Recurrence in Stage I and II Triple-Negative Breast Cancer: Analysis of Clinicopathologic and Imaging Factors

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Research article

Keywords: Breast, triple-negative breast cancer, recurrence, mammography, ultrasonography, magnetic resonance imaging

Posted Date: August 6th, 2019

DOI: https://doi.org/10.21203/rs.2.12471/v1

Abstract

Background To describe the outcomes of patients with early stage triple-negative breast cancer (TNBC) and to investigate whether certain imaging and clinicopathologic factors were associated with recurrence in patients with early stage TNBC. Methods We identified stage I and II TNBC patients treated between 2009 and 2011. Data included patient and tumor characteristics, time of recurrence, and findings on mammography, ultrasonography, and magnetic resonance imaging (MRI). Kaplan-Meier method was used to estimate recurrence free survival and Cox proportional hazards model was used to determine the association between imaging and clinicopathologic factors and recurrence. Results The study included 702 patients with mean age of 49.0 years (range, 24–82 years) and mean follow-up of 61 months (range, 6 - 93 months). Overall, 115 (115/702, 16.4%) had recurrence. Clinicopathologic factors associated with recurrence included increasing tumor size, positive nodal status, ki-67 index more than 14, presence of lymphovascular invasion (LVI), mastectomy, and neoadjuvant or adjuvant chemotherapy. Imaging factors associated with recurrence included moderate or marked background parenchymal enhancement on MRI. After controlling for all potential confounders, tumor size, nodal status, LVI, and adjuvant chemotherapy were independently associated with recurrence. Conclusion Sixteen percent of patients with early stage TNBC experienced recurrence, with 3 and 5 year recurrence rates being 12.4% and 15.3%, respectively. Tumor size, nodal status, LVI, and adjuvant chemotherapy were independently associated with recurrence, while none of the imaging factors showed association.

Background

Triple-negative breast cancer (TNBC) is a heterogenous collection of breast cancers showing negativity for hormonal receptor markers and human epidermal growth factor receptor 2 (HER2) overexpression, and accounts for 12–17% of all breast cancers [1]. Although a remarkable histologic heterogeneity lies within the TNBC classification, there are distinguishing clinical features between TNBC and non-TNBC. TNBC shows an aggressive nature, poor prognosis, and unresponsiveness to targeted therapies [2], while the patterns of recurrence are also different. Many studies have reported higher recurrence rates in TNBC patients ranging 5.7% to 27%, compared to hormone receptor positive tumors [3]. The pattern of recurrence is difference in that the majority of recurrences of TNBC occur within the first 5 years of diagnosis while more than 50% of estrogen receptor (ER)-positive breast cancers recur between 5 and 10 years after the first surgery [4, 5]. Previous studies suggest that TNBC are at increased risk of developing locoregional recurrence regardless of the local therapies such as breast conserving operation, mastectomy, or axillary lymph node dissection [6, 7]. Furthermore, distant metastasis and mortality rate following locoregional recurrence is higher in TNBC compared to other subtypes [8].

Risk factors for recurrence in TNBC, such as increasing tumor size, positive nodal status, lymphovascular invasion (LVI), increasing stage, and type of chemotherapy, have been suggested by previous studies [9, 10]. A recent study showed that the absence of preoperative magnetic resonance imaging (MRI) and the presence of dense breast tissue at mammography were associated with an increased risk of recurrence in TNBC, while another study demonstrated that peritumoral edema was associated with worse recurrence-

free survival [11, 12]. However, to the best of our knowledge there has been no reported study evaluating the associations between the risk of recurrence and preoperative conventional imaging features, including mammography, ultrasonography (US), and MRI, for predicting recurrence in TNBC. In particular, this study is meaningful in that the population is limited to early stage TNBC patients who are expected to show relatively lower recurrence rates. Therefore, the purpose of this study was to describe the outcomes of patients with early stage TNBC and to investigate whether certain imaging and clinicopathologic factors are associated with recurrence in patients with early stage TNBC.

Methods

Study design

Our institutional review board approved this retrospective study, and the requirement for informed consent was waived. Eight hundred seventy-three consecutive patients with TNBC who underwent surgery between January 2009 and December 2011 were retrospectively identified. Patients were determined as having the TNBC subtype according to immunohistochemical staining. Positive staining for ER or progesterone receptor (PR) was defined as strong nuclear staining in at least 3/8 of the tumor cells examined. HER2 positivity was defined as a score of 3+ in immunohistochemical staining or HER2 gene amplification by fluorescence in situ hybridization. Out of 873 patients, 130 stage III or IV patients, 23 patients with unavailable preoperative images, three with a history of silicone breast injections, and two with a personal history of breast cancer were excluded. An additional 10 patients with less than 6 months' follow-up and three patients without clear medical record whether they received radiotherapy were excluded. Therefore, the final population cohort included 702 patients with TNBC. Patients were divided into groups according to whether they experienced recurrence or not.

