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Effects of Marital Status on Prognosis in Women with Infiltrating Ductal Carcinoma of the Breast: A Real-World 1: 1 Propensity-Matched Study

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Tian Lan***
BCD 2 **Yunyan Lu***
CD 1 **Hua Luo**
BE 1 **Junling He**
CF 1 **Jiawei He**
EF 1 **Zujian Hu**
A 1 **Haibin Xu**

1 Department of Breast Surgery, Hangzhou Hospital of Traditional Chinese Medicine, Hangzhou, Zhejiang, P.R. China
2 Department of Cardiology, The First People's Hospital of Xiaoshan District, Hangzhou, Zhejiang, P.R. China

* Tian Lan and Yunyan Lu contributed equally to this work

Corresponding Authors: Haibin Xu, e-mail: haibin0512@126.com, Tian Lan, e-mail: lan_tian_lt@163.com
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Background: The effects of marital status on infiltrating ductal carcinoma of breast cancer (IDC) have not been studied in detail. This study investigated the impact of marital status on IDC patients.

Material/Methods: SEER databases were searched from 2010 to 2015 for subjects who were married, divorced, single, and widowed. The influence of marital status on breast cancer-specific survival (BCSS) and overall survival (OS) of IDC patients was investigated through multivariate Cox regression analysis and Kaplan-Meier analysis. To prevent bias, propensity score matching (PSM) analysis was performed.

Results: The 5-year OS was 89.6% in married patients, 84.9% in divorced patients, 83.5% in single patients, and 71.3% in widowed patients ($p < 0.001$). The 5-year BCSS were 92.9%, 90.2%, 87.6%, and 86.4%, respectively ($p < 0.001$). Multivariate Cox regression analysis revealed that marriage was a protective factor for patients with IDC in terms of OS (divorced: HR, 1.27; 95% CI, 1.21–1.32; $p < 0.001$; single: HR, 1.36; 95% CI, 1.31–1.42; $p < 0.001$; widowed: HR, 1.42; 95% CI, 1.36–1.48; $p < 0.001$) and BCSS (divorced: HR, 1.15; 95% CI, 1.09–1.21; $p < 0.001$; single: HR, 1.27; 95% CI, 1.21–1.33; $p < 0.001$; widowed: HR, 1.32; 95% CI, 1.25–1.40; $p < 0.001$). Following subgroup and PSM analysis, married patients were shown to have better OS and BCSS as opposed to divorced, single, or widowed patients.

Conclusions: We identify marital status as a predictor of survival in those with IDC. Widowed patients showed the highest mortality risk.

MeSH Keywords: **Breast Neoplasms • Marital Status • Prognosis • SEER Program**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/923630>

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Background

Breast cancer is a common tumor in women, with ~279 100 new cases and 42 690 deaths in 2020 alone [1]. Infiltrating ductal carcinoma of breast cancer (IDC) accounts for ~70–80% of breast cancers globally [2,3]. Although advances in treatment have reduced the mortality rate of IDC, the increasing incidence of IDC is still a serious problem [4]. Therefore, it is urgent to explore potential risk factors contributing to IDC development. The risk factors for breast cancer include reproductive risk factors [5], lifestyle [6], family history [7], and genetic predisposition [8]. Psychological and social factors are also emerging as key indicators of cancer development [9].

Marital status is a key sociocultural variable that influences cancer patients. Marital status can predict the outcomes of rectal cancer [10], ovarian serous carcinoma [11], pancreatic cancer [12], and non-small cell lung cancer [13]. Similarly, marital status has been suggested as a predictive factor for breast cancer survival [14–17]. Breast cancer is highly heterogeneous, with a range of pathologies, biological behavior, and prognosis that differ from other histological subtypes [18,19]. However, most previous reports did not distinguish histologic subtypes or molecular subtypes. In addition, significant imbalances in baseline characteristics exist amongst the studied groups based on marital status. The effects of marital status on the prognosis of IDC patients therefore require assessment.

In this study, 1: 1 propensity score matching (PSM) was performed to explore the influence of marital status on IDC prognosis in the Surveillance, Epidemiology, and End Results (SEER) database.

