HHS Public Access

Author manuscript

Med Oncol. Author manuscript; available in PMC 2015 October 07.

Published in final edited form as:

Med Oncol. 2011 September ; 28(3): 738–744. doi:10.1007/s12032-010-9526-z.

Medullary carcinoma of the breast: a population-based perspective

Steve R. Martinez,
Department of Surgery, University of California Davis, Davis, CA, USA

Division of Surgical Oncology, University of California Davis, Davis, CA, USA

UC Davis Cancer Center, 4501 X Street, Suite 3010, Sacramento, CA 95817, USA

Shannon H. Beal,
Department of Surgery, University of California Davis, Davis, CA, USA

Robert J. Canter,
UC Davis Cancer Center, 4501 X Street, Suite 3010, Sacramento, CA 95817, USA

Steven L. Chen,
UC Davis Cancer Center, 4501 X Street, Suite 3010, Sacramento, CA 95817, USA

Vijay P. Khatri, and
UC Davis Cancer Center, 4501 X Street, Suite 3010, Sacramento, CA 95817, USA

Richard J. Bold
UC Davis Cancer Center, 4501 X Street, Suite 3010, Sacramento, CA 95817, USA

Steve R. Martinez: steve.martinez@ucdmc.ucdavis.edu

Abstract

Prognostic factors specific to medullary carcinoma of the breast (MCB) are unknown. Our objective was to identify patient and tumor factors predictive of overall survival (OS) in a large cohort of MCB patients. The Surveillance, Epidemiology, and End Results database was used to identify patients with MCB diagnosed from 1988 to 2004. Patient, tumor, and treatment factors were compared by univariate analysis via the Kaplan–Meier method and survival differences detected using the log-rank test. A multivariate Cox proportional hazards model controlled for patient age, race, type of surgery, radiotherapy, tumor size, number of lymph node metastases (LNM), lymph node yield (LNY), estrogen receptor (ER) and progesterone receptor (PR) status, and extent of disease. On univariate analysis of 3,348 patients, factors influencing OS included age, race, tumor size, ER status, type of surgery, radiotherapy, LNM, LNY, and extent of disease ($P < 0.001$). On multivariate analysis, advancing age ($P < 0.001$), black race ($P < 0.001$), regional metastases ($P < 0.001$), distant metastases ($P < 0.001$), increasing tumor size ($P < 0.001$), ER positivity ($P = 0.003$), and increasing LNM ($P < 0.001$) were associated with decreased OS. An OS benefit was seen in PR-positive patients ($P = 0.002$) and in those with increasing LNY ($P < 0.001$). Even among node-negative patients, increasing LNY was associated with improved OS ($P < 0.001$). Tumor size, LNM, regional and distant metastases, PR status, age, and race are

Correspondence to: Steve R. Martinez, steve.martinez@ucdmc.ucdavis.edu.

important prognostic factors in MCB. ER positivity was associated with decreased OS, which may reflect inaccuracy in diagnosing MCB or a significant biologic variant. The improved OS seen with increasing LNY in node-negative patients suggests MCB may be currently understaged.

Keywords

Medullary carcinoma of the breast; SEER; Prognosis; Survival

Introduction

Only 3–5% of all breast cancers are characterized as medullary carcinoma of the breast (MCB). MCB is distinguished by prominent (>75%) syncytial growth, well-circumscribed margins, nuclear pleomorphism, and a diffuse lymphoid infiltrate an absence of an intraductal component or microglandular features [1]. Several known poor prognostic factors are common to MCB, including large tumor size, high nuclear grade, and hormone receptor negativity. Despite this, MCB has superior survival compared to infiltrating ductal carcinoma, with 10-year survival rates up to 84% [1–4].

Prognostic factors specific to MCB are relatively unknown. Determination of these factors is important to identify patients at greatest risk for disease recurrence and death, as these patients may benefit from more aggressive treatment. Our objective was to identify patient- and tumor-specific factors influencing survival in a large cohort of patients with MCB.

Methods

Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute. All histologically confirmed cases of MCB identified in the SEER database inclusive of years 1988 through 2004 were eligible. We excluded patients with known secondary cancers and those identified by death certificate or autopsy. Characteristics of the SEER database, including the registries represented and the data fields included, have been reported by our group previously [5–7].