Data collection

The data included clinicopathologic characteristics such as patient age, tumor size on final pathology specimen (T1 vs. T2), lymph node involvement (N0 vs. N1), histology (ductal vs. other), grade (I/II vs. III), ki-67 index, presence of LVI, presence of an extensive intraductal component (EIC), type of surgery (mastectomy vs. breast conserving operation), resection margin status, receipt of radiation therapy, and type of chemotherapy (adjuvant vs. neoadjuvant chemotherapy). Ki-67 cut-off value of 14 was adopted to distinguish between low and high Ki-67 expression which was used for subtyping immunohistochemistry-based breast cancer [13]. For mammographic features, breast density (non-dense vs. dense), presentation of the tumor (non-visible vs. asymmetry vs. mass), shape (oval/round vs. irregular), margins (circumscribed vs. not circumscribed), and the presence of malignant calcifications were evaluated. For US features, shape (oval/round vs. irregular), margins (circumscribed vs. not circumscribed), and posterior features were evaluated. For MRI features, background parenchymal enhancement (BPE), amount of fibroglandular tissue (FGT), presentation of the tumor (mass vs. non-mass), shape (oval/round vs. irregular), margins (circumscribed vs. not circumscribed), enhancement pattern (homogenous vs. heterogenous vs. rim), kinetics (persistent vs. plateau vs. washout), presence of

intratumoral necrosis, and T2 peritumoral edema were evaluated. Imaging findings were retrospectively reviewed by breast imaging specialists (H.J.E. and J.H.C., with 5 and 20 years of breast imaging experience, respectively). Breast cancer recurrence was classified either local (limited to the ipsilateral breast or chest wall and/or axillary, infraclavicular, or supraclavicular lymph nodes) or distant (metastasis to other parts of the body). The time to recurrence and sites of recurrence were recorded. Recurrent cancer was diagnosed clinically, radiologically, and/or pathologically. Patients were censored at the date of the last clinical contact.

Statistical analysis

Cox proportional hazards model was used to analyze the effect on recurrence-free survival by clinicopathologic variables (age, size and histology of the tumor, multiplicity, bilaterality, nodal status, histologic grade, ki-67 index, presence of LVI, presence of EIC, type of surgery, resection margn status, receipt of radiation therapy, type of chemotherapy) and imaging variables (breast density, presentation of the tumor, shape, margin, and the presence of malignant calcifications for mammographic features, shape, margin, and posterior features for US features, BPE, amount of FGT, presentation of the tumor, shape, margin, enhancement pattern, kinetics, presence of intratumoral necrosis, and T2 peritumoral edema for MRI features). Multivariable analysis in Cox proportional hazards model was performed by backward elimination considering variables with a p value of less than 0.2 in univariable analysis. The Kaplan-Meier method was used to estimate recurrence free survival. All variables were presented mean and standard deviation for continuous variables and number of case and percentages for categorical variables. Statistical analysis was performed using SAS 9.4 software (SAS Institutes, Cary, NC), and $p < 0.05$ was considered statistically significant.

Results

Patients

The study cohort included 702 patients with a mean age of 49.0 ± 10.9 years (range, 24–82 years) and a mean follow-up of 61 months (range, 6 - 93 months), with all the patients being Asian. The majority were originally diagnosed with invasive ductal carcinoma (637/702, 90.7%). There were 289 patients (289/702, 41.2%) with stage I disease and 413 patients (413/702, 58.8%) with stage II disease. Of the 702 patients, 621 received either adjuvant (548/702, 78.1%) or neoadjuvant chemotherapy (73/702, 10.4%). Most patients received radiation therapy (555/702, 79.1%) and breast conserving operation (557/702, 79.3%). The patient characteristics are summarized in Table 1.

Recurrence

Overall, 587 patients (587/702, 83.6%) had no evidence of recurrence, while 115 (115/702, 16.4%) had recurrence, including 38 (38/115, 33.0%) with locoregional recurrence, 42 (42/115, 36.5%) with distant recurrence, 19 (19/115, 16.5%) with contralateral breast cancer, and 16 (16/115, 13.9%) with recurrences in multiple sites.

Of the 38 locoregional recurrences, 25 were in the ipsilateral regional nodes, 12 in the ipsilateral breast, and 4 in the postmastectomy chest wall. In the 42 with distant recurrences, the lung was the most common site (n = 28), followed by bone (n = 10), brain (n = 9), and liver (n = 6). The mean time to recurrence was 26.8 months, with a range of 4–78 months. The 3 year recurrence rate was 12.4%, and the 5 year recurrence rate was 15.3% (Figure 1).