Material and Methods

Patients

The SEER 18 regions database [Incidence-SEER 18 Regs Research Data (with additional treatment fields), Nov 2017 Sub (1975-2016 varying)] was used, encompassing ~28% of the U.S. population. Patients diagnosed from 2010 to 2015 were collected due to the lack of availability of Her2 information prior to 2010. Inclusion criteria were as follows: (1) age ≥ 18 years at diagnosis; (2) accessible marital information; (3) histology ICD-O-3 (International Classification of Diseases for Oncology, 3rd edition) limited to infiltrating duct carcinoma (8500/3); and (4) survival times ≥ 1 month. Patients with missing or incomplete demographic, clinicopathological, treatment, or follow-up information were excluded.

Clinicopathological variables

Marital status, gender, age at diagnosis, ethnicity, median household income, insurance status, tumor grade, tumor size,

lymph node, metastasis, TNM stage, ER, PR, Her2, molecular subtype, treatment regimens, and prognostic information were assessed. Patients were divided into those who were married, single, divorced, and widowed based on marital status. Age was categorized as 18–49 years, 50–59 years, 60–69 years, 70–79 years, and ≥ 80 years. Ethnicity was classified into white, black, American Indian/Alaska Native (AI), and Asian or Pacific Islander (API). Socioeconomic status was divided into Quartile 1 ($< \$52 620$), Quartile 2 ($\$52 621–\$60 890$), Quartile 3 ($\$60 891–\$74 440$), and Quartile 4 ($> \$74 441$). Tumor grade IV was combined with grade III. TNM staging was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC) and classed into stage I to stage IV. Radiation and chemotherapy were categorized as “yes” and “no/unknown”.

Statistical analyses

Baseline features were compared using the chi-square test. The primary endpoints were overall survival (OS) and breast cancer-specific survival (BCSS). Kaplan-Meier (KM) curves were used to investigate survival differences amongst the groups. Log-rank tests were applied for group comparisons. Prognostic factors were identified using multivariate Cox proportional hazard assessments.

PSM can reduce selection bias and mimic randomized controlled trials [20,21], and was employed to reassess the influence of marital status. PSM was performed using 1: 1 nearest neighbor matching with a caliper of 0.01. Standardized differences (SD) were used to assess the changes in variables before and after PSM. $SD \leq 0.1$ were employed to denote significant balances in the baseline covariate [22].

Statistical analyses were performed using R (version 3.5.2, <https://www.r-project.org/>). R packages, including tableone, rms, survival, survminer, ggplot2, cobalt, and MatchIt, were used. Assessments were 2-sided. P-value < 0.05 was deemed statistically significant.

Results

Clinicopathological characteristics

From 2010 to 2015, 183 260 patients with IDC were included. Clinicopathological characteristics in each group are presented in Table 1. Those who were widowed tended to be in the older age groups of 60–69 (22.8%), 70–79 (33.9%), and ≥ 80 years (33.8%). The single group had more black patients (23.4%), while the married group had more Asian/Pacific Islander patients (7.1%). Compared to those who were divorced, single, and widowed, married patients tended to have earlier stage (53.4%), smaller tumor sizes (62.6%), negative lymph

Table 1. The characteristics of patients with breast cancer according to marital status in the SEER database.

