Original Study

Features Associated With Long-Term Survival in Patients With Metastatic Breast Cancer

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Abstract

Of women diagnosed with metastatic breast cancer (MBC), 20% to 30% survive ≥5 years. We identified clinicopathologic and socioeconomic features associated with MBC survival. Diagnosis of de novo MBC, premenopausal status, estrogen receptor-positive status, and HER2-positive status were positively associated whereas triple-negative status, brain metastases, and visceral with bone metastases were inversely associated with long-term survival in our study population.

Background: Of women diagnosed with metastatic breast cancer (MBC), 20% to 30% survive ≥5 years. We evaluated data from a large breast cancer program to identify features associated with MBC survival. **Patients and Methods:** Women diagnosed with MBC in or after 1999 were included. Long-term MBC survival was defined as ≥5 years from date of MBC diagnosis (n = 122), short-term MBC survival as ≤2 years (n = 191). Differences were assessed using *t* tests, Wilcoxon–Mann–Whitney tests, χ^2, and Fisher exact tests. Odds ratios (ORs) were calculated using multivariate logistic regression models. **Results:** Long-term survivors were significantly ($P < .05$) younger, premenopausal, partnered, had estrogen receptor (ER)-positive, progesterone receptor-positive, and HER2-positive disease, lower Charlson Comorbidity Index, lower rates of visceral metastases, and higher household income. After adjustment for potential confounders, de novo MBC, premenopausal status, ER-positive status, and HER2-positive status remained significantly positively associated with long-term survival (respectively: OR, 2.68 [95% confidence interval (CI), 1.48-4.88]; OR, 1.96 [95% CI, 1.02-3.79]; OR, 3.74 [95% CI, 1.72-8.14]; OR, 2.88 [95% CI, 1.61-5.14]). Triple-negative status, visceral with bone metastases, and brain metastases remained negatively associated with long-term survival (respectively: OR, 0.12 [95% CI, 0.05-0.29]; OR, 0.18 [95% CI, 0.07-0.47]; OR, 0.16 [95% CI, 0.04-0.60]). Partner status and household income were significant in univariate but not multivariate analyses. **Conclusion:** Diagnosis of de novo MBC, premenopausal status, ER-positive status, and HER2-positive status were positively associated whereas triple-negative status, brain metastases, and visceral with bone metastases were inversely associated with long-term survival. These findings can be applied to better prognosticate survival for MBC patients.

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Introduction

Breast cancer (BC) is the second leading cause of cancer death among women in the United States.[1,2] In 2019, 40,920 women are expected to die of this disease.[3] Most of these deaths will be because of complications from metastatic BC (MBC), also known as stage IV disease.[4] At BC diagnosis, 6% of women already have stage IV disease, which is defined as de novo MBC.[3,4] In addition, despite treatment of early-stage BC, 20% to 30% of patients diagnosed at early stage eventually progress to MBC.[4,5] MBC has a median survival of only 2 to 3 years.[6] According to the latest Surveillance, Epidemiology, and End Results data (2008-2014), the 5-year survival rate for MBC is 27%.[3]

Known features associated with long-term MBC survival include hormone receptor-positive BC, and having nonvisceral and bone metastases.[7-9] Characteristics associated with short-term survival include triple-negative disease,[7,8] having visceral metastases[10,11] and having brain metastases.[11] There is some debate regarding long-term survival in HER2-positive MBC patients. HER2-positive MBC in older studies was associated with poor survival but after

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1999 with the availability of trastuzumab, it has been associated with improved survival.[8,11] Interestingly, some recent studies show no long-term survival benefit for HER2-positive disease.[7]

Data on factors associated with MBC survival are limited to analyses of large national databases from several countries including the United States,[11-13] The Netherlands,[8,14] Sweden,[10] France,[15] and Australia.[16] Many characteristics such as age, time interval between initial diagnosis and MBC diagnosis, and de novo MBC status have not been clearly shown to be linked to survival and have had mixed results between different studies. Patient age at diagnosis has been reported to be associated with survival in certain studies,[10,11,15] whereas others have reported it as not significant.[16] A short time interval to recurrence from initial BC to MBC (<24 months) has been reported to be associated with decreased survival[14] in some studies but was not significant in other studies.[15] De novo MBC has been associated with survival in HER2-positive patients.[17] However, it had variable results in terms of survival in other subsets of MBC patients.[14]

