Primary Tumor Location is Associated with Prognosis for Women with Breast Cancer

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Abstract

Background: The prognostic impact of tumor location on breast cancer patients is not consistent and still controversial. We aimed to investigate the prognostic role of primary tumor location on the survival of patients with breast cancer.

Methods: Using the Surveillance, Epidemiology, and End Results database, we identified 53,905 patients diagnosed with tumors in the lower quadrants (n=11,065), upper quadrants (n=38,974), or central and nipple (n=3,866). Chi-squared test was used to compare categorical variables across the groups. Cox proportional hazard models were applied to estimate the factors associated with prognosis.

Results: Compared with the other quadrants, patients with central and nipple lesions showed generally more unfavorable clinicopathologic features and worse breast cancer-specific survival (BCSS) and overall survival (OS). Multivariate Cox analysis showed a higher hazard ratio (HR) for tumor location of central and nipple (BCSS: HR, 1.145, p = 0.036, 95% confidence interval [CI], 1.009-1.299; OS: HR, 1.118, p = 0.024, 95% CI: 1.015-1.232), while lower HR were observed for upper quadrants (BCSS: HR, 0.888, p = 0.004, 95% CI: 0.818-0.964; OS: HR, 0.930, p = 0.023, 95% CI: 0.873-0.990). Multivariate logistic regression indicated that tumors located in central and nipple were more likely to be inoperable disease (HR, 1.460, 95% CI: 1.300-1.640, p < 0.001), while tumors located in upper quadrants tend to be operable disease (HR, 0.895, p = 0.005, 95% CI, 0.829-0.967).

Conclusion: Tumors located in central and nipple had negative contact with BCSS and OS, while tumor located in upper quadrants had favorable contact with survival.

Introduction

Breast cancer is currently the first most common malignancy in the USA and the second leading cause of cancer mortality in women[1]. Up to now, a number of clinicopathological factors, including hormone receptor (HR) status, human epidermal growth factor receptor-2 (HER2) expression, Ki-67 level, tumor size, pathological grade, and lymph node (LN) status, have been identified as powerful indicators predicting prognosis and guiding adjuvant treatments[2–5]. Furthermore, multigenic molecular tests (i.e. Oncotype DX, MammaPrint, EndoPredict, and Prosigna)) have been developed and facilitated risk stratification of tumors into low-risk or high-risk groups, which helped predict recurrence and guide chemotherapy[6, 3, 7]. Despite of all these remarkable prognostic factors, patients with the same subtype are still bearing different survival outcomes. It is essential to find more effective parameters to help tailor personalized therapy for each individual.

Previous studies have occasionally reported the influence of primary tumor location on the prognosis of breast cancer, but the results are not consistent and still controversial. Tumors most frequently located in the upper outer quadrant (UOQ). Sohn et al.[8] reported that patients with tumors in the UOQ were associated with an independent contribution to better survival than that of patients with tumors in other quadrants. Some other studies have reported that patients with medial tumors showed lower survival rates than those with lateral tumors [9, 10]. Meanwhile, patients with non-UOQ tumors especially lower inner quadrant (LIQ) have been demonstrated with worse survival[11, 12]. Moreover, tumors in central portion have been verified to have a worse prognosis in some reports[13, 14]. Furthermore, Kroman et al.[15] found the risk of dying increased significantly (up to 21%) with increasing distance of tumor location from the axilla. Despite of all these studies, some other authors have reported no correlation between tumor location and breast cancer survival[16, 17]. Although upper inner quadrant (UIQ) is also one of inner quadrants like LIQ, its prognostic influence was quite different from that of LIQ. Axillary lymph-node metastases (ALNM) is less frequent observed in the UIQ (20.6%) compared with all other quadrants (33.2%)[18]. Hwang et al. [19] analyzed 63,388 patients with primary breast cancer from the Korean Breast Cancer Registry and found the survival rate of UIQ was not inferior to those of UOQ or lower outer quadrant (LOQ). Levi et al.[20] included 4,562 patients and concluded compared to tumors located in UOQ, the HR was 1.02 for UIQ, 1.20 for LOQ, and 1.55 for LIQ. Sarp et al.[12] identified 1,522 women with breast cancer recorded at the population-based Geneva Cancer Registry and demonstrated the 10-year specific survival was 94% for patients with tumors in UOQ, 96% for the UIQ, 91% for the LOQ, the 88% for the LIQ. All these studies have verified the different prognostic influence of tumors in LIQ, and Kamakura et al.[21] elucidated the recurrence-free survival rate was lower in patients with the lower quadrantss carcinoma than other regions. Based on above studies, we first reclassified primary tumor sites into 3 groups such as: lower quadrants (including LIQ and LOQ), upper quadrants (including UIQ and UOQ), and central and nipple. To describe prognostic value of tumor location for patients with breast cancer, we performed a population-based, nationally representative cohort study using the National Cancer Institute's SEER database.