Characteristic	Married	Divorced	Single	Widowed	pvalue
	107899	22826	29535	23000	
Subtype (%)					
HR-/HER2- (triple negative)	13281 (12.3)	3099 (13.6)	4247 (14.4)	2668 (11.6)	<0.001
HR-/HER2+ (HER2 enriched)	5801 (5.4)	1217 (5.3)	1636 (5.5)	1063 (4.6)	
HR+/HER2- (Luminal A)	75459 (69.9)	15806 (69.2)	19598 (66.4)	17097 (74.3)	
HR+/HER2+ (LuminalB)	13358 (12.4)	2704 (11.8)	4054 (13.7)	2172 (9.4)	
Age (%)					
18-49	28875 (26.8)	4655 (20.4)	10349 (35.0)	440 (1.9)	<0.001
50-59	30248 (28.0)	6646 (29.1)	8601 (29.1)	1728 (7.5)	
60-69	29621 (27.5)	7127 (31.2)	6773 (22.9)	5251 (22.8)	
70-79	14942 (13.8)	3438 (15.1)	2762 (9.4)	7806 (33.9)	
≥80	4213 (3.9)	960 (4.2)	1050 (3.6)	7775 (33.8)	
Race (%)					
White	87818 (81.4)	17685 (77.5)	19926 (67.5)	18499 (80.4)	<0.001
Black	7669 (7.1)	3601 (15.8)	6915 (23.4)	2709 (11.8)	
API	11850 (11.0)	1381 (6.1)	2440 (8.3)	1672 (7.3)	
AI	562 (0.5)	159 (0.7)	254 (0.9)	120 (0.5)	
Gender (%)					
Male	990 (0.9)	114 (0.5)	239 (0.8)	74 (0.3)	<0.001
Female	106909 (99.1)	22712 (99.5)	29296 (99.2)	22926 (99.7)	
Median household income (%)					
Quartile1	27103 (25.1)	6644 (29.1)	7528 (25.5)	7309 (31.8)	<0.001
Quartile2	26289 (24.4)	5551 (24.3)	8608 (29.1)	5554 (24.1)	
Quartile3	26613 (24.7)	5634 (24.7)	6145 (20.8)	5307 (23.1)	
Quartile4	27894 (25.9)	4997 (21.9)	7254 (24.6)	4830 (21.0)	
Insurance (%)					
Insured	106504 (98.7)	22291 (97.7)	28505 (96.5)	22800 (99.1)	<0.001
Uninsured	1395 (1.3)	535 (2.3)	1030 (3.5)	200 (0.9)	
Grade (%)					
I	22865 (21.2)	4636 (20.3)	5175 (17.5)	5039 (21.9)	<0.001
II	45042 (41.7)	9290 (40.7)	11695 (39.6)	10280 (44.7)	
III	39992 (37.1)	8900 (39.0)	12665 (42.9)	7681 (33.4)	
Stage (%)					
I	57607 (53.4)	11354 (49.7)	12855 (43.5)	11995 (52.2)	<0.001
II	36396 (33.7)	7871 (34.5)	10999 (37.2)	7671 (33.4)	
III	10732 (9.9)	2653 (11.6)	4104 (13.9)	2415 (10.5)	
IV	3164 (2.9)	948 (4.2)	1577 (5.3)	919 (4.0)	
Tumor size (%)					
T0/1	67595 (62.6)	13348 (58.5)	15363 (52.0)	13685 (59.5)	<0.001
T2	32257 (29.9)	7275 (31.9)	10237 (34.7)	7134 (31.0)	
T3	5121 (4.7)	1258 (5.5)	2261 (7.7)	1023 (4.4)	
T4	2926 (2.7)	945 (4.1)	1674 (5.7)	1158 (5.0)	

Table 1 continued. The characteristics of patients with breast cancer according to marital status in the SEER database.

Characteristic	Married	Divorced	Single	Widowed	pvalue
	107899	22826	29535	23000	
Node status (%)					
N0	72833 (67.5)	14922 (65.4)	18271 (61.9)	16259 (70.7)	<0.001
N1	26627 (24.7)	5760 (25.2)	8092 (27.4)	4922 (21.4)	
N2	5422 (5.0)	1375 (6.0)	1980 (6.7)	1141 (5.0)	
N3	3017 (2.8)	769 (3.4)	1192 (4.0)	678 (2.9)	
Metastasis (%)					
M0	104735 (97.1)	21878 (95.8)	27958 (94.7)	22081 (96.0)	<0.001
M1	3164 (2.9)	948 (4.2)	1577 (5.3)	919 (4.0)	
Bone M (%)					
Yes	1988 (1.8)	583 (2.6)	1015 (3.4)	532 (2.3)	<0.001
No	105911 (98.2)	22243 (97.4)	28520 (96.6)	22468 (97.7)	
Brain M (%)					
Yes	177 (0.2)	60 (0.3)	98 (0.3)	51 (0.2)	<0.001
No	107722 (99.8)	22766 (99.7)	29437 (99.7)	22949 (99.8)	
Liver M (%)					
Yes	840 (0.8)	237 (1.0)	401 (1.4)	198 (0.9)	<0.001
No	107059 (99.2)	22589 (99.0)	29134 (98.6)	22802 (99.1)	
Lung M (%)					
Yes	927 (0.9)	298 (1.3)	501 (1.7)	376 (1.6)	<0.001
No	106972 (99.1)	22528 (98.7)	29034 (98.3)	22624 (98.4)	
ER (%)					
Negative	20377 (18.9)	4596 (20.1)	6303 (21.3)	3982 (17.3)	<0.001
Positive	87522 (81.1)	18230 (79.9)	23232 (78.7)	19018 (82.7)	
PR (%)					
Negative	30772 (28.5)	6946 (30.4)	9220 (31.2)	6507 (28.3)	<0.001
Positive	77127 (71.5)	15880 (69.6)	20315 (68.8)	16493 (71.7)	
HER2 (%)					
Negative	88740 (82.2)	18905 (82.8)	23845 (80.7)	19765 (85.9)	<0.001
Positive	19159 (17.8)	3921 (17.2)	5690 (19.3)	3235 (14.1)	
Surgery (%)					
No surgery	4341 (4.0)	1339 (5.9)	2326 (7.9)	1872 (8.1)	<0.001
BCS	61159 (56.7)	12834 (56.2)	15175 (51.4)	13208 (57.4)	
Mastectomy	42399 (39.3)	8653 (37.9)	12034 (40.7)	7920 (34.4)	
Radiation (%)					
None/unknown	46773 (43.3)	10292 (45.1)	14297 (48.4)	12574 (54.7)	<0.001
Yes	61126 (56.7)	12534 (54.9)	615238(51.6)	10426 (45.3)	
Chemotherapy (%)					
No/unknown	56299 (52.2)	12055 (52.8)	14119 (47.8)	17161 (74.6)	<0.001
Yes	51600 (47.8)	10771 (47.2)	15416 (52.2)	5839 (25.4)	