Because much of what is known of features associated with survival in MBC comes from analyses of large national databases, several variables that are not readily available in these databases have not yet been well investigated. For instance, there is little known about the effects of partner status, employment status, and income on survival in MBC. In addition, the effects of clinical diagnoses such as hypertension and Charlson Comorbidity Index (CCI) have been difficult to assess and control for in previous studies. MBC patients' baseline comorbidities as well as socioeconomic factors influence prognosis[18] and high CCI is a known risk factor for worse overall BC survival.[19,20]

African American race has also been linked to poor survival in many studies in HER2-positive MBC[13] as well as in other subsets of MBC patients.[11,12] Data from large national databases are difficult to control for social determinants of health and patient comorbidities to truly understand the reasons why race is associated with poorer survival. Moreover, tumor biology differs with different racial backgrounds that might also affect prognosis.[18,21]

Previous studies have limited and often lack data on socioeconomic variables as well as patients' baseline comorbidities. In addition, there is ongoing debate regarding certain characteristics such as HER2-positive status, patient age, de novo MBC, and time interval between initial BC and MBC diagnosis and their associations with MBC survival. To address limitations in previous studies, we used data from patients seen at a large, urban BC program in the United States to identify clinicopathologic and socioeconomic features associated with survival at the time of MBC diagnosis.

Patients and Methods

Study Population

The current study was a retrospective analysis of a large BC program in a cancer center in western Pennsylvania, United States. The center has an ongoing MBC database of >1400 women with MBC. The database was created in 1999 and is designed to capture demographic, clinical (including tumor characteristics), and symptom information of women who underwent routine MBC clinical care at our BC program. The start date of January 1999 reflects the temporal demarcation of routine HER2 testing and the commercial availability and routine clinical use of trastuzumab in the treatment of HER2-positive BC. In total there are 38 different baseline characteristics, demographic, and historical items captured for each subject in the database with 15 variables abstracted monthly. Variables abstracted monthly include treatment, response to treatment, reason for treatment change, and supportive therapies.

In January 2018, we evaluated the database for long-term MBC survivors (≥5-year survival from date of MBC diagnosis) and short-term MBC survivors (≤2-year survival from date from MBC diagnosis) and identified n = 122 and n = 191 subjects, respectively. Short-term survival was defined as ≤2 years from date of MBC diagnosis to be just below the median survival time. Long-term survival was defined as ≥5 years because only a small percentage of women survive >5 years. This is consistent with previous studies, which also have used this definition.[7,9,22] These subjects were included in the current analyses. Women included in the database (n = 1425) who did not meet long-term or short-term survivor criteria were excluded.

Data Collection and Variables

Clinical, pathologic, and socioeconomic patient characteristics were abstracted from medical records, and included: overall survival (OS) after initial BC diagnosis and after MBC diagnosis, age at initial BC diagnosis and at MBC diagnosis, time between initial BC and MBC diagnosis, year of initial diagnosis, body mass index (BMI), race, partner status at MBC diagnosis, employment status at MBC diagnosis, household income, history of hypertension, menopausal status at initial BC diagnosis, CCI at MBC diagnosis, tumor receptor status (estrogen receptor [ER], progesterone receptor [PR], HER2) at initial BC diagnosis, tumor stage at initial BC diagnosis, tumor type (ductal, lobular, other) at initial BC diagnosis, and site(s) of initial metastases. These variables were chosen because they are all potential prognostic features and were available at the time of MBC diagnosis.