In the univariate analysis for recurrence, factors significantly associated with recurrence included increasing tumor size, positive nodal status, ki-67 index more than 14, presence of LVI, mastectomy, and neoadjuvant or no adjuvant chemotherapy. Compared with T1 patients, patients with an increased tumor size were more likely to have a recurrence, with hazard ratios (HR) of 1.92 and 6.75 for T2 and T3 tumors, respectively. Patients with positive axillary nodes also had a significantly higher risk of recurrence (HR = 1.92 for N1 tumors). Patients with recurrences were also more likely to have ki-67 index more than 14 (HR = 3.46), presence of LVI (HR = 3.27), received mastectomy (HR = 1.92), neoadjuvant chemotherapy (HR = 2.00), or to not have received adjuvant chemotherapy (HR = 1.79) (Table 1).

Imaging findings

Out of 702 patients, 692 (98.6%), 693 (98.7%), and 293 (41.7%) had available mammographic, US, and MRI examinations, respectively, for the radiologist to review. Imaging features of the subjects are summarized in Table 2. On mammography, tumors tended to present as a mass (586/692, 84.7%), with oval or round shape (295/586, 50.3%), with not circumscribed margins (477/586, 81.4%), and without microcalcifications (507/692, 73.3%). On US, tumors tended to present as an oval or round shaped mass (390/693, 56.3%), with not circumscribed margins (491/693, 70.9%), and with posterior acoustic enhancement (447/693, 68.8%). On MRI, tumors tended to present as a mass (276/293, 94.2%), with oval or round shape (179/276, 64.9%), not circumscribed margins (173/276, 62.7%), rim enhancement (140/293, 47.8%), washout kinetics (267/292, 91.4%), no intratumoral necrosis (176/293, 60.1%), and the presence of T2 peritumoral edema (191/293, 65.2%). In the univariate analysis for recurrence, imaging factors significantly associated with recurrence included moderate or marked BPE on MRI. Patients with moderate or marked BPE had a higher risk of recurrence, with a HR of 1.94 (Table 2, Figure 2,Figure 3). After controlling for all potential confounders in a multivariate anlalysis, increasing tumor size, positive nodal status, the presence of LVI, and not receiving adjuvant chemotherapy were independent associated with recurrence (Table 3).

Discussion

In this study, 16% of patients with early stage TNBC had recurrence, with the mean time to recurrence being 26.8 months (range, 4–78 months). On mammography, US, and MRI, tumors tended to present as an oval or round shaped mass and with not circumscribed margins. On MRI, tumors tended to show rim enhancement, washout kinetics, no intratumoral necrosis, and peritumoral edema. Factors significantly associated with recurrence included increasing tumor size, positive nodal status, ki-67 index above 14, presence of LVI, mastectomy, and neoadjuvant or adjuvant chemotherapy. After controlling for all

potential confounders, tumor size, LVI, and adjuvant chemotherapy were identified as independently associated with recurrence.

Locoregional and distant recurrence rates were found to be 5.4% and 11.0%, respectively, in this study. The ranges of locoregional and distant recurrence rates reported in the literature are wide, from 4.6% to 22%, and 16.9% to 33.9%, respectively. Our study population was early stage TNBC patients, and therefore the lower locoregional and distant recurrence rates in comparison with previous reports that included stage III or stage IV patients are explainable [4, 9, 14]. Although local recurrence rate was not significantly lower in early stage TNBC patients when compared with previous results, there was still a remarkably lower distant recurrence rate in comparison with the TNBC group as a whole. In addition, the mean follow-up period was 61 months in the present study, and most recurrences occur within the first 4 years after diagnosis and treatment in this unique subtype of breast cancer [10, 14].

Increasing tumor size and the presence of LVI were associated with poorer prognosis and recurrence in the present study, with this being in agreement with other previously published studies [3, 15-17]. We found that receipt of neoadjuvant chemotherapy was associated with recurrence, while receipt of adjuvant chemotherapy was inversely associated with recurrence. This could be explained by that generally neoadjuvant chemotherapy is preferred to adjuvant chemotherapy in the case with the larger tumor size, metastatic lymph nodes, for the conserving surgery. Actually, the mean tumor size was 3.5 cm in 73 patients with neoadjuvant chemotherapy, and 2.2 cm in 541 patients with adjuvant chemotherapy in our study.

The strength of the present study is that the associations between the risk of recurrence and preoperative conventional imaging features in early TNBC patients were evaluated. Moderate or marked BPE on MRI was associated with recurrence according to the multivariate analysis. With regard to BPE and recurrence risk, moderate or marked BPE on baseline MRI has been reported to be associated with an increased recurrence rate in a neoadjuvant chemotherapy setting [18]. Although higher BPE was eliminated after multivariate analysis, the present study, which included only 10% of patients with neoadjuvant chemotherapy, also demonstrated an association with recurrence in the univariate analysis. Future studies on BPE could verify the association between BPE and prognosis.