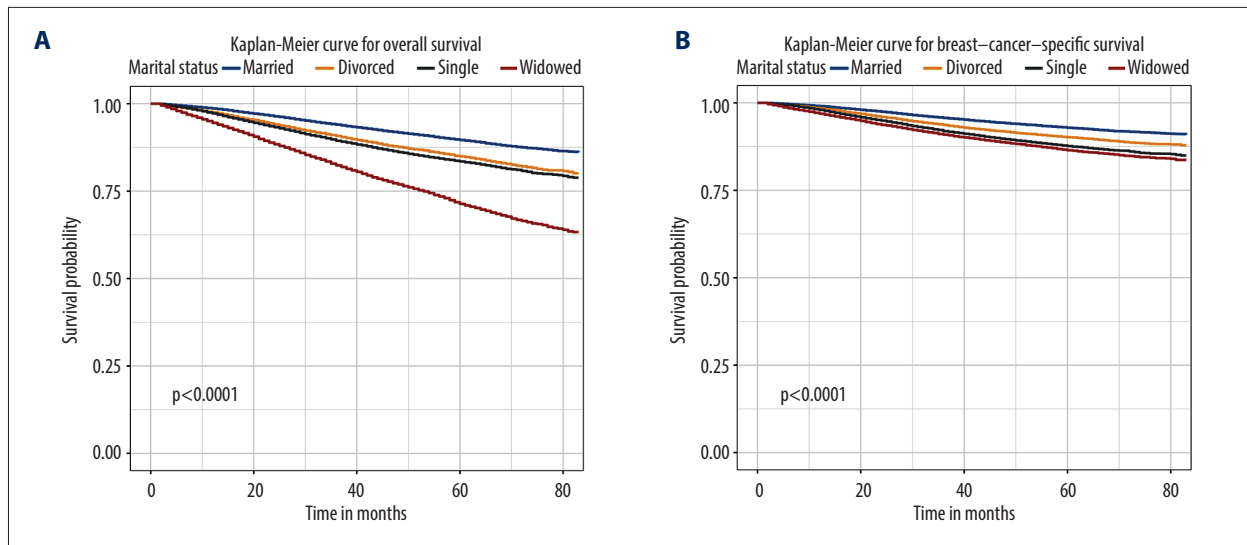


Figure 1. Overall survival (A) and breast cancer-specific survival (B) curve of breast cancer patients based on marital status (married, divorced, widowed, and single).

Table 2. Impact of marital status on the OS by univariate and multivariate survival analysis before PSM.