If information on menopausal status was missing from the medical records, women were classified as premenopausal if younger than 45 years at initial BC diagnosis and postmenopausal if older than 55 years; menopausal status was designated as missing if between 45 and 55 years of age. ER and PR status was defined as positive if ≥10% positive staining for ER and PR and defined as negative if <10% positive staining for ER and PR. HER2 status was determined using immunohistochemistry and, if equivocal fluorescence in situ hybridization analysis. Annual household income was determined according to patient's zip code categorization in US Census data. Year of initial diagnosis ranged from 1999 to 2017. To account for longitudinal improvements in supportive therapies for MBC, patients were grouped into 3 categories of 5- to 7-year time intervals: 1999 to 2004, 2005 to 2010, and 2011 to 2017. Throughout these time periods there were some improvements in further medical treatments for MBC as well as in improvements in palliative and supportive care services available for MBC patients.

Statistical Analyses

Differences between long-term and short-term MBC survivors were assessed using *t* tests or Wilcoxon–Mann–Whitney tests for continuous variables and χ^2 tests or Fisher exact tests for categorical variables. In addition, odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for long-term survival were calculated

Table 1 Clinical, Pathological, and Socioeconomic Characteristics of Long-Term and Short-Term Survivors

Variable	Long-Term Survivors (n = 122)[a]	Short-Term Survivors (n = 191)[a]	P[b]
Age at Initial Dx, Years	51.4 ± 13.0	55.8 ± 13.8	.006
Age at Metastatic Dx, Years	53.2 ± 12.7	57.8 ± 13.6	.003
Overall Survival, Years	9.8 ± 3.4	3.0 ± 2.1	<.0001
Survival After MBC Dx, Years	8.0 ± 2.5	1.0 ± 0.6	<.0001
Time Between Initial Dx and MBC Dx, Months	21.5 ± 28.4	24.1 ± 25.1	.04
Year of Initial Diagnosis			<.0001
1999-2004	66 (54.1)	69 (36.1)	
2005-2010	55 (45.1)	84 (44.0)	
2011-2017	1 (0.8)	38 (19.9)	
Body Mass Index	28.4 ± 6.4	30.0 ± 7.5	.11
Race			.43
White	114 (93.4)	170 (90.9)	
Black	8 (6.6)	17 (9.1)	
Partnered, Yes	85 (70.3)	110 (58.8)	.04
Employed, Yes	55 (46.6)	79 (44.1)	.67
Household Income, USD	57,615 ± 19,721	52,740 ± 16,642	.03
History of Hypertension, Yes	36 (30.8)	62 (36.5)	.32
Menopausal Status			.01
Premenopausal	54 (52.9)	61 (37.2)	
Postmenopausal	48 (47.1)	103 (62.8)	
Charlson Comorbidity Index			.03
<10	107 (93.4)	143 (83.6)	
≥10	8 (7.0)	28 (16.4)	
ER-Positive, Yes	94 (77.1)	101 (53.4)	<.0001
PR-Positive, Yes	72 (59.5)	73 (39.3)	.0005
HER2-Positive, Yes	57 (50.0)	47 (24.9)	<.0001
Triple-Negative, Yes	7 (5.8)	64 (33.7)	<.0001
De Novo MBC, Yes			<.0001
Yes	55 (48.3)	46 (24.7)	
No	59 (51.8)	140 (75.3)	
Stage at Initial Dx			.0002
I	6 (5.3)	20 (10.8)	
II	32 (28.1)	61 (32.8)	
III	21 (18.4)	59 (31.7)	
IV	55 (48.3)	46 (24.7)	
Type of Breast Cancer			.54
Ductal	100 (84.8)	153 (87.9)	
Lobular	14 (11.9)	14 (8.1)	
Other	4 (3.4)	7 (4.0)	
Site of Metastases			.0007
Visceral + bone +/- non-visceral	14 (11.6)	40 (20.9)	
Bone with or without nonvisceral	51 (42.2)	43 (22.5)	
Nonvisceral	21 (17.4)	33 (17.3)	
Visceral with or without nonvisceral	31 (25.6)	53 (27.8)	
Brain with or without additional site	4 (3.3)	22 (11.5)	

Data are presented as meant ± SD or n (%).
Abbreviations: Dx = diagnosis; ER = estrogen receptor; MBC = metastatic breast cancer; PR = progesterone receptor.
[a]Numbers do not always add up to the total number of short-term survivors or long-term survivors because of missing information.
[b]The *t* test or Wilcoxon–Mann–Whitney test for continuous and χ^2 test or Fisher exact test for categorical variables.