There are several limitations to this study. First, this study was conducted at a single institution including only Asian as a retrospective study, and selection bias was a possibility. Second, the mean follow-up period (61 months, range: 6 - 93 months) was less than 10 years and 37 % (259/702) of our patients had less than 5 year follow-up. Therefore, we could not analyze the survival rate. However, considering that most of the locoregional or distant metastases occur during the first 5 years, this study provides meaningful results in a group of early stage TNBC [10, 14]. Third, the exclusion of all terms with *p*-value greater than 0.20 from the multivariate analysis limits the possibility of finding incremental effects. We grouped TNBC patients according to immunohistochemical staining, which still includes heterogenous molecular subtypes. However, this study restricted subjects to an early stage TNBC group, who are

expected to show a relatively lower recurrence rate. Furthermore, we analyzed not only already recognized clinicopathologic factors, but also preoperative imaging factors.

Conclusions

In conclusion, 16% of patients with early stage TNBC experienced a locoregional, distant, or contralateral breast recurrence, with 3 year and 5 year recurrence rates of 12.5% and 15.4%, respectively. Tumor size, nodal status, LVI, and adjuvant chemotherapy were independently associated with recurrence, while none of the imaging features showed association.

Abbreviations

Triple-negative breast cancer (TNBC), estrogen receptor (ER), lymphovascular invasion (LVI), magnetic resonance imaging (MRI), ultrasonography (US), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), extensive intraductal component (EIC), background parenchymal enhancement (BPE), amount of fibroglandular tissue (FGT)

Declarations

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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Contributions

All authors have made substantial contributions to acquisition of data, or analysis and interpretation of data. They have been involved in drafting the manuscript or revising it critically for important intellectual content. The authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Each author – namely HJE, JHC, WJC, EYC, HJS, HHK – has participated sufficiently in the work to take public responsibility for appropriate portions of the content.

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Ethics approval and consent to participate

This study was approved by the institutional review board of Asan Medical Center, and the need for informed consent was waived due to the retrospective design of the study.

Competing interests

The authors declare that they have no competing interests.

Publisher’s Note

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Tables

Table 1. Univariate Cox Proportional Hazard Analysis of Clinicopathologic Factors with Recurrences

Variable	All (n = 702)	Recurrence				
		No (n = 587)	Yes (n = 115)	*P* value	HR	95% CI
Age (years)	49.0 ± 10.9	49.10 ± 10.9	48.25 ± 11.4	0.5419	1.00	0.98, 1.01
Pathologic tumor size				<.001		
T1	345 (49.2)	305 (52.0)	40 (34.8)		1	
T2	350 (49.9)	279 (47.5)	71 (61.7)	0.001	1.92	1.30, 2.83
T3	7 (1.0)	3 (0.5)	4 (3.5)	<.001	6.75	2.41, 18.89
Pathologic lymph node				<.001		
N0	521 (74.2)	450 (76.7)	71 (61.7)		1	
N1	181 (25.8)	137 (23.3)	44 (38.3)		1.92	1.32, 2.80
Histology				0.870		
IDC	637 (90.7)	532 (90.6)	105 (91.3)		1	
Others	65 (9.3)	55 (9.4)	10 (8.7)		0.95	0.50, 1.81
Histology grade[a]				0.380		
1 or 2	132 (18.8)	107 (18.3)	25 (21.7)		1	
3	569 (81.2)	479 (81.7)	90 (78.3)		0.82	0.53, 1.28
Ki-67 (%)[a]				0.035		
<14	58 (11.6)	55 (13.1)	3 (3.8)		1	
≥14	441 (88.4)	365 (86.9)	76 (96.2)		3.46	1.09, 10.97
LVI				<.001		
No	592 (84.3)	516 (87.9)	76 (66.1)		1	
Yes	110 (15.7)	71 (12.1)	39 (33.9)		3.27	2.22, 4.81
EIC				0.806		
No	582 (82.9)	486 (82.8)	96 (83.5)		1	
Yes	120 (17.1)	101 (17.2)	19 (16.5)		0.94	0.58, 1.54
Multiplicity				0.201		
No	611 (87.0)	515 (87.7)	96 (83.5)		1	
Yes	91 (13.0)	72 (12.3)	19 (16.5)		1.38	0.84, 2.26
Bilaterality				0.297		

No	690 (98.3)	575 (98.0)	115 (100)		1	
Yes	12 (1.7)	12 (2.0)	0 (0)		0.23	0.01, 3.70
Surgery				0.001		
Mastectomy	145 (20.7)	109 (18.6)	36 (31.3)		1	
BCO	557 (79.3)	478 (81.4)	79 (68.7)		0.52	0.35, 0.77
Radiation therapy				0.222		
No	147 (20.9)	119 (20.3)	28 (24.3)		1	
Yes	555 (79.1)	468 (79.7)	87 (75.7)		0.77	0.50, 1.17
Neoadjuvant Chemotherapy				0.006		
No	629 (89.6)	533 (90.8)	96 (83.5)		1	
Yes	73 (10.4)	54 (9.2)	19(16.5)		2.00	1.22, 3.28
Adjuvant Chemotherapy				0.005		
No	154 (21.9)	119 (20.3)	35 (30.4)		1	
Yes	548 (78.1)	468 (79.7)	80 (69.6)		0.56	0.38, 0.84
Margin involvement				0.498		
No	691 (98.4)	577 (98.3)	114 (99.1)		1	
Yes	11 (1.6)	10 (1.7)	1 (0.9)		0.51	0.07, 3.63