Methods

Patients

As an authoritative 18 population-based cancer registries, the SEER program collects and publishes cancer incidence and survival data, which covers approximately 28% of the US population (http://seer.cancer.gov/). Subjects had to meet the following criteria for inclusion: (1) age at diagnosis between 18 and 75 years old; (2) histological type was limited to infiltrating duct carcinoma (International Classification of Diseases for Oncology, third revision, ICD-O-3, 8500); (3) known tumor size and lymph node status; (4) surgically resected with pathology specimen and confirmed by pathological diagnosis; (5) known survival time and cause of death; (6) known HR and HER2 status; (7) known surgery type; (8) unilateral breast cancer; and (9) breast cancer as the first and only malignant tumor. According to the site codes of ICD-O-3, we reclassified primary tumor sites into 3 groups such as: lower quadrants (ICD-O codes C50.5, C50.3), upper quadrants (ICD-O codes C50.2, C50.4), and central and nipple (ICD-O codes C50.0, C50.1). We derived a dataset of 53,905 female breast cancer patients diagnosed from 2010 to 2012, including 38,974 (72.3%) patients with tumors in upper quadrants, 11,065 (20.5%) patients in lower quadrants, and 3,866 (7.2%) patients in central and nipple.

Statistical analysis

Cases of yearly diagnosed breast cancer patients were extracted via the SEER*Stat software (version 8.3.6). Baseline characteristics by tumor location were compared using chi-square tests. Breast cancer-specific survival (BCSS) was calculated from the date of diagnosis to the date of breast cancer-specific death, and overall survival (OS) was calculated from the time of diagnosis to the time of death by any cause. Kaplan-Meier estimates of BCSS and OS were plotted by tumor location and analyzed across groups with log-rank tests. In addition, risk factors associated with prognosis were analyzed using Cox proportional hazard models. Logistic regression model was utilized to present the relationship between the tumor location and inoperable disease. All computed p values were two-sided, and a p value of less than 0.05 was considered statistically significant. All analyses were performed using the R 2.15.3 software.

Results

Baseline characteristics of patients stratified by tumor location

An initial analysis of the demographic and clinical characteristics of all 53,905 patients were summarized in Table 1. The median follow-up time was 61 months. The most common tumor location was the upper quadrants (72.3%), followed by tumors located in lower quadrants (20.5%), and the central and nipple region (7.2%). Compared with the other quadrants, patients with central and nipple lesions showed generally more unfavorable clinicopathologic features (older age, higher proportion of patients with stage II/III/IV, more patients with T2/T3/T4, and more patients with positive LN). Patients with central and nipple lesions were observed with less lumpetomy surgery rate and a significantly lower incidence of HR-/HER2- (triple-negative) subtype (all $p < 0.001$).

Table 1
Baseline characteristics of breast cancer patients from the SEER database stratified by tumor location.

Variables	Subgroup	No. (%) of patients			
		Lower quadrants (n = 11,065)	**Upper quadrants (n = 38,974)**	**Central and nipple (n = 3,866)**	P
Literality	Left	5,781(52.2)	19,705(50.6)	1,988(51.4)	0.006
	Right	5,284(47.8)	19,269(49.4)	1,878(48.6)	
Age	< 60	5,630(50.9)	20,346(52.2)	1,779(46.0)	< 0.001
	≥ 60	5,435(49.1)	18,628(47.8)	2,087(54.0)	
Race	White	8,659(78.3)	30,623(78.6)	3,074(79.5)	0.001
	Black	1,310(11.8)	4,407(11.3)	362(9.4)	
	Other	1,045(9.4)	3,731(9.6)	412(10.7)	
	Unknown	51(0.5)	213(0.5)	18(0.5)	
Grade	I	2,073(18.7)	8,250(21.2)	673(17.4)	< 0.001
	II	4,486(40.5)	15,402(39.5)	1,721(44.5)	
	III and UD	4,254(38.4)	14,483(37.2)	1,381(35.7)	
	Unknown	252(2.3)	839(2.2)	91(2.4)	
pT	pT0	1(0.0)	7(0.0)	0(0.0)	< 0.001
	pT1	7,260(65.6)	24,702(63.4)	2,103(54.4)	
	pT2	3,271(29.6)	11,967(30.7)	1,291(33.4)	
	pT3	302(2.7)	1,669(4.3)	246(6.4)	
	pT4	231(2.1)	629(1.6)	226(5.8)	
pN	pN0	7,731(69.9)	27,115(69.6)	2,228(57.6)	< 0.001
	pN1	2,518(22.8)	8,828(22.7)	1,175(30.4)	
	pN2	553(5.0)	2,030(5.2)	300(7.8)	
	pN3	263(2.4)	1,001(2.6)	163(4.2)	
M stage	M0	10,896(98.5)	38,444(98.6)	3,774(97.6)	< 0.001
	M1	169(1.5)	530(1.4)	92(2.4)	
TNM stage	I	6,178(55.8)	21,324(54.7)	1,699(43.9)	< 0.001
	II	3,711(33.5)	13,351(34.3)	1,435(37.1)	
	III	1,007(9.1)	3,769(9.7)	640(16.6)	
	IV	169(1.5)	530(1.4)	92(2.4)	
Surgery	Lumpetomy	6740(60.9)	25,099(64.4)	1,668(43.1)	< 0.001
	Mastectomy	4,325(39.1)	13,875(35.6)	2,198(56.9)	
Breast subtype	HR+/HER2-	7,702(69.6)	27,185(69.8)	2,776(71.8)	< 0.001
	HR+/HER2+	1,324(12.0)	4,205(10.8)	480(12.4)	
	HR-/HER2+	611(5.5)	1,883(4.8)	244(6.3)	
	HR-/HER2-	1,428(12.9)	5,701(14.6)	366(9.5)	