Table 2 Results From the Multivariate Analyses[a]

Variable	OR	95% CI	Adjusted for[b]
Age at Initial Diagnosis	0.97	0.95-1.00	ER, PR, and HER2 status, de novo, and CCI
Age at Diagnosis of Metastases	0.97	0.95-1.00	ER, PR, and HER2 status, de novo, and CCI
Household Income (Above vs. Below Mean[c])	1.37	0.77-2.41	Age, ER, PR, and HER2 status, de novo, and CCI
Partner Status (Yes vs. No)	1.38	0.74-2.58	Age, ER, PR and HER2 status, de novo, and CCI
Menopausal Status (Pre- vs. Post)	1.96	1.02-3.79	ER, PR, and HER2 status, de novo, and CCI
CCI (≥10 vs. <10)	0.37	0.12-1.16	Age, ER, PR, and HER2 status, and de novo
ER-Positive (Positive vs. Negative)	3.74	1.72-8.14	Age, PR, and HER2 status, de novo, and CCI
PR-Positive (Positive vs. Negative)	1.11	0.55-2.26	Age, ER, and HER2 status, de novo, and CCI
HER2-Positive (Positive vs. Negative)	2.88	1.61-5.14	Age, ER, and PR status, de novo, and CCI
Triple-Negative (Yes vs. No)	0.12	0.05-0.29	Age, de novo, and CCI
De Novo MBC (Yes vs. No)	2.68	1.48-4.88	Age, ER, PR, and HER2 status, and CCI
Site of Metastases			Age, ER, PR, and HER2 status, de novo, and CCI
Bone with or without nonvisceral	1.0	Reference	
Visceral and bone with or without nonvisceral	0.18	0.07-0.47	
Nonvisceral	0.68	0.28-1.69	
Visceral with or without nonvisceral	0.88	0.40-1.87	
Brain with or without additional site	0.16	0.04-0.60	

Abbreviations: CCI = Charlson Comorbidity Index; ER = estrogen receptor; MBC = metastatic breast cancer; OR = odds ratio; PR = progesterone receptor.
[a]Long-term survivors were compared with short-term survivors, that is, the odds of being a long-term survivor is shown.
[b]Age is age at MBC diagnosis (continuous); ER status (positive, negative); PR status (positive, negative); HER2 status (positive, negative); CCI (≥10 vs. <10); and de novo (yes, no).
[c]Used mean annual household income of the total study population (USD$54,636).

using multivariate logistic regression models. All significance tests were 2-sided; *P* values <.05 were considered significant. All analyses were performed with use of the SAS statistical software package (SAS version 9.4, SAS Institute Inc, Cary, NC).

Results

Selected Characteristics of the Study Population

The study population included 122 long-term MBC survivors and 191 short-term MBC survivors. Selected characteristics are presented according to survivor status in Table 1. All patients included in this analysis were initially diagnosed with BC on or after January 1, 1999. All included patients were female, and most were white and originally diagnosed with ductal carcinoma. Mean OS after initial BC diagnosis for the long-term survivors was 9.8 (SD, 3.4; range, 5.1-17.9) years and 3.0 (SD, 2.1; range, 0.2-9.5) years for the short-term survivors. Mean survival after MBC diagnosis was 8.0 (SD, 2.5; range, 5.0-15.2) years and 1.0 (SD, 0.6; range, 0.8-2.1) years for, respectively, long-term survivors and short-term survivors.

