tumor subtypes among men with breast cancer. The majority of our patients had HR-positive tumors; however, HER2 overexpression was observed in 14.9% of patients, and 3.6% of patients had TN tumors; this observation has potential prognostic and treatment implications. Among men with breast cancer, we observed

differences in tumor subtype among different racial/ethnic groups. Non-Hispanic black men were numerically more likely to have TN tumors and ER-positive/PR-negative tumors than non-Hispanic black men.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

REFERENCES

- Giordano SH, Cohen DS, Buzdar AU, Perkins G, Hortobagyi GN. Breast carcinoma in men: a population-based study. *Cancer*. 2004;101:51-57.
- Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin*. 2011;61:212-236.
- Giordano SH, Buzdar AU, Hortobagyi GN. Breast cancer in men. *Ann Intern Med*. 2002;137:678-687.
- Korde LA, Zujewski JA, Kamin L, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. *J Clin Oncol*. 2010;28:2114-2122.
- Anderson WF, Althuis MD, Brinton LA, Devesa SS. Is male breast cancer similar or different than female breast cancer? *Breast Cancer Res Treat*. 2004;83:77-86.
- Stalsberg H, Thomas DB, Rosenblatt KA, et al. Histologic types and hormone receptors in breast cancer in men: a population-based study in 282 United States men. *Cancer Causes Control*. 1993;4:143-151.
- Leach IH, Ellis IO, Elston CW. c-erb-B-2 expression in male breast carcinoma. *J Clin Pathol*. 1992;45:942.
- Rayson D, Erlichman C, Suman VJ, et al. Molecular markers in male breast carcinoma. *Cancer*. 1998;83:1947-1955.
- Gattuso P, Reddy VB, Green LK, Castelli MJ, Wick RM. Prognostic factors for carcinoma of the male breast. *Int J Surg Pathol*. 1995;2:199-206.
- Bloom KJ, Govil H, Gattuso P, Reddy V, Francescatti D. Status of HER-2 in male and female breast carcinoma. *Am J Surg*. 2001;182:389-392.
- Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA*. 2006;295:2492-2502.
- Klijn JG, Blamey RW, Boccardo F, Tominaga T, Duchateau L, Sylvester R. Combined tamoxifen and luteinizing hormone-releasing hormone (LHRH) agonist versus LHRH agonist alone in premenopausal advanced breast cancer: a meta-analysis of 4 randomized trials. *J Clin Oncol*. 2001;19:343-353.
- Telli ML, Chang ET, Kurian AW, et al. Asian ethnicity and breast cancer subtypes: a study from the California Cancer Registry. *Breast Cancer Res Treat*. 2011;127:471-478.
- Bauer KR, Brown M, Creech C, Schlang NC, Caggiano V. Data quality assessment of HER2 in the Sacramento region of the California Cancer Registry. *J Regist Manage*. 2007;34:4-7.
- Parise CA, Bauer KR, Brown MM, Caggiano V. Breast cancer subtypes as defined by the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2) among women with invasive breast cancer in California, 1999-2004. *Breast J*. 2009;15:593-602.
- Muir D, Kanthan R, Kanthan SC. Male versus female breast cancers. A population-based comparative immunohistochemical analysis. *Arch Pathol Lab Med*. 2003;127:36-41.
- Curigliano G, Colleoni M, Renne G, et al. Recognizing features that are dissimilar in male and female breast cancer: expression of p21Waf1 and p27Kip1 using an immunohistochemical assay. *Ann Oncol*. 2002;13:895-902.
- Arslan UY, Oksuzoglu B, Ozdemir N, et al. Outcome of non-metastatic male breast cancer: 118 patients. *Med Oncol*. 2012;29:554-560.
- Chavez-Macgregor M, Litton J, Chen H, et al. Pathologic complete response in breast cancer patients receiving anthracycline- and taxane-based neoadjuvant chemotherapy: evaluating the effect of race/ethnicity. *Cancer*. 2010;116:4168-4177.
- Sparano J, Wang W, Stears V, et al. Black race is associated with a worse outcome in patients with hormone receptor positive, Her2-normal breast cancer treated with chemohormonal therapy [abstract]. *Cancer Res*. 2010;69(suppl 3). Abstract 494s.
- O'Malley C, Shema S, White E, Glaser S. Incidence of male breast cancer in California, 1988-2000: racial/ethnic variation in 1759 men. *Breast Cancer Res Treat*. 2005;93:145-150.
- Arpino G, Weiss H, Lee AV, et al. Estrogen receptor-positive, progesterone receptor-negative breast cancer: association with growth factor receptor expression and tamoxifen resistance. *J Natl Cancer Inst*. 2005;97:1254-1261.
- Neven P, Pochet N, Drijkoningen M, et al. Progesterone receptor in estrogen receptor-positive breast cancer: the association between HER-2 and lymph node involvement is age related. *J Clin Oncol* 24:2595, 2006; author reply 2595-2597.
- Thakkar JP, Mehta DG. A review of an unfavorable subset of breast cancer: estrogen receptor positive progesterone receptor negative. *Oncologist*. 2011;16:276-285.
- Yu KD, Liu GY, Di GH, et al. Progesterone receptor status provides predictive value for adjuvant endocrine therapy in older estrogen receptor-positive breast cancer patients. *Breast*. 2007;16:307-315.