Characteristics	5-year OS	Univariate analysis		Multivariate analysis		
		Log rank χ^2	P value	HR	95% CI	P value
Marital status		4346.6	<0.001			
Married	89.6%			Reference		
Divorced	84.9%			1.27	1.21–1.32	<0.001
Single	83.5%			1.36	1.31–1.42	<0.001
Widowed	71.3%			1.42	1.36–1.48	<0.001
Age		9737.8	<0.001			
18–49	89.6%			Reference		
50–59	89.6%			3.42	3.28–3.57	<0.001
60–69	88.9%			1.51	1.46–1.56	<0.001
70–79	82.3%			1.05	1.02–1.09	0.001
≥80	57.2%			0.98	0.95–1.01	0.161
Race		1063.9	<0.001			
White	86.1%			Reference		
Black	78.4%			1.24	1.19–1.29	<0.001
API	91.0%			0.75	0.71–0.80	<0.001
AI	83.8%			1.29	1.09–1.53	0.004
Gender		108.6	<0.001			
Male	75.0%			Reference		
Female	85.8%			0.73	0.65–0.83	<0.001

Table 2 continued. Impact of marital status on the OS by univariate and multivariate survival analysis before PSM.

Characteristics	5-year OS	Univariate analysis		Multivariate analysis		
		Log rank χ^2	P value	HR	95% CI	P value
Median household income		701.2	<0.001			
Quartile 1	82.1%			Reference		
Quartile 2	85.2%			0.8	0.77–0.82	<0.001
Quartile 3	86.8%			1.01	0.98–1.04	0.473
Quartile 4	88.9%			0.99	0.96–1.02	0.658
Insurance		122.0	<0.001			
Uninsured	78.9%			Reference		
Insured	85.8%			0.75	0.68–0.82	<0.001
Grade		3373.4	<0.001			
I	92.8%			Reference		
II	88.0%			1.24	1.17–1.30	<0.001
III	79.3%			1.84	1.74–1.94	<0.001
Stage		27296.3	<0.001			
I	92.9%			Reference		
II	85.6%			1.83	1.75–1.90	<0.001
III	70.1%			4.52	4.31–4.74	<0.001
IV	32.3%			10.28	9.72–10.88	<0.001
Subtype		3036.7	<0.001			
HR–/HER2– (triple negative)	74.3%			Reference		
HR–/HER2+ (HER2 enriched)	81.6%			0.52	0.49–0.56	<0.001
HR+/HER2– (Luminal A)	87.9%			0.48	0.46–0.50	<0.001
HR+/HER2+ (Luminal B)	86.7%			0.42	0.40–0.44	<0.001
Surgery		17876.6	<0.001			
No surgery	44.0%			Reference		
BCS	90.8%			0.42	0.40–0.44	<0.001
Mastectomy	83.6%			0.48	0.46–0.50	<0.001
Radiation		2212.4	<0.001			
None/unknown	81.1%			Reference		
Yes	89.5%			0.74	0.71–0.76	<0.001
Chemotherapy		55.0	<0.001			
No/unknown	86.4%			Reference		
Yes	84.8%			0.78	0.75–0.81	<0.001

OS – overall survival; PSM – propensity score matching; HR – hazard ratio; CI – confidence interval.

Table 3. Impact of marital status on the BCSS by univariate and multivariate survival analysis before PSM.

Characteristics	5-year OS	Univariate analysis		Multivariate analysis		
		Log rank χ^2	P value	HR	95% CI	P value
Marital status		1200.1	<0.001			
Married	92.9%			Reference		
Divorced	90.2%			1.15	1.09–1.21	<0.001
Single	87.6%			1.27	1.21–1.33	<0.001
Widowed	86.4%			1.32	1.25–1.40	<0.001
Age		1228.9	<0.001			
18–49	90.6%			Reference		
50–59	91.4%			2.04	1.93–2.15	<0.001
60–69	92.9%			1.34	1.29–1.40	<0.001
70–79	91.0%			1.08	1.03–1.12	<0.001
≥80	82.7%			0.96	0.92–1.00	0.040
Race		1194.6	<0.001			
White	91.6%			Reference		
Black	83.8%			1.27	1.21–1.33	<0.001
API	93.6%			0.8	0.74–0.86	<0.001
AI	89.5%			1.27	1.03–1.57	0.026
Gender		23.2	<0.001			
Male	86.5%			Reference		
Female	90.9%			0.88	0.74–1.05	0.145
Median household income		468.0	<0.001			
Quartile 1	88.7%			Reference		
Quartile 2	90.3%			0.80	0.77–0.84	<0.001
Quartile 3	91.8%			1.00	0.97–1.04	0.846
Quartile 4	93.0%			1.04	1.00–1.07	0.067
Insurance		304.8	<0.001			
Uninsured	81.3%			Reference		
Insured	91.1%			0.74	0.67–0.81	<0.001
Grade		5565.4	<0.001			
I	98.2%			Reference		
II	93.7%			2.01	1.82–2.22	<0.001
III	83.9%			3.71	3.36–4.10	<0.001
Stage		38639.6	<0.001			
I	97.9%			Reference		
II	91.2%			2.93	2.74–3.12	<0.001
III	75.2%			8.98	8.37–9.63	<0.001
IV	35.7%			24.52	22.72–26.47	<0.001