Note.—Except where indicated, data are numbers of patients or tumors, with percentages in parentheses. BCO = breast conservation surgery, CI = confidence interval, EIC = extensive intraductal component, HR = hazard ratio, IDC = invasive ductal carcinoma, LVI = lymphovascular invasion

[a]Histologic grade data and Ki-67 proliferation index data were available for 701 and 499 patients, respectively.

Table 2. Univariate Cox Proportional Hazard Analysis of Imaging Factors with Recurrences

Variable	All	Recurrence				
		No	Yes	*P* value	Hazard Ratio	95% CI
Mammogram[a]	692					
Density				0.069		
Non dense	219 (31.6)	191 (33.0)	28 (24.6)		1	
Dense	473 (68.4)	387 (67.0)	86 (75.4)		1.49	0.97, 2.28
Presentation				0.516		
Non visible	52 (7.5)	45 (7.8)	7 (6.1)		1	
Asymmetry	54 (7.8)	48 (8.3)	6 (5.3)	0.788	0.86	0.29, 2.56
Mass	586 (84.7)	485 (83.9)	101 (88.6)	0.505	1.30	0.60, 2.79
Shape				0.177		
Oval or round	295 (50.3)	251 (51.8)	44 (43.6)		1	
Irregular	291 (49.7)	234 (48.2)	57 (56.4)		1.31	0.89, 1.94
Margin				0.746		
Circumscribed	109 (18.6)	89 (18.4)	20 (19.8)		1	
Not circumscribed	477 (81.4)	396 (81.6)	81 (80.2)		0.92	0.57, 1.50
Calcification				0.215		
No	507 (73.3)	429 (74.2)	78 (68.4)		1	
Yes	185 (26.7)	149 (25.8)	36 (31.6)		1.28	0.87, 1.91
Ultrasonography[a]						
Shape				0.131		
Oval or round	390 (56.3)	334 (57.6)	56 (46.9)		1	
Irregular	303 (43.7)	246 (42.4)	57 (53.1)		1.33	0.92, 1.92
Margin				0.485		
Circumscribed	202 (29.1)	172 (29.7)	30 (26.5)		1	
Not circumscribed	491 (70.9)	408 (70.3)	83 (73.5)		1.16	0.76, 1.76
Posterior features				0.555		
No	201 (29.0)	164 (28.3)	37 (32.7)		1	
Enhancement	447 (64.5)	380 (65.5)	67 (59.3)	0.340	0.82	0.55, 1.23

Shadowing	45 (6.5)	36 (6.2)	9 (8.0)	0.884	1.06	0.51, 2.19
MRI[a]						
BPE				0.049		
Minimal or mild	244 (83.3)	211 (85.1)	33 (73.3)		1	
Moderate or marked	49 (16.7)	37 (14.9)	12 (26.7)		1.94	1.00, 3.76
Amount of FGT				0.701		
a or b	53 (19.1)	46 (18.5)	7 (15.6)		1	
c or d	240 (81.9)	202 (81.5)	38 (84.4)		1.17	0.52, 2.62
Presentation				0.692		
Mass	276 (94.2)	233 (94.0)	43 (95.6)		1	
Non mass	17 (5.8)	15 (6.0)	2 (4.4)		0.75	0.18, 3.01
Shape				0.214		
Oval or round	179 (64.9)	155 (66.5)	24 (55.8)		1	
Irregular	97 (35.1)	78 (33.5)	19 (44.2)		1.47	0.80, 2.68
Margin				0.702		
Circumscribed	103 (37.3)	88 (37.8)	15 (34.9)		1	
Not circumscribed	173 (62.7)	145 (62.2)	28 (65.1)		1.13	0.60, 2.12
Enhancement				0.378		
Homogenous	27 (9.2)	21 (8.5)	6 (13.3)		1	
Heterogeneous	126 (43.0)	111 (44.8)	15 (33.3)	0.190	0.53	0.21, 1.37
Rim	140 (47.8)	116 (46.8)	24 (53.4)	0.499	0.73	0.30, 1.80
Kinetics[b]				0.493		
Persistent	11 (3.8)	11 (4.4)	0 (0)		1	
Plateau	14 (4.8)	13 (5.3)	1 (2.2)	0.550	2.70	0.10, 70.28
Washout	267 (91.4)	223(90.3)	44 (97.8)	0.300	4.49	0.26, 76.76
Intraturmoral necrosis				0.134		
No	176 (60.1)	144 (58.1)	32 (71.1)		1	
Yes	117 (39.9)	104 (41.9)	13 (28.9)		0.6	0.32, 1.16
T2 peritumoral edema				0.405		

No	102 (34.8)	89 (35.9)	13 (28.9)	1	
Yes	191 (65.2)	159 (64.1)	32 (71.1)	1.32	0.69, 2.51

[a]Out of 702 patients, 692 (98.6%), 693 (98.7%), and 293 (41.7%) had available mammographic, US, and MRI examinations, respectively

[b]Out of 693 patients, 692 had available kinetics.