Univariate estimates of survival were made for known and suspected prognostic variables using the Kaplan–Meier method; we compared survival curves using the log-rank test. Variables subjected to univariate analysis included patient age (≤50 years or >50 years), sex, race/ethnicity (white, black, Hispanic, Asian, Native American), tumor grade (I–II, III–IV), tumor size (≤20 vs. >20 mm), lymph node yield (LNY median split at ≤13, >13), lymph node status (LNS, positive vs. negative), type of surgery (none, lumpectomy, mastectomy, lymph node dissection only, surgery not otherwise specified), radiation (yes, no), estrogen receptor (ER) and progesterone receptor (PR) status (positive, negative, equivocal), and extent of disease (local, regional, metastatic). We constructed Cox proportional hazards models that included all variables from the univariate analysis regardless of statistical significance, with the exception of sex; too few male patients were in our study to be included in the multivariate analysis. Age, tumor size, LNY, and number of lymph node metastases (LNM) were analyzed as continuous variables. Survival was calculated as the number of completed months between the date of diagnosis and whichever occurred first:

date of death, date last known to be alive, or 31 December 2004. The survival endpoint for the present study was overall survival (OS). Patients who were lost to follow-up or survived beyond 31 December 2004 were coded as censored observations. The remaining variables were analyzed as categorical or ordinal variables as appropriate. Analyses were conducted using STATA version 11 (StataCorp, College Station, Texas).

Results

Patient, tumor, and treatment characteristics

Patient and tumor characteristics are presented in Table 1. Briefly, our population included 3,348 patients with MCB. Of these, the median age was 50 years. Most patients were white (72%) women (99.9%). SEER categorizes the extent of disease into three broad stages: localized (disease confined to the breast), regional (disease confined to regional lymph nodes), and metastatic (disease spread to distant sites). Most patients (97.8%) had local or regional disease at the time of diagnosis. The median tumor size was 22 mm. The majority of patients had tumors that were ER and PR negative (56.8 and 58.4%, respectively); a fourth of patients had incomplete data regarding ER and PR status. Tumor grade was high (III–IV) in 50.7% of patients and unknown in 43.2%. Lymph nodes were not examined in 7% of patients and the number of lymph nodes examined was unavailable in another 2%. Of those with complete lymph node information, the median LNY was 13. Overall, two-thirds of patients (71.7%) had no lymph node metastases. Less than 1% of patients received no surgical treatment; 98.6% of patients received either lumpectomy (55.1%) or mastectomy (43.5%). The majority of patients did not receive adjuvant radiation therapy (51.2%).

Survival analysis: entire population

For the population as a whole, the 10-year OS rate was 78%. Log-rank assessments of survival differences between or among the survival curves are reported in Table 1. Sex, tumor grade, and PR status did not achieve significance. All remaining variables demonstrated differences significant at the $P < 0.001$ level.

For patients >50 years old, 10-year survival was 16.6% lower than that of patients <50 years old ($P < 0.001$). Ten-year survival for blacks was 69.6% compared to 79.8% for whites. Patients with regional and distant metastases had 10-year survival rates of 68.1 and 25.0%, respectively. Tumors confined to the breast, however, were associated with an 83.4% 10-year survival. Ten-year survival was 73.3% for tumors >22 mm compared to 82.8% for those ≤22 mm. Ten-year survival rates were 70.3% vs. 80.8% in ER-positive and ER-negative patients, respectively. We report 10-year survival rates of 67.5% for those with LNM and 81.9% for those without LNM. Patients with a LNY > 13 had an 8.9% survival advantage at 10 years over patients in which 13 or fewer lymph nodes were examined. A trend toward improved OS was seen in patients who underwent lumpectomy (10 year survival 82.3%) compared to those who had a mastectomy (10 year survival 73.7%). Similarly, patients receiving radiotherapy had improved OS (10 year survival 80.5%) compared to those who did not (10 year survival 75.7%) on univariate analysis.