P values are from Chi-square test and were significant at < 0.05. SEER: Surveillance, Epidemiology, and End Results; HR: hormone receptor; HER2: human epidermal growth factor receptor 2.

Marital status	Married	6,344(57.3)	22,310(57.2)	2,092(54.1)	0.004
	Not married	4,201(38.0)	14,791(38.0)	1,584(41.0)	
	Unknown	520(4.7)	1,873(4.8)	190(4.9)	

P values are from Chi-square test and were significant at < 0.05. SEER: Surveillance, Epidemiology, and End Results; HR: hormone receptor; HER2: human epidermal growth factor receptor 2.

Comparison Of Survival Among The Three Groups

Using the lower quadrants population as a reference, we found the 5-year BCSS of patients with central and nipple lesions was significantly lower than that of the lower quadrants population (90.5% *vs* 93.2%, $p < 0.001$), while patients of the upper quadrants showed significantly better BCSS (93.8% *vs* 93.2%, $p = 0.01$) (Fig. 1A). Similarly, the 5-year OS of the patients with tumors in central and nipple were markedly lower than that of the lower quadrants population (84.5% *vs* 88.9%, $p < 0.001$), while patients with tumors in the upper quadrants showed significantly better OS (89.8% *vs* 88.9%, $p = 0.004$) (Fig. 1B). To balance the effect of distinct distribution of baseline prognostic factors among different groups, univariate and multivariate Cox proportional hazards models were used. Laterality ($p = 0.042$), race, grade, TNM stage, surgery type, breast subtype, marital status, and tumor location (all $p < 0.001$) were responsible for BCSS. Similarly, the significant predictors of OS were laterality ($P = 0.044$), age, race, grade, TNM stage, surgery type, breast subtype, marital status, and tumor location (all $p < 0.001$) (Table 2). After multivariate analysis, we found that race, grade, TNM stage, surgery type, breast subtype, and marital status were significant independent predictors of both OS and BCSS (all $p < 0.001$). Tumor location of central and nipple was confirmed as an independent risk factor with higher HRs in terms of both BCSS and OS (BCSS: hazard ratio [HR], 1.145, $p = 0.036$, 95% confidence interval [CI], 1.009–1.299; OS: HR, 1.118, $p = 0.024$, 95% CI, 1.015–1.232) (Table 2), while lower HRs were observed for tumor location of upper quadrants (BCSS: HR, 0.888, $p = 0.004$, 95% CI, 0.818–0.964; OS: HR, 0.930, $p = 0.023$, 95% CI, 0.873–0.990).

Table 2
Univariate and multivariate Cox proportional model of factors associated with breast cancer-specific survival and overall survival.