Note.- a = almost entirely fat, b= scattered fibroglandular tissue, c = heterogeneous fibroglandular tissue, d= extreme fibroglandular tissue, BPE = background parenchymal enhancement, FGT = fibroglandular tissue,

Table 3. Multivariate Cox Proportional Hazard Analysis of Recurrences

Variable	Recurrence		
	P value	HR	95% CI
Pathologic tumor size	0.004		
T1		1	
T2	0.035	1.54	1.03, 2.30
T3	0.002	4.99	1.77, 14.04
Pathologic lymph node	0.039		
N0		1	
N1		1.53	1.02, 2.28
LVI	<.001		
No		1	
Yes		2.79	1.85, 4.21
Adjuvant chemotherapy	<.001		
No		1	
Yes		0.49	0.32, 0.73

Note.— CI = confidence interval, HR = hazard ratio, LVI = lymphovascular invasion

Figures

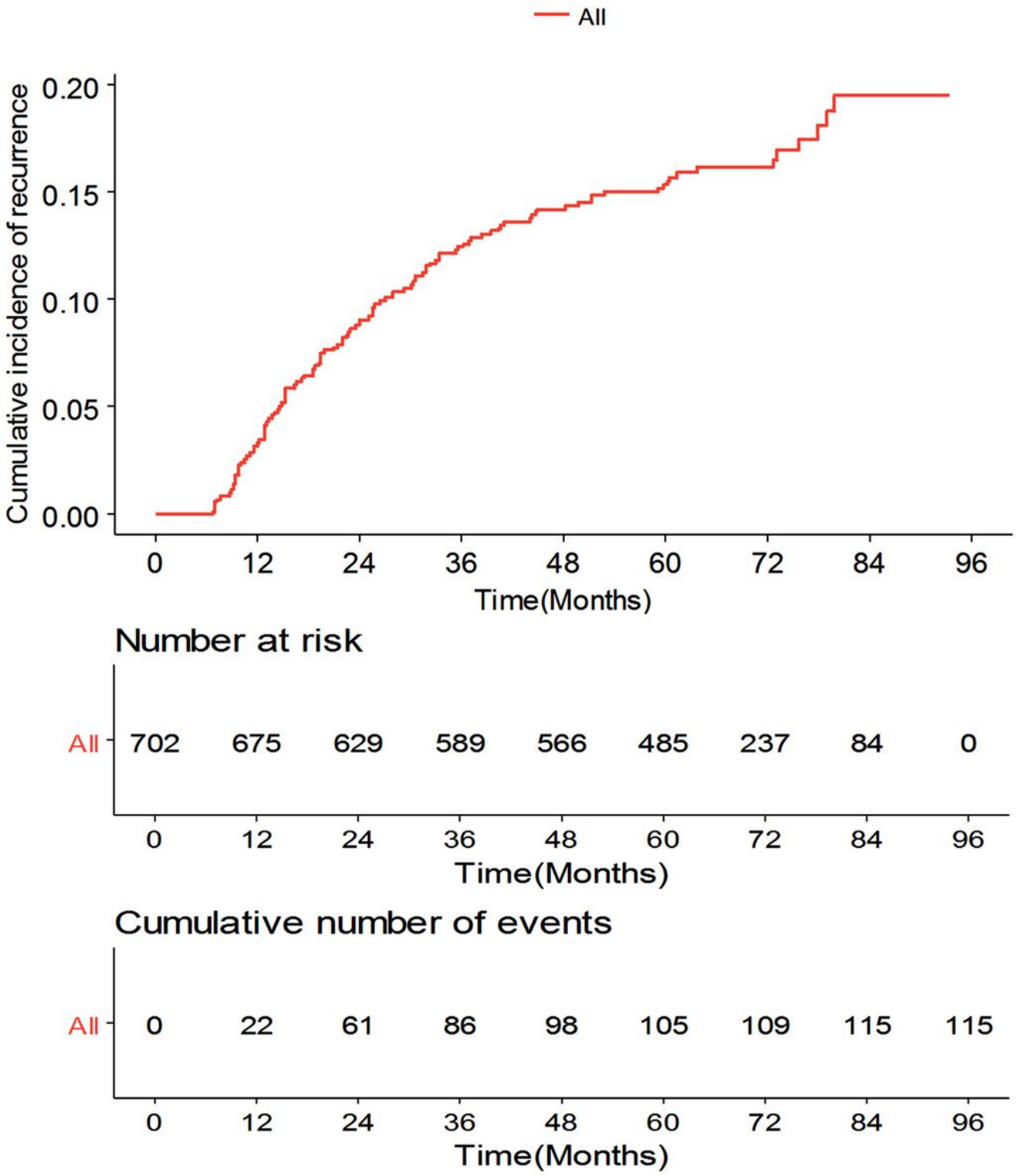

Figure 1