Results of the multivariate analysis of all patients are summarized in Table 2. With age as a continuous variable, this survival difference persisted on multivariate analysis (HR 1.04, CI: 1.04–1.05, $P < 0.001$). Racial differences were also found in our cohort, with blacks faring worse on multivariate analysis (HR 1.84, CI: 1.52–2.25, $P < 0.001$).

The poorer prognosis in patients with regional (HR 1.60, CI: 1.32–1.93, $P < 0.001$) and distant metastasis (HR 4.36, CI: 2.66–7.12, $P < 0.001$) was maintained on multivariate analysis. Increasing tumor size was associated with a higher risk of death (HR 1.01, CI: 1.01–1.01, $P < 0.001$). We identified ER-positive status as predicting a poorer prognosis (HR 1.51, CI: 1.15–1.98, $P = 0.003$). A survival benefit was observed in PR-positive patients on multivariate analysis (HR 0.61, CI: 0.44–0.83, $P = 0.002$). A worse OS was seen in patients with increasing numbers of positive lymph nodes (HR 1.10, CI: 1.07–1.12, $P < 0.001$). Increasing LNY was associated with lower rates of mortality (HR 0.96, CI: 0.95–0.97, $P < 0.001$) even among node-negative patients (HR 0.96, CI: 0.94–0.97, $P < 0.001$). Lumpectomy did not confer a survival advantage relative to those receiving mastectomy (HR 0.94, CI: 0.76–1.16, $P = 0.54$). No survival benefit to the receipt of RT was noted (HR 0.86, CI: 0.70–1.04, $P = 0.14$).

Survival analysis: non-metastatic patients undergoing lumpectomy or mastectomy

We performed a subset multivariate analysis on our patients. This analysis excluded patients with known metastatic disease and further included only those patients treated with lumpectomy or mastectomy for their primary tumor. The subset population consisted of 3,125 patients. Results of the subset analysis are reported in Table 3. Factors associated with an increased risk of mortality included increased patient age (HR 1.04, CI: 1.04–1.05; $P < 0.001$), black race (HR 1.95, CI: 1.60–2.37; $P < 0.001$), increasing tumor size (HR 1.01, CI: 1.01–1.02; $P < 0.001$), increasing number of metastatic nodes (HR 1.12, CI: 1.10–1.14; $P < 0.001$), ER positivity (HR 1.47, CI: 1.12–1.94; $P = 0.006$), and ER status unknown (HR 5.55, CI: 1.71–17.99; $P = 0.004$). Factors associated with a decreased risk of mortality included increasing LNY (HR 0.96, CI: 0.95–0.97; $P < 0.001$), PR positivity (HR 0.69, CI: 0.50–0.94; $P = 0.02$), and PR status unknown (HR 0.21, CI: 0.07–0.68; $P = 0.009$).

Discussion

This is the largest analysis of MCB to date. Our study demonstrated that MCB shares several prognostic factors with infiltrating ductal carcinoma. Among these are advancing age, increasing tumor size and number of lymph node metastases, and the presence of distant metastases all of which decrease OS. We also identified several factors uniquely predictive of survival in MCB.

Lymph node status is the most important factor predicting survival in patients with invasive ductal and lobular carcinoma. The number of LNM not only correlates with OS but is an important determinant of treatment. Patients receiving mastectomy are routinely offered chest wall radiation when LNM are ≥4. The significance of LNM in MCB was previously reported [1, 8–10]. Reinfuss et al. demonstrated a poorer 10-year survival in MCB patients with LNM (58.8%) compared to those without LNM (97.1%), but identified no other significant prognostic factors [10]. In the largest series prior to the present study, Fisher et

al. compared the effect of LNM in MCB by categorizing patients into those with and without LNM. Ten-year survival rates for those without LNM were 68.7–80.2%. Patients with LNM not receiving chemotherapy had 10-year survival rates of 44.4–50.0% [9]. Our OS was similar, with 10-year survival rates of 67.5 and 81.9% in those with and without LNM, respectively. Ridolfi et al. identified a trend of poorer OS in MCB patients with axillary LNM, but this did not reach statistical significance [1]. To the best of our knowledge, no other studies have assessed LNY as a prognostic factor for MCB. We found that increasing LNY, even among node-negative patients, was associated with improved survival. This suggests significant understaging in patients with lower LNY.