Variables	Subgroup	BCSS				OS			
		Univariable		**Multivariable**		**Univariable**		**Multivariable**	
		Hazard ratio	P	**Hazard ratio**	P	**Hazard ratio**	P	**Hazard ratio**	P
Location	Lower quadrants	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	Upper quadrants	0.899(0.828, 0.975)		0.888(0.818, 0.964)		0.913(0.857, 0.972)		0.930(0.873, 0.990)	
	Central and nipple	1.416(1.249, 1.605)		1.145(1.009, 1.299)		1.412(1.283, 1.554)		1.118(1.015, 1.232)	
Laterality	Left	1	0.042			1	0.044		
	Right	0.933(0.873, 0.997)				0.949(0.903, 0.999)			
Age	< 60	1	0.170			1	< 0.001	1	< 0.001
	≥ 60	0.955(0.893, 1.020)				1.869(1.774, 1.970)		2.325(2.203, 2.454)	
Race	White	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	Black	1.878(1.725, 2.043)		1.165(1.068, 1.271)		1.525(1.424, 1.634)		1.137(1.057, 1.217)	
	Other	0.703(0.613, 0.806)		0.670(0.585, 0.769)		0.614(0.551, 0.684)		0.651(0.585, 0.726)	
	Unknown	0.114(0.029, 0.457)		0.140(0.035, 0.558)		0.158(0.066, 0.380)		0.183(0.076, 0.441)	
Grade	I	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	II	3.487(2.892, 4.205)		2.111(1.747, 2.551)		1.532(1.402, 1.676)		1.171(1.069, 1.283)	
	III and UD	11.417(9.546, 13.656)		3.870(3.206, 4.671)		3.065(2.817, 3.334)		1.700(1.546, 1.869)	
	Unknown	5.666(4.241, 7.568)		2.506(1.868, 3.361)		1.870(1.540, 2.271)		1.258(1.033, 1.531)	
TNM stage	I	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	II	4.146(3.751, 4.582)		2.788(2.515, 3.091)		2.155(2.026, 2.292)		1.888(1.769, 2.015)	
	III	13.539(12.223, 14.997)		8.209(7.358, 9.159)		5.126(4.784, 5.493)		4.225(3.914, 4.561)	
	IV	47.755(42.116, 54.148)		31.532(27.662, 35.994)		15.326(13.847, 16.963)		13.204(11.876, 14.680)	
Surgery	Lumpetomy	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	Mastectomy	2.568(2.400, 2.748)		1.306(1.216, 1.403)		1.868(1.776, 1.965)		1.304(1.235, 1.377)	
Breast subtype	HR+/HER2-	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	HR+/HER2+	1.307(1.163, 1.469)		0.709(0.630, 0.998)		1.077(0.987, 1.175)		0.808(0.739, 0.884)	

Abbreviations: BCSS, breast cancer-specific survival; OS, overall survival; UD, undifferentiated; HR: hormone receptor; HER2: human epidermal growth factor receptor

	HR-/HER2+	2.503(2.208, 2.837)		1.082(0.951, 1.231)		1.641(1.479, 1.821)		1.009(0.906, 1.124)	
	HR-/HER2-	4.091(3.799, 4.404)		2.202(2.029, 2.389)		2.492(2.348, 2.645)		1.805(1.687, 1.929)	
Marital status	Married	1	< 0.001	1	< 0.001	1	< 0.001	1	< 0.001
	Not married	1.509(1.410, 1.615)		1.350(1.260, 1.447)		1.949(1.850, 2.053)		1.663(1.577, 1.754)	
	Unknown	1.208(1.030, 1.417)		1.140(0.972, 1.447)		1.441(1.277, 1.625)		1.318(1.168, 1.486)	

Abbreviations: BCSS, breast cancer-specific survival; OS, overall survival; UD, undifferentiated; HR: hormone receptor; HER2: human epidermal growth factor receptor

Subgroup Analyses By Tnm Stage And Breast Subtype

We next assessed the prognostic value of tumor location in various subgroups. We found that upper quadrants exhibited better survival rates than lower quadrants for BCSS and OS (all $p < 0.05$) in patients with TNM stage I–II (Fig. 2A, 2B; Fig. 3A, 3B), while patients with central and nipple lesions exhibited worse survival rates than upper quadrants for BCSS ($p < 0.05$) in patients with TNM stage II, and for OS ($p < 0.05$) in patients with TNM stage I–III (Fig. 2B; Fig. 3A, 3B, 3C). Dramatically, we found that upper quadrants exhibited worse survival rates than lower quadrants for BCSS and OS in patients with TNM stage IV (BCSS: 39.0% *vs* 50.9%, $p = 0.015$; OS: 36.5% *vs* 46.6%, $p = 0.01$) (Fig. 2D; Fig. 3D). This poor prognostic value of BCSS and OS of central and nipple lesions could be drawn for patients with all breast subtypes (all $p < 0.05$), while the better survival rates for BCSS and OS of the upper quadrants comparing lower quadrants only persisted in HER2-/HR+ (BCSS: $p = 0.002$; OS: $p = 0.001$) (Supplementary Fig. 1A, Supplementary Fig. 2A), and triple-negative cancer (BCSS: $p = 0.04$; OS: $p = 0.056$) (Supplementary Fig. 1D, Supplementary Fig. 2D).