Table 3 continued. Impact of marital status on the BCSS by univariate and multivariate survival analysis before PSM.

Characteristics	5-year OS	Univariate analysis		Multivariate analysis		
		Log rank χ^2	P value	HR	95% CI	P value
Subtype		4705.1	<0.001			
HR-/HER2- (triple negative)	79.1%			Reference		
HR-/HER2+ (HER2 enriched)	85.6%			0.43	0.40–0.47	<0.001
HR+/HER2- (Luminal A)	93.5%			0.41	0.39–0.43	<0.001
HR+/HER2+ (Luminal B)	90.9%			0.32	0.30–0.34	<0.001
Surgery		19591.4	<0.001			
No surgery	51.9%			Reference		
BCS	95.7%			0.33	0.31–0.36	<0.001
Mastectomy	88.7%			0.45	0.42–0.47	<0.001
Radiation		922.3	<0.001			
None/unknown	88.5%			Reference		
Yes	92.8%			0.86	0.82–0.89	<0.001
Chemotherapy		1605.0	<0.001			
No/unknown	94.0%			Reference		
Yes	87.3%			0.85	0.82–0.90	<0.001

BCSS – breast cancer-specific survival; PSM – propensity score matching; HR – hazard ratio; CI – confidence interval.

nodes (67.5%), and no metastasis (97.1%). Patients in the widowed group were least likely to have received radiation (45.3%) or chemotherapy (25.4%).

Effects of marital status on OS and BCSS

The OS and BCSS of patients with IDC were assessed using Kaplan-Meier analysis. Significant differences in OS were observed based on marital status ($p < 0.0001$) (Figure 1A). The 5-year OS was 89.6% in married patients, and 71.3%, 84.9%, and 83.5% in those who were widowed, single, and divorced, respectively (Table 2). The BCSS of the 4 marital subgroups also differed (Figure 1B). The 5-year BCSS was 92.9% in the married group, 90.2% in the divorced group, 87.6% the single group, and 86.4% in the widowed group ($p < 0.001$) (Table 3).

Univariate analysis demonstrated that ethnicity, age, gender, income, insurance status, tumor grade, stage, subtype, surgical therapy, radiation therapy, and chemotherapy were significantly associated with OS (Table 2) and BCSS (Table 3) (all $p < 0.001$).

Results from multivariate Cox regression analysis revealed marriage as a protective factor for OS (divorced: HR, 1.27; 95% CI, 1.21–1.32; $p < 0.001$; single: HR, 1.36; 95% CI, 1.31–1.42; $p < 0.001$; and widowed: HR, 1.42; 95% CI, 1.36–1.48; $p < 0.001$) (Table 2)

and BCSS (divorced: HR, 1.15; 95% CI, 1.09–1.21; $p < 0.001$; single: HR, 1.27; 95% CI, 1.21–1.33; $p < 0.001$; and widowed: HR, 1.32; 95% CI, 1.25–1.40; $p < 0.001$) (Table 3) in patients with IDC. Molecular subtype, insurance, surgery, radiation therapy, and chemotherapy showed a highly significant association with OS and BCSS.

To reduce the effect of confounders, IDC patients were stratified according to clinical features. We also identified marital status as an independent prognostic indicator of OS (Figure 2) and BCSS (Figure 3) in all subgroups.

Survival analysis after 1: 1 PSM

To minimize the confounding factors and assess the impact of marital status, we performed 1: 1 PSM. Three 1: 1 matched cohorts were obtained: a divorced and married cohort, a single and married cohort, and a widowed and married cohort. The demographic and clinicopathological features between 2 groups in the 2 cohorts were balanced (Table 4). The absolute mean differences in all variables across the groups were less than 0.1 following PSM assessment (Figure 4). Married patients showed better BCSS and OS in the divorced-married cohort (Figure 5A, 5B), the single-married cohort (Figure 5C, 5D), and the widowed-married cohort (Figure 5E, 5F).