Ridolfi et al. showed tumor size ≥3 cm to be associated with a 10-year survival of 55% while tumors <3 cm had 10-year survival rates of 92% [1]. In our study, the median size of tumors was 22 mm. We categorized patients as having tumors that were 22 mm or less vs. those that were >22 mm. Ten-year survival for those with smaller tumors was 83% compared to 73% for those with tumors >22 mm. Tumor size continued to be a significant prognostic factor on multivariate analysis with a 1% increased risk of death associated with each increasing mm in tumor size.

Only 1.1% (n = 37) of our patient population had distant metastases at diagnosis. The 10-year survival in this group was 25.0%. As expected, distant metastases predicted a worse OS. To the best of our knowledge, this is the first description of OS in this group. Racial and ethnic disparities in treatment and outcomes have been reported extensively in invasive ductal and lobular breast carcinoma, even after adjusting for access to health care, treatment differences, and socioeconomic status [11–13]. In our study, black patients had an 84% increased risk of death relative to their white counterparts. To our knowledge, this is the first report of racial disparities in survival for patients with MCB. While our study could not adjust for disparities in access to health care or socioeconomic status, we were able to control for other potential tumor-related, treatment-related, and patient-related confounders in our multivariate analysis. The survival disadvantage attributed to black patients may not be due to breast-specific factors, as our outcome measure for this study was OS.

ER positivity is rare in MCB [10, 14–16]. In our study, only 547 (16.3%) patients had ER-positive tumors. Unlike infiltrating ductal and lobular carcinomas, ER positivity in MCB was associated with poorer OS. This may reflect a biologic variant. Numerous microarray studies based on gene clustering have described distinct molecular profiles of breast cancer and classified them into basal-like, erbB-2, and luminal/ER-positive types to further define the biologic behavior and prognosis of breast carcinomas [17, 18]. Webster et al. identified a subgroup of ER-positive patients with a significantly worse prognosis with gene clustering [7]. Oh et al. similarly identified two subgroups of patients within the luminal/ER-positive subtype and demonstrated decreased OS in the group that overexpressed genes of increased proliferation and antiapoptosis [19]. Therefore, ER positivity does not necessarily indicate a survival advantage but is likely influenced by other biologic determinants. Pinto et al. reported no survival difference in patients with ER-positive/Her-2/neu-positive carcinomas compared to the ER-negative/Her-2/neu-positive group, suggesting a hormone therapy resistance [20]. These studies indicate that gene interplay can modify the prognostic effects of previously studied factors such as ER status.

Interestingly, although the rate of PR-positive tumors was low in our study (14%), patients with PR-positive tumors had superior rates of OS, which is in accordance with the pattern seen in patients with invasive ductal and lobular carcinoma, but not previously reported in the MCB literature.

We performed an additional subanalysis of patients that excluded those with metastatic disease. This analysis was performed to remove any potential bias in the survival analysis contributed by these patients with documented poor survival. We also excluded patients who did not undergo surgery or who had undefined surgical procedures. Only patients who received lumpectomy or mastectomy were included. All trends noted in the analysis including all patients were also seen in the subanalysis of non-metastatic lumpectomy and mastectomy patients.

MCB represents <5% of all breast cancers in the U.S. and is difficult to study prospectively. We used the SEER database both to study a larger cohort of patients with MCB and to better capture national trends in treatment and outcomes. The limitations of SEER data are recognized. Histologic diagnoses may be less consistent in SEER compared to studies with individual pathologic review of specimens. In a reevaluation of 135 MCB tumors from 1977 to 1982, interobserver and intraobserver agreement rates of 72% and 63–77% were noted, respectively [21]. Using three different sets of diagnostic criteria for MCB, consensus could be reached on a MCB diagnosis in 70, 87, and 96% of cases, respectively [22]. Many studies have shown survival rates of atypical MCB to fall between that of typical MCB and infiltrating ductal carcinoma [1, 3, 9]. The worse overall survival of ER-positive tumors may be reflective of a stronger prognostic effect of atypical histology, but this cannot be confirmed using SEER data. Similarly, quality control with respect to the adequacy of surgery is difficult to determine. Finally, we have no information from SEER regarding the use of adjuvant chemotherapy or hormonal therapy, which can influence OS. SEER data collection began in 1973, but we chose to limit our analysis to cases diagnosed from 1988 to 2004 to take advantage of more modernized surgical care and more complete data fields. This may impede our ability for long-term follow-up in a disease that has a 10-year OS of 84– 92% reported by others [1, 3, 10, 16], and 78% in our current study.