Tumors Location Is Related To Tumor Resectability

To clarify the reasons leading to poor prognosis of tumors in central and nipple, we analyzed the relationship between tumor location and inoperable disease of breast cancer (TNM stage III/IV, except for T3N1M0). Variables that were significant ($p < 0.001$) in the univariate logistic analysis (age, race, grade, tumor size, breast subtype, marital status, and tumor location) were further included in the multivariate logistic regression analysis. Tumors located in central and nipple were more likely to be inoperable diseases (HR, 1.460, $p < 0.001$, 95% CI, 1.300–1.640), while tumors located in the upper quadrants tend to be operable diseases (HR, 0.895, $p = 0.005$, 95% CI, 0.829–0.967) (Table 3).

Table 3
Univariate and multivariate Logistic regression model of factors associated with inoperable disease.

Variables	Subgroup	Univariable		Multivariable	
		Hazard ratio	P	**Hazard ratio**	P
Laterality	Left	1	0.876		
	Right	0.995(0.941, 1.053)			
Age	< 60	1	< 0.001	1	< 0.001
	≥ 60	0.679(0.641, 0.720)		0.889(0.834, 0.947)	
Race	White	1	< 0.001	1	0.007
	Black	1.541(1.423, 1.669)		1.097(1.004, 1.198)	
	Other	1.036(0.940, 1.142)		0.916(0.825, 1.017)	
	Unknown	0.542(0.322, 0.913)		0.569(0.329, 0.983)	
Grade	I	1	< 0.001	1	< 0.001
	II	3.421(3.013, 3.885)		2.208(1.936, 2.519)	
	III and UD	6.914(6.110, 7.824)		2.906(2.540, 3.325)	
	Unknown	4.168(3.333, 5.212)		2.193(1.725, 2.788)	
Tumor size	≤ 20mm	1	< 0.001	1	< 0.001
	20-50mm	5.944(5.540, 6.378)		4.758(4.422, 5.119)	
	> 50mm	22.314(20.255, 24.582)		16.991(15.362, 18.794)	
	Unknown	120.765(67.304, 216.693)		91.057(50.547, 164.032)	
Breast subtype	HR+/HER2-	1	< 0.001	1	< 0.001
	HR+/HER2+	1.972(1.818, 2.139)		1.243(1.137, 1.359)	
	HR-/HER2+	2.587(2.331, 2.871)		1.362(1.212, 1.530)	
	HR-/HER2-	1.779(1.648, 1.921)		0.866(0.792, 0.946)	
Marital status	Married	1	< 0.001	1	< 0.001
	Not married	1.274(1.202, 1.350)		1.162(1.090, 1.239)	
	Unknown	1.026(0.893, 1.178)		1.029(0.887, 1.194)	
Location	Lower quadrants	1	< 0.001	1	< 0.001
	Upper quadrants	0.974(0.907, 1.047)		0.895(0.829, 0.967)	
	Central and nipple	1.839(1.654, 2.046)		1.460(1.300, 1.640)	

Abbreviations: UD, undifferentiated; HR: hormone receptor; HER2: human epidermal growth factor receptor 2.

Discussion

Studies on tumor location of different subsets of breast cancer data, however, have produced some inconsistent results. Some studies showed breast cancer patients with tumors located in medial, lower, or central regions may indicate adverse prognostic outcomes[19, 11, 12, 20, 14, 10, 21]. Whereas other studies didn't show association between tumor location and breast cancer prognosis[16, 17]. In light of all of these evidences, we hypothesize this lack of consensus and disparate outcomes is partially owing to lack of standardized division of the breast. In our study, we reviewed prior researches and first introduced triple-classification of tumor location as upper quadrants, lower quadrants, and central and nipple. Our classification method seemed to be more reasonable, which helped to lead to more moderate results.

In the current study, we found patients with tumors in central and nipple exhibited more unfavorable clinicopathologic characteristics (older age, higher proportion of patients with stage II/III/IV, more patients with T2/T3/T4, and more patients with positive LN), and these clinicopathologic features could partially explain the worse prognosis of tumors in central and nipple. This may because X-rays can hardly penetrate in the nipple–areolar complex, as a result, tumors in central and nipple were harder to be detected and may reach a substantially larger size when mammography could screen out. Ansari et al.[22] reported that breast cancer located closer to the nipple have a higher incidence of metastases to axillary LN, which is in accordance with our study. Our finding is similar to Gill's study[14], which concluded that the HR of central tumors for overall survival was 1.46 mostly due to their more advanced stages. Besides, Ji et al. also demonstrated tumors in the central and nipple portion is an independent adverse factor for BCSS and OS[13].