Univariate Analyses

In univariate analyses of the demographic variables (ie, age at initial diagnosis, age at MBC diagnosis, time between initial and metastatic diagnosis, year of initial diagnosis, BMI, race, partner status, employment status, income status, and menopausal status), long-term survivors were significantly younger at initial BC diagnosis and at MBC diagnosis, more often partnered, had higher annual household income, and were more often premenopausal compared with short-term survivors. As noted in the Patients and Methods section, patients were categorized in 3 "year of initial diagnosis" groups. Long-term and short-term survivors differed significantly for year of initial diagnosis when taking all 3 groups into account (see Table 1). However, only 1 long-term survivor was initially diagnosed between 2011 and 2017, likely because follow-up time was not yet long enough to classify as long-term survivor when diagnosed in this time period. Limiting the analysis to only the first 2 groups (1999-2004 and 2005-2010), no significant difference between long-term and short-term survivors was observed ($P = .14$). Time between initial BC diagnosis and MBC diagnosis was significantly longer for short-term MBC survivors ($P = .04$; mean, 24.1 months vs. 21.5 months). This is likely because of the greater proportion of subjects diagnosed with de novo MBC in the long-term survival group. When limiting the analyses to subjects not diagnosed with de novo MBC, time between initial BC diagnosis and MBC diagnosis was significantly longer for long-term MBC survivors ($P = .005$; mean, 31.1 months vs. 41.5 months). No significant differences were observed for BMI, race, and employment status.

In univariate analyses of the clinicopathologic variables (ie, tumor receptor [ER, PR, HER2, triple-negative] status, de novo MBC, stage at initial diagnosis, tumor type, site of metastases, history of hypertension, and CCI) long-term survivors were significantly more often ER-positive, PR-positive, and HER2-positive at initial BC diagnosis and diagnosed with de novo MBC than short-term survivors. They also had significantly lower CCI and lower rates of visceral and brain metastases. Short-term survivors were significantly more often diagnosed with triple-negative initial BC compared with long-term survivors. No significant differences were observed for history of hypertension and initial BC tumor type (ductal, lobular, and other).

Multivariate Analyses

We subsequently conducted multivariate analyses to evaluate whether variables found to be significant in the univariate analyses remained significant after adjustment for potential confounding factors. ORs and corresponding 95% CIs were calculated for long-term survival using multivariate logistic regression models. Results are presented in Table 2 and as follows. Diagnosis of de novo MBC, premenopausal status, ER-positive status, and HER2-positive status remained significantly positively associated with long-term survival (respectively, OR, 2.68 [95% CI, 1.48-4.88]; OR, 1.96 [95% CI, 1.02-3.79]; OR, 3.74 [95% CI, 1.72-8.14]; OR, 2.88 [95% CI, 1.61-5.14]), whereas triple-negative status remained negatively associated with long-term survival (OR, 0.12 [95% CI, 0.05-0.29]). Using the most commonly observed metastasis sites as reference group (ie, bone with or without nonvisceral metastases), having visceral and bone metastases, and having brain metastases remained negatively associated with long-term survival (respectively, OR, 0.18 [95% CI, 0.07-0.47]; OR, 0.16 [95% CI, 0.04-0.60]).

Table 2 shows results for logistic regression models that included age at MBC diagnosis as a variable. We repeated these analyses with age at initial BC diagnosis included in the models instead and observed similar results (data not shown). Additional adjustment for the other factors that were found significantly associated with survival in the univariate analyses (eg, partner status) did not change the estimates significantly (ie, not more than 10%) and therefore, these variables were not included in the multivariate model (data not shown). Age at initial BC diagnosis, age at MBC diagnosis, partner status, household income, CCI, and PR status were no longer significantly associated with survival in the multivariate analysis.

Discussion

In this study, we retrospectively analyzed clinicopathologic and socioeconomic features in short-term survivors and long-term survivors with MBC. We found that de novo MBC was associated with improved survival in univariate analyses as well as after adjustment for age, tumor receptor status, and CCI. This is one of the first studies to show this association. A previous study reported that de novo HER2-positive MBC was associated with survival.[17] In another study, de novo status of MBC was associated with increased survival compared with patients with a short time to recurrence (<24 months) but had no survival difference compared with patients with longer time to recurrence (>24 months).[14] This is interesting and in line with findings from the current study, which showed that, when analyses were limited to subjects not diagnosed with de novo MBC, time between initial BC diagnosis and MBC diagnosis was significantly longer for long-term MBC survivors ($P = .005$; mean 31.1 months vs. 41.5 months). Shorter time interval to recurrence has been linked to decreased survival in some studies[10] and has been not significant in multivariate analyses in others.[15] In our study, de novo MBC status as well as longer time interval between initial and MBC diagnosis (when excluding de novo MBC patients) are both associated with long-term survival.