Conclusion

Our objective was to identify patient- and tumor-specific factors influencing survival in a large cohort of patients with MCB. Many prognostic factors relevant to invasive ductal and lobular breast carcinomas are important for MCB as well. Among these, we have identified a dramatic disparity in OS among black patients with MCB. ER positive MCB patients demonstrate poorer OS compared to their ER-negative counterparts. Furthermore, our findings indicate that MCB is likely being currently understaged due to inadequate lymphadenectomy. Even among nodenegative patients, increasing LNY improved survival.

Acknowledgments

Supported by Grant Number UL1 RR024146 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NNCRR or NIH.

Information on NCRR is available at http://www.ncrr.nih.gov/. Information on Re-engineering the Clinical Research Enterprise can be obtained from http://nihroadmap.nih.gov/clinicalresearch/overview-translational.asp.

References

1. Ridolfi RL, Rosen PP, Port A, Kinne D, Mike V. Medullary carcinoma of the breast: a clinicopathologic study with 10 year follow-up. Cancer. 1977; 40(4):1365–1385. [PubMed: 907958]
2. Bloom HJ, Richardson WW, Field JR. Host resistance and survival in carcinoma of breast: a study of 104 cases of medullary carcinoma in a series of 1, 411 cases of breast cancer followed for 20 years. Br Med J. 1970; 3(5716):181–188. [PubMed: 5448777]
3. Rapin V, Contesso G, Mouriesse H, Bertin F, Lacombe MJ, Piekarski JD, Travagli JP, Gadenne C, Friedman S. Medullary breast carcinoma. A reevaluation of 95 cases of breast cancer with inflammatory stroma. Cancer. 1988; 61(12):2503–2510. [PubMed: 2835145]
4. Vu-Nishino H, Tavassoli FA, Ahrens WA, Haffty BG. Clinicopathologic features and long-term outcome of patients with medullary breast carcinoma managed with breast-conserving therapy (BCT). Int J Radiat Oncol Biol Phys. 2005; 62(4):1040–1047. [PubMed: 15990007]
5. Beal SH, Martinez SR, Canter RJ, Chen SL, Khatri VP, Bold RJ. Survival in 12,653 breast cancer patients with extensive axillary lymph node metastasis in the anthracycline era. Med Oncol. [Epub ahead of print].
6. Chen SL, Martinez SR. The survival impact of the choice of surgical procedure after ipsilateral breast cancer recurrence. Am J Surg. 2008; 196(4):495–499. [PubMed: 18809050]
7. Webster LR, Lee SF, Ringland C, Morey AL, Hanby AM, Morgan G, Byth K, Mote PA, Provan PJ, Ellis IO, et al. Poor-prognosis estrogen receptor-positive breast cancer identified by histopathologic subclassification. Clin Cancer Res. 2008; 14(20):6625–6633. [PubMed: 18927304]
8. Black CL, Morris DM, Goldman LI, McDonald JC. The significance of lymph node involvement in patients with medullary carcinoma of the breast. Surg Gynecol Obstet. 1983; 157(6):497–499. [PubMed: 6648768]
9. Fisher ER, Kenny JP, Sass R, Dimitrov NV, Siderits RH, Fisher B. Medullary cancer of the breast revisited. Breast Cancer Res Treat. 1990; 16(3):215–229. [PubMed: 2085673]
10. Reinfuss M, Stelmach A, Mitus J, Rys J, Duda K. Typical medullary carcinoma of the breast: a clinical and pathological analysis of 52 cases. J Surg Oncol. 1995; 60(2):89–94. [PubMed: 7564387]
11. Chlebowski RT, Chen Z, Anderson GL, Rohan T, Aragaki A, Lane D, Dolan NC, Paskett ED, McTiernan A, Hubbell FA, et al. Ethnicity and breast cancer: factors influencing differences in incidence and outcome. J Natl Cancer Inst. 2005; 97(6):439–448. [PubMed: 15770008]
12. Henson DE, Chu KC. Levine PH: histologic grade, stage, and survival in breast carcinoma: comparison of African American and Caucasian women. Cancer. 2003; 98(5):908–917. [PubMed: 12942556]
13. Newman LA, Mason J, Cote D, Vin Y, Carolin K, Bouwman D. Colditz GA: African-American ethnicity, socioeconomic status, and breast cancer survival: a meta-analysis of 14 studies involving over 10, 000 African-American and 40, 000 White American patients with carcinoma of the breast. Cancer. 2002; 94(11):2844–2854. [PubMed: 12115371]
14. Ponsky JL, Gliga L, Reynolds S. Medullary carcinoma of the breast: an association with negative hormonal receptors. J Surg Oncol. 1984; 25(2):76–78. [PubMed: 6694404]
15. Silfversward C, Gustafsson JA, Gustafsson SA, Humla S, Nordenskjold B, Wallgren A, Wrange O. Estrogen receptor concentrations in 269 cases of histologically classified human breast cancer. Cancer. 1980; 45(8):2001–2005. [PubMed: 6245787]
16. Vo T, Xing Y, Meric-Bernstam F, Mirza N, Vlastos G, Symmans WF, Perkins GH, Buchholz TA, Babiera GV, Kuerer HM, et al. Long-term outcomes in patients with mucinous, medullary, tubular, and invasive ductal carcinomas after lumpectomy. Am J Surg. 2007; 194(4):527–531. [PubMed: 17826073]
17. Bertucci F, Finetti P, Cervera N, Charafe-Jauffret E, Mamessier E, Adelaide J, Debono S, Houvenaeghel G, Maraninchi D, Viens P, et al. Gene expression profiling shows medullary breast