Compared with lower quadrants, we elucidated the favorable prognostic value of upper quadrants in various subgroups of breast cancer patients. Accordingly, pertinent studies have reported better prognosis of patients with tumors in UOQ[23, 8], and tumors in LIQ have been verified as worse prognostic factor in breast cancer[24, 12]. Anatomically, the lymphatics from the lower portion of the breast appear to occasionally communicate with those under the diaphragmatic region or peritoneal plexus by passing through the sheath of rectus abdominis, and Kamakura and colleagues[21] revealed that a lower quadrants tumor location was a significant prognostic factor for recurrence, especially soft tissue and visceral recurrence. Furthermore, we hypothesized that the worse prognosis of tumors in lower quadrants is partially because of possible hidden internal mammary node (IMN). Vendrell-Torné et al.[25] found that drainage from the LIQ in 30% of cases occurred exclusively to IMN. In particular, Shahar et al.[26] recently reported that drainage to the internal mammary chain was significantly more seem in lower tumors comparing upper tumors (lower 36.4% *vs* upper 14.6%, $p = 0.003$). Adjuvant chemotherapy has become a standardized therapy to reduce mortality in LN positive patients[27], while adjuvant radiotherapy of the internal mammary chain is still controversial[28]. Hwang et al.[19] revealed LIQ tumors showed worse OS in LN negative patients who received no chemotherapy, but similar OS was seen in patients who received chemotherapy. Because of possible hidden IMN metastasis, lower tumors could be under-staged and under-treated, leading to worse survival outcomes.

Inevitably, there are some limitations in the present study. First, our study is retrospective in nature, further validations from other institutions are merited. Secondly, we had no access to details of chemotherapy regimens, radiation or other adjuvant therapies. Thus, no definitive statements can be made with respect to whether the trends we presented are caused by treatment differences. Despite of these shortcomings, we first introduced this triple-classification and obtained remarkable results, it contributes to the growing literature regarding prognostic value of tumor location on breast cancer.

In summary, we have provided evidence that the tumor location of central and nipple was an independent adverse prognostic factor, while the tumor location of upper quadrants was an independent favorable prognostic factor. Further studies are impending to verify whether tumor location could help guide more personalized treatment algorithms.

Declarations

Abbreviations

SEER, Surveillance, Epidemiology, and End Results; BCSS, breast cancer-specific survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; UD, undifferentiated; HR: hormone receptor; HER2, human epidermal growth factor receptor 2; LIQ, lower inner quadrant; LOQ, lower outer quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant; LN, lymph node; ALNM, axillary lymph-node metastases; ICD-O-3, International Classification of Diseases for Oncology, third revision; IMN, internal mammary node.

Declarations

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No.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Author's contributions

Zhuowei Tang, Yuzhu Ji: Study design, data collections, statistical analysis, writing and manuscript preparation.

Xiaohong Zhang, Weiyun Xu, Lijuan Zhao: data analysis, writing and manuscript preparation.

Jing Zhang, Li Long, Jing Feng,Yixue Wen: supervised the entire project.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

The authors agree for publication.