Time to recurrence for 702 patients with early stage triple-negative breast cancer. Data illustrate the overall cohort, those with a locoregional recurrence only, those with distant recurrence only, those with contralateral breast recurrence only, and those with multiple site recurrence.

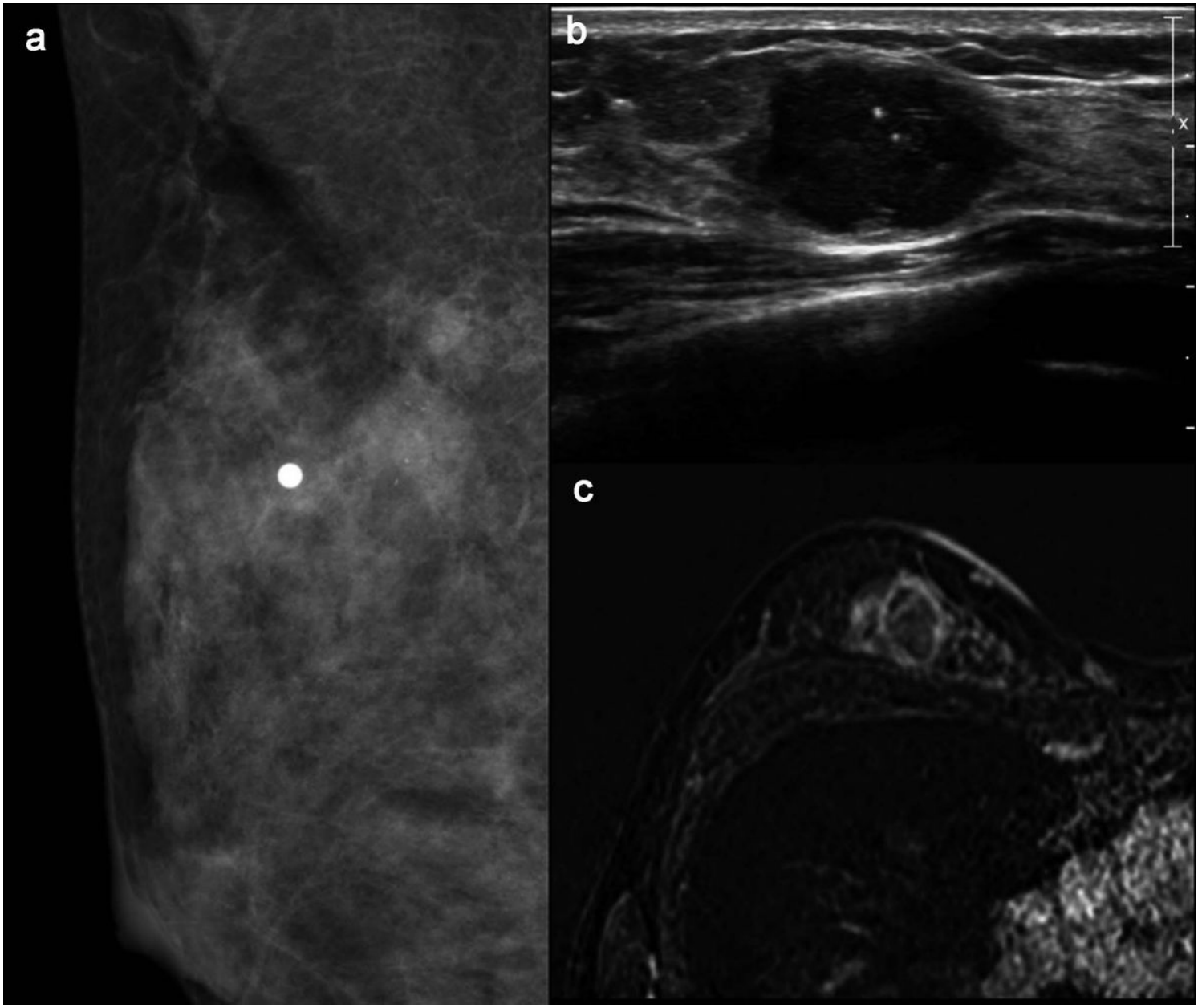

Figure 2

A 30 year old female who experienced metastasis to lung at 33 month follow-up after breast conserving operation, radiation and adjuvant chemotherapy for stage 1A tumor in right breast. (a) Right mediolateral oblique mammogram shows dense breast tissue and an irregular not circumscribed mass with calcifications. (b) US shows an ovoid mass with angular margin with posterior acoustic enhancement. (c) MRI shows a round rim enhancing mass.