cancer is a subgroup of basal breast cancers. Cancer Res. 2006; 66(9):4636–4644. [PubMed: 16651414]

18. Sorlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, Hastie T, Eisen MB, van de Rijn M, Jeffrey SS, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A. 2001; 98(19):10869–10874. [PubMed: 11553815]
19. Oh DS, Troester MA, Usary J, Hu Z, He X, Fan C, Wu J, Carey LA, Perou CM. Estrogen-regulated genes predict survival in hormone receptor-positive breast cancers. J Clin Oncol. 2006; 24(11):1656–1664. [PubMed: 16505416]
20. Pinto AE, Andre S, Pereira T, Nobrega S, Soares J. C-erbB-2 oncoprotein overexpression identifies a subgroup of estrogen receptor positive (ER+) breast cancer patients with poor prognosis. Ann Oncol. 2001; 12(4):525–533. [PubMed: 11398888]
21. Pedersen L, Holck S, Schiodt T, Zedeler K, Mouridsen HT. Interand intraobserver variability in the histopathological diagnosis of medullary carcinoma of the breast, and its prognostic implications. Breast Cancer Res Treat. 1989; 14(1):91–99. [PubMed: 2605345]
22. Gaffey MJ, Mills SE, Frierson HF Jr, Zarbo RJ, Boyd JC, Simpson JF, Weiss LM. Medullary carcinoma of the breast: interobserver variability in histopathologic diagnosis. Mod Pathol. 1995; 8(1):31–38. [PubMed: 7731939]

Table 1

Medullary breast cancer characteristics in 3,348 patients, SEER 1988–2004

Variable	*N* (%)	*P* value
Age		
≤50	1,713 (51.2)	<0.001
>50	1,635 (48.8)	
Sex		
Female	3,343 (99.9)	=0.31
Male	5 (0.1)	
Race/ethnicity		
White	2,410 (72.0)	<0.001
Black	660 (19.7)	
Asian	229 (6.8)	
Native American	33 (1.0)	
Other	16 (0.5)	
Extent of disease		
Local	2,283 (68.2)	<0.001
Regional	992 (29.6)	
Metastatic	37 (1.1)	
Unknown	36 (1.1)	
Size (mm)		
≤22	1,663 (49.7)	<0.001
>22	1,534 (45.8)	
Unknown	151 (4.5)	
Grade		
I–II	204 (6.1)	=0.92
III–IV	1,697 (50.7)	
Unknown	1,447 (43.2)	
ER status		
Negative	1,902 (56.8)	<0.001
Positive	547 (16.3)	
Equivocal	40 (1.2)	
Unknown	859 (25.7)	
PR status		
Negative	1,955 (58.4)	=0.14
Positive	470 (14.0)	
Equivocal	29 (0.9)	
Unknown	894 (26.7)	
Lymph node status (LNS)		
Negative	2,401 (71.7)	<0.001
Positive	947 (28.3)	
Lymph node examined (LNY)		