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Figures

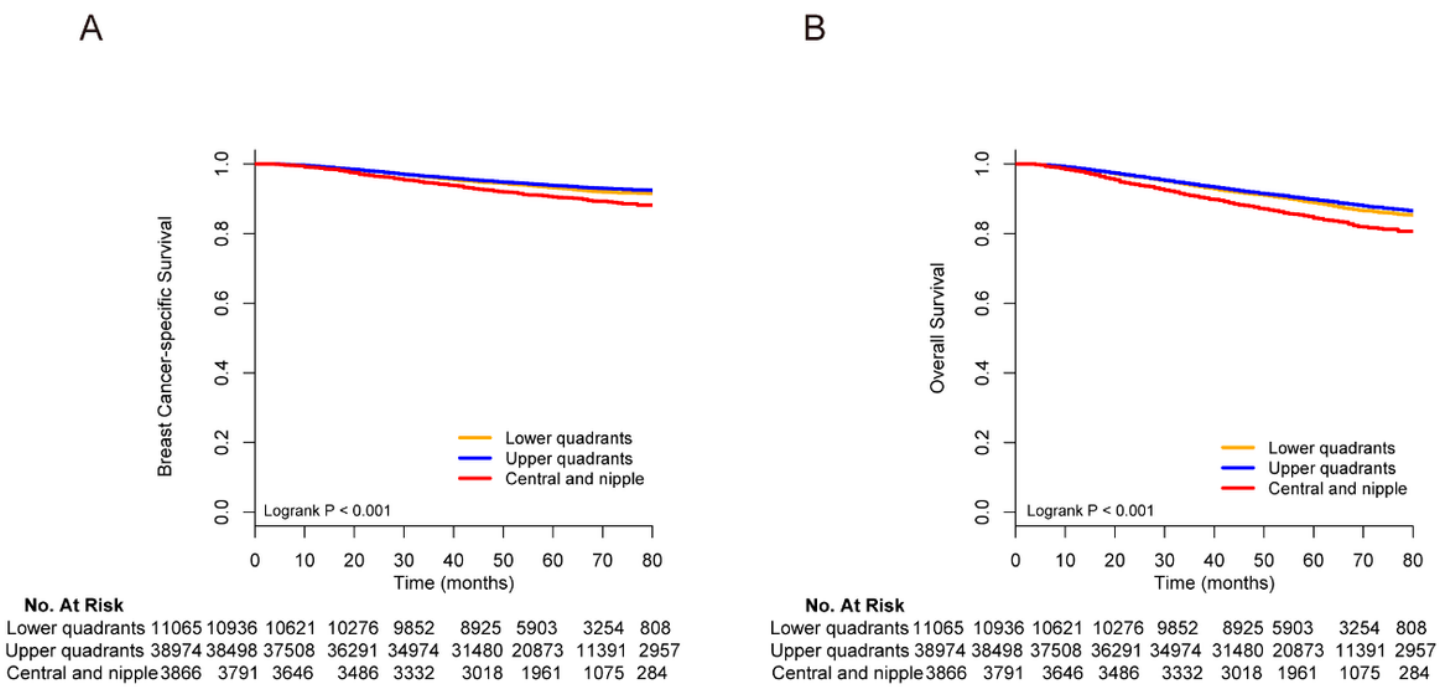

Figure 1

Relationship between tumor location and breast cancer-specific survival and overall survival in all patients. (A) breast cancer-specific survival (BCSS); (B) overall survival (OS).

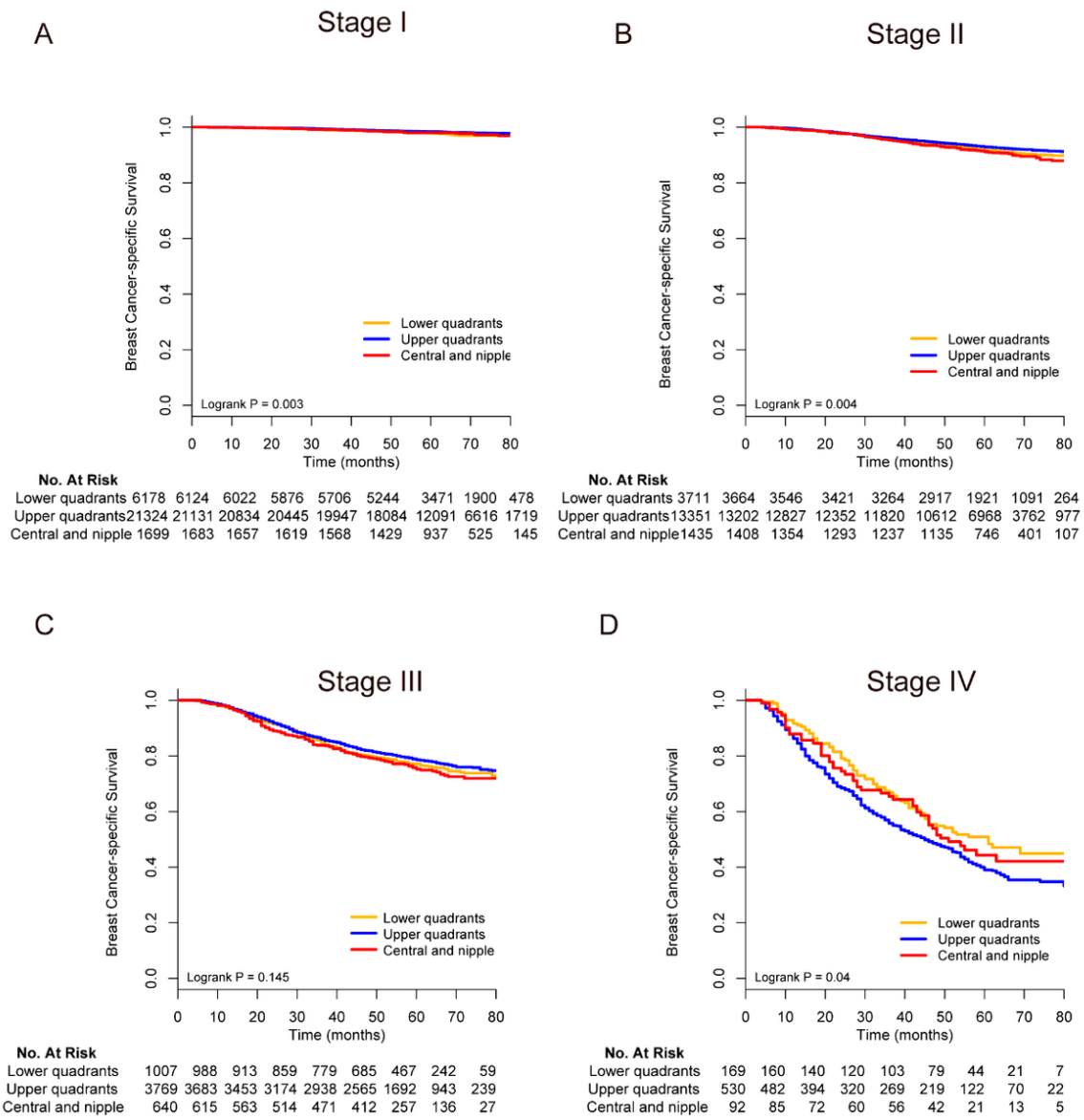

Figure 2

Relationship between tumor location and breast cancer-specific survival stratified by TNM stage. (A) Stage I; (B) Stage II; (C) Stage III; (D) Stage IV.