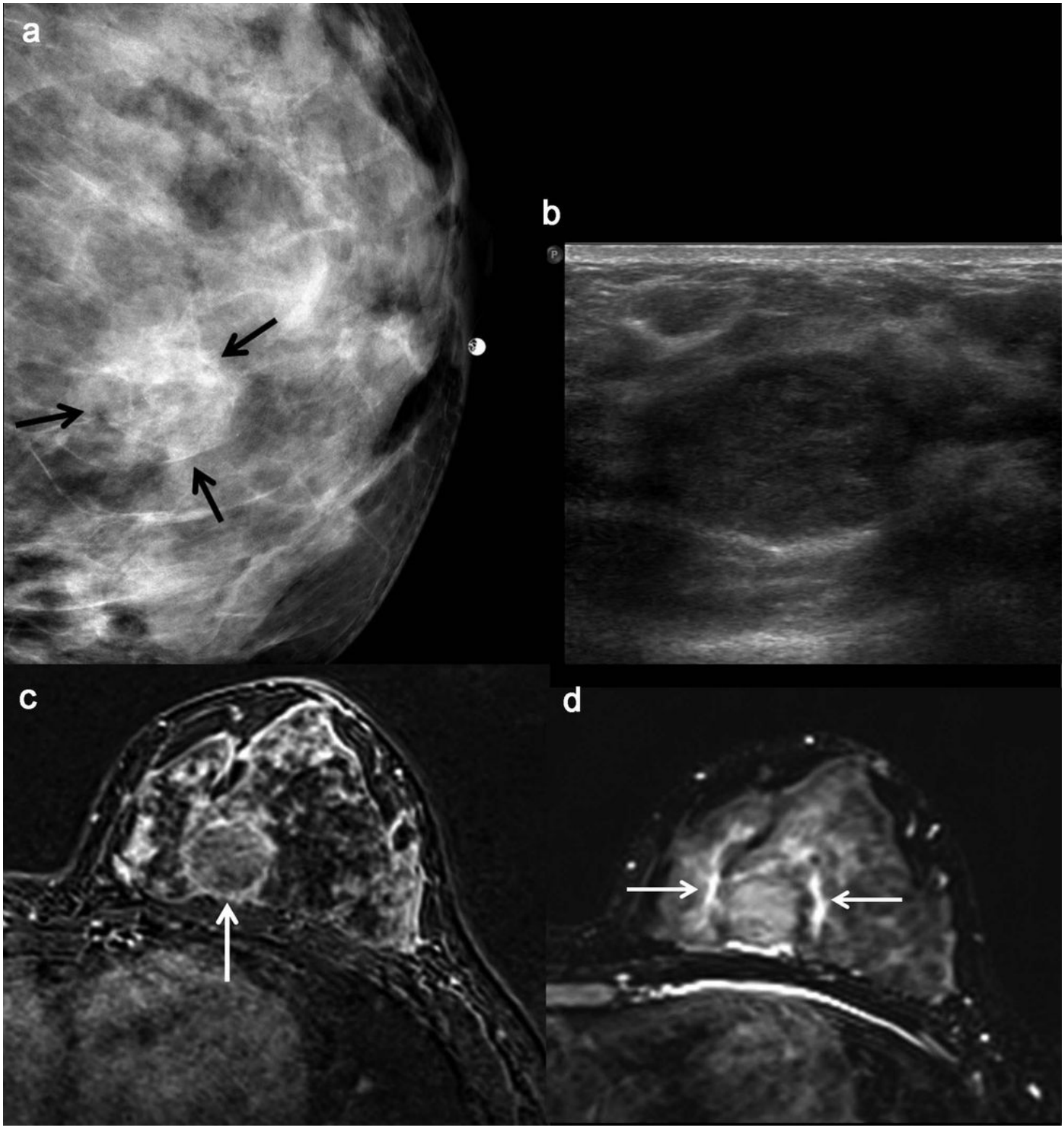

Figure 3

A 36 year old female who experienced metastasis to ipsilateral axillary lymph node at 33 month follow-up after mastectomy, radiation and adjuvant chemotherapy for stage 2B tumor in left breast. (a) Left craniocaudal compression magnification shows dense breast tissue and an irregular, not circumscribed mass with calcifications (arrows). (b) US shows an ovoid mass with microlobulated margin with posterior

acoustic enhancement. (c, d) MRI shows moderate background enhancement and a round heterogenous enhancing mass (arrows) with peritumoral edema on T2 weighted image.