We hypothesize that the better survival outcomes for patients diagnosed with de novo MBC is because they have not previously been exposed to chemotherapy or hormone therapy. Therefore, the tumor is treatment-naive and has not yet accumulated somatic mutations and resistance to first-line MBC treatments. Supporting this, previous studies have shown that patients who received previous hormone therapy[12] and/or previous systemic adjuvant therapy[10,11] experienced worse survival than those who were treatment-naive at the start of MBC. Additionally, the biology of de novo MBC might be inherently less aggressive compared with the tumor biology of MBC patients with a history of early stage BC. Further studies comparing primary initial BC with corresponding MBC tissues as well as comparing recurrent MBC tissues with de novo MBC tissues for genomic and immunologic differences are needed to further investigate the biologic mechanism of action responsible for the positive association of de novo MBC with survival.

This study is one of the first studies to show that premenopausal status is associated with increased survival when adjusted for stage at initial diagnosis, tumor receptor status, and CCI. Age was associated with survival in univariate analysis. However, in multivariate analysis age at initial BC diagnosis and age at MBC diagnosis were no longer significantly associated with survival. A previous study of a population-based cancer registry in Stockholm, Sweden indicated that age younger than 60 years after the year 2000 conferred a survival benefit in MBC.[10] Analysis of data from 2010 to 2013 in the National Cancer Database showed survival benefit for age younger than 60 compared with age older than 60 years.[11] However, in a study using the New South Wales Central Cancer Registry (from 2001 to 2007), there was no survival difference between women with MBC who were younger than 40 years old and those who were older than 40 years old.[16] In older studies, younger age and premenopausal status were associated with worse survival outcomes.[23] In more recent studies (from the 2000s and onward), there seems to be mixed data regarding age and survival. It appears age might be a "u-shaped" variable and the group with the survival benefit might be women ages 40 to 60 years. This can explain the reason in our study that premenopausal status was associated with better survival in the univariate and multivariate analysis, although age at initial and age at MBC diagnosis was only associated with survival in the univariate but not in the multivariate analysis.

In multivariate analyses, we found that ER-positive and HER2-positive status were independently associated with increased survival and that triple-negative status was associated with decreased survival. Previous studies have shown that patients who were ER-negative experienced worse survival in MBC[12] whereas ER-positive and HER2-positive status, consistent with our results, were associated with improved MBC survival.[8] There is one recent study that did not show increased survival in patients with HER2-positive MBC, but this study investigated features associated with MBC survival of ≥10 years.[7] Triple-negative status in MBC is a well known predictor of poor survival.[7,8] Patients with the longest MBC survival are patients who are hormone receptor positive as well as HER2-positive, with the median survival historically reported at 34.4 months.[8]

Our results are in line with and support the current literature showing the importance and prognostic value in terms of survival for ER-positive and HER2-positive status as well as the poor survival outcomes for triple-negative status. Interestingly, our study did in fact have a small subset of triple-negative MBC patients who were long-term survivors (n = 7). This suggests that despite the overall poor prognosis for long-term survival with triple-negative disease (OR, 0.12 [95% CI, 0.06-0.30]), there are some unique features that led this small cohort of women to become long-term survivors.

Previous studies have shown that luminal subtype and family history of BC, with or without breast cancer genes 1 or 2 (*BRCA1* or *BRCA2*) mutation, confer an independent survival benefit regardless of tumor receptor status.[7,9] In addition, hormone receptor-negative patients' mutations in phosphoinositol-3-kinase-pathway genes and microenvironment maintenance have been reported associated with increased survival.[22] Genomic and immunologic studies on these triple-negative patients' initial and MBC tissues can help to further elucidate the factors responsible for long-term survival of triple-negative patients.