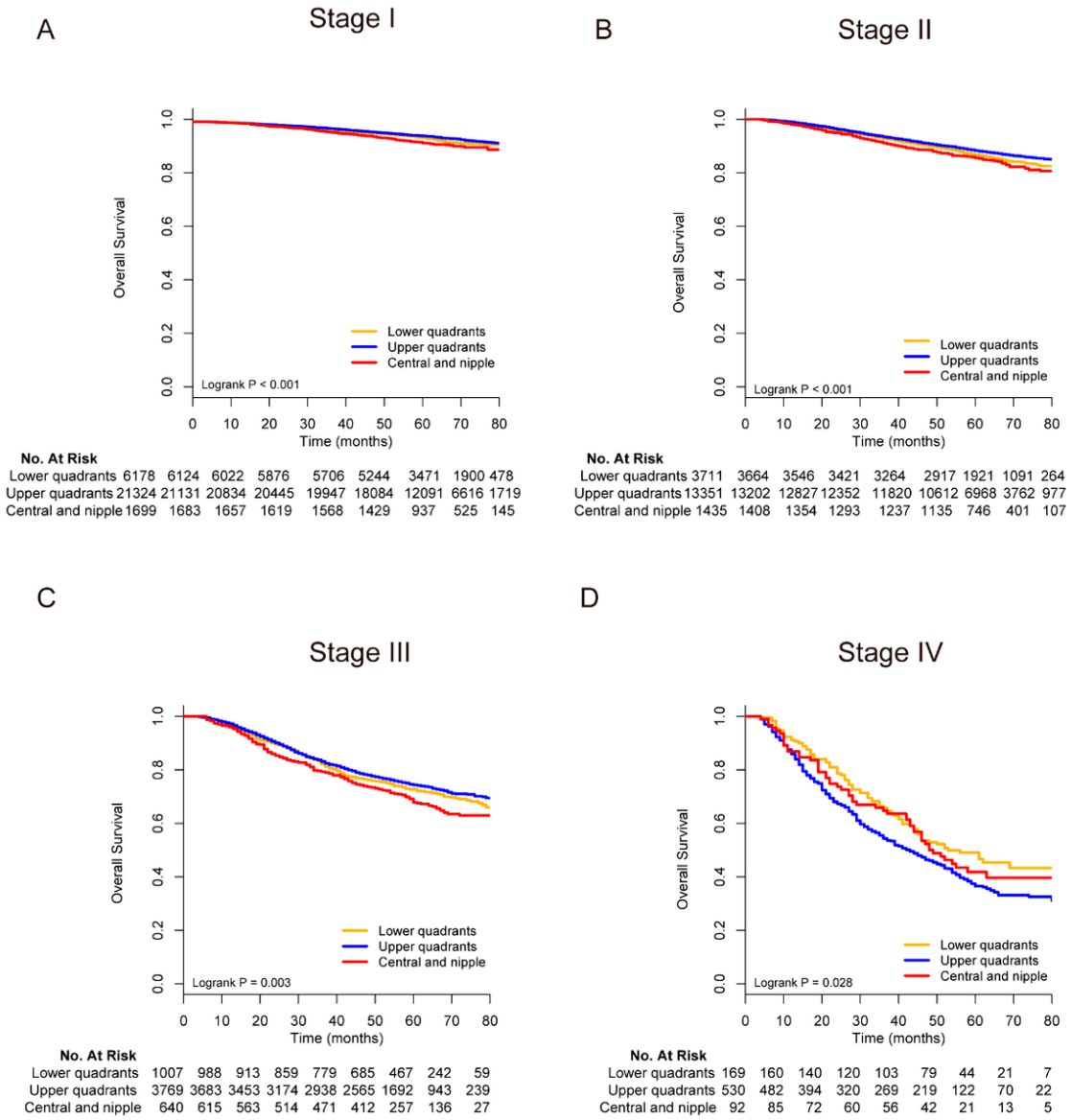

Figure 3

Relationship between tumor location and overall survival stratified by TNM stage. (A) Stage I; (B) Stage II; (C) Stage III; (D) Stage IV.

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