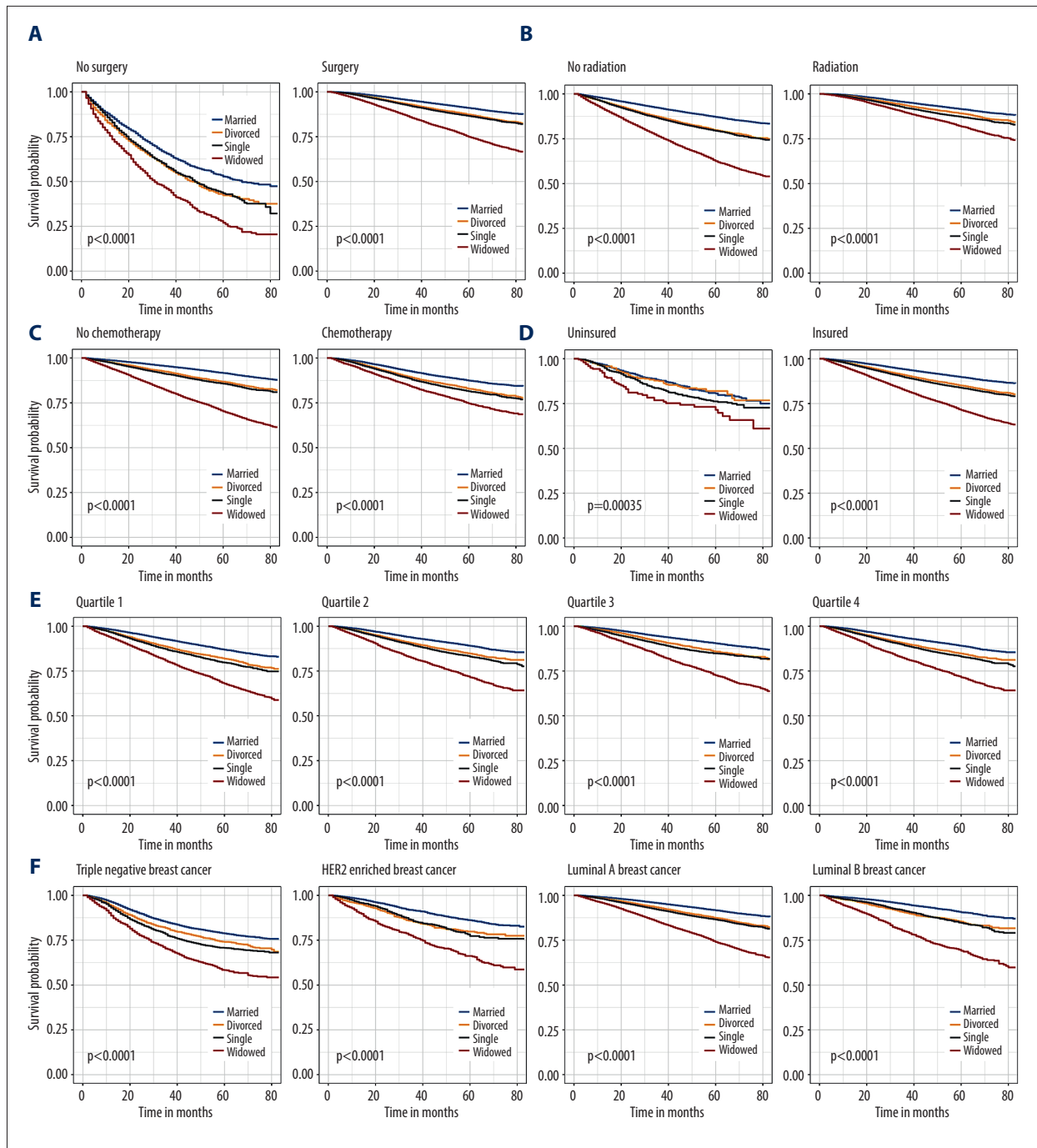


Figure 2. Kaplan-Meier analysis for overall survival in subgroups stratified by surgery (A), radiation (B), chemotherapy (C), insurance status (D), median household income (E), and subtype (F).