Our results are also consistent with previous literature regarding sites of metastases and survival. This study showed site of initial metastasis was associated with survival in MBC whereas long-term survivors have less visceral and less brain metastases compared with short-term survivors. In the multivariate analyses, visceral and bone metastases and brain metastases were inversely associated with survival. Previous studies have shown similar results showing site of metastases was associated with survival, whereas patients with MBC with visceral metastases and brain metastases had worse outcomes.[10,11]

We found in the univariate analyses that positive partner status was associated with survival. However, in the multivariate analyses this association was no longer significant. A previous large study of 1020 MBC patients reported that having never been married was associated with poor survival using a multivariate model.[12] In this report, medical records "partner" status was classified as a dichotomous legally "married," rather than the broader category of "partnered" according to patient report. In that context the partner status of the patients represented in the older medical records might be under-reported. Future research is needed to study the effects of partner status with a consistent definition on survival in MBC. In particular, this is important because if not having a partner is associated with decreased survival than extra support services could be offered to these patients to help improve survival.

In this study, race (white or black) was not associated with survival in the univariate analysis but we had poor representation of black patients and, therefore, were underpowered to find an association. Most of our study population was white with 93.4% white patients in the long-term survivor arm and 90.9% white patients in the short-term survivor arm. National Cancer Database data from 2010 to 2013 determined that race (white vs. African American) had a significant effect on survival.[11] Another large study showed poorer survival in MBC for patients who were African American.[12] It has also been shown that in HER2-positive MBC, black patients have significantly lower overall and progression-free survival.[13]

Higher median household income was also found associated with survival in our study in univariate analyses. However this association did not remain significant in the multivariate analysis. There is very limited literature on the effects of income on survival in MBC. Future research on this topic with more sophisticated geospatial analysis measuring neighborhood deprivation and not merely income is necessary.

Strength and Limitations

The strengths of this study are that we were able to collect and analyze data on a large number of demographic, clinicopathologic, and socioeconomic variables that might influence survival in MBC and had long-term follow-up of subjects diagnosed with BC. An additional strength of this study is that it examined variables associated with survival in an era in which anti-HER2 therapy was readily available. Limitations include the relatively small study population and poor representation of minority populations. In addition, it should be noted that multiple comparisons might lead to chance findings.

Conclusion

In this study we aimed to find which clinicopathologic and socioeconomic features were associated with survival in MBC. This study is one of the first to show that de novo MBC and premenopausal status are associated with survival in MBC after adjustment for potential confounders. In addition, this study showed that ER-positive and HER2-positive status were associated with increased survival and that triple-negative status was associated with decreased survival. Brain metastases and visceral with bone metastases were associated with worse survival. This study also showed an association with income and partner status with survival in the univariate analyses. These findings can easily be applied to clinical practice to help predict the length of survival at MBC diagnosis. More studies, including large multicenter prospective cohort analyses are needed to confirm our results regarding the survival benefit de novo MBC confers. Future research investigating genomic and immunologic differences as well as social determinants of health among MBC patients will help to further elucidate additional features associated with survival.

Clinical Practice Points

- Tumor receptor status (ER-positive and HER2-positive) was associated with long-term survival in MBC whereas triple-negative status was associated with decreased survival.
- Premenopausal status was associated with long-term survival in MBC when adjusted for CCI and tumor receptor status. However, age at initial BC diagnosis and age at MBC were no longer significantly associated with survival after adjustment for CCI and tumor receptor status.
- Diagnosis of de novo MBC was associated with long-term survival in MBC when adjusted for age, tumor receptor status, and CCI.
- Brain metastases and visceral coupled with bone metastases and were inversely associated with MBC survival.
- Partner status and income were associated with survival in MBC in univariate analyses but were no longer significant after adjustment for potential confounders.

Disclosure

Adam Brufsky, MD, PhD is a consultant for Eisai, Roche, Lilly, Novartis, Pfizer, Agendia, Myriad, Celgene, and Sandoz.

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