Variable	*N* (%)	*P* value
≤13	1,713 (51.2)	<0.001
>13	1,635 (48.8)	
Surgery		
Mastectomy	1,457 (43.5)	<0.001
Lumpectomy	1,845 (55.1)	
None	25 (0.7)	
LND only	8 (0.2)	
Surgery, NOS	13 (0.4)	
Radiation		
No	1,713 (51.2)	<0.001
Yes	1,513 (45.2)	
Unknown	122 (3.6)	

Table 2

Multivariate model of overall survival, all patients, SEER 1988–2004

Variable	Hazard ratio	95% Confidence interval	*P* value
Increasing age	1.04	1.04–1.05	<0.001
Race/ethnicity			
White	–		–
Black	1.84	1.52–2.25	<0.001
Asian	1.04	0.73–1.51	0.80
Native American	1.54	0.76–3.12	0.23
Extent of disease			
Local	–	–	–
Regional	1.60	1.32–1.93	<0.001
Metastatic	5.65	3.43–9.30	<0.001
Unknown	1.91	0.83–4.40	0.13
Tumor size (mm)	1.01	1.01–1.01	<0.001
Grade			
I–II	–	–	–
III–IV	1.03	0.71–1.48	0.88
Unknown	0.95	0.66–1.37	0.78
ER status			
Negative	–	–	–
Positive	1.51	1.15–1.98	0.003
Equivocal	0.88	0.36–2.19	0.79
Unknown	6.12	1.96–19.19	0.002
PR status			
Negative	–	–	–
Positive	0.61	0.44–0.83	0.002
Equivocal	0.53	0.23–1.25	0.15
Unknown	0.18	0.059–0.58	0.004
Number of lymph node metastases	1.10	1.07–1.12	<0.001
Lymph node yield	0.96	0.95–0.97	<0.001
Surgery			
Mastectomy	–	–	–
Lumpectomy	0.94	0.76–1.16	0.54
None	1.96	0.70–5.44	0.20
Node dissection only	***	***	***
Surgery NOS	2.33	1.02–5.33	0.04
Radiation			
No	–	–	–
Yes	0.86	0.70–1.04	0.14

Table 3

Multivariate model of overall survival, patients undergoing lumpectomy or mastectomy with no distant metastases, SEER 1988–2004

Variable	Hazard ratio	95% Confidence interval	*P* value
Increasing age	1.04	1.04–1.05	<0.001
Race/ethnicity			
White	–	–	–
Black	1.95	1.60–2.37	<0.001
Asian	1.03	0.71–1.49	=0.88
Native American	1.59	0.79–3.22	0.20
Tumor size (mm)	1.01	1.01–1.02	<0.001
Grade			
I–II	–	–	–
III–IV	1.12	0.77–1.63	0.56
Unknown	1.06	0.73–1.55	0.75
ER status			
Negative	–	–	–
Positive	1.47	1.12–1.94	0.006
Equivocal	0.91	0.37–2.27	0.85
Unknown	5.55	1.71–17.99	0.004
PR status			
Negative	–	–	–
Positive	0.69	0.50–0.94	0.02
Equivocal	0.67	0.26–1.71	0.40
Unknown	0.21	0.07–0.68	0.009
Number of lymph node metastases	1.12	1.10–1.14	<0.001
Lymph node yield	0.96	0.95–0.97	<0.001
Surgery			
Mastectomy	–	–	–
Lumpectomy	0.85	0.68–1.06	0.15
Radiation			
No	–	–	–
Yes	0.96	0.78–1.19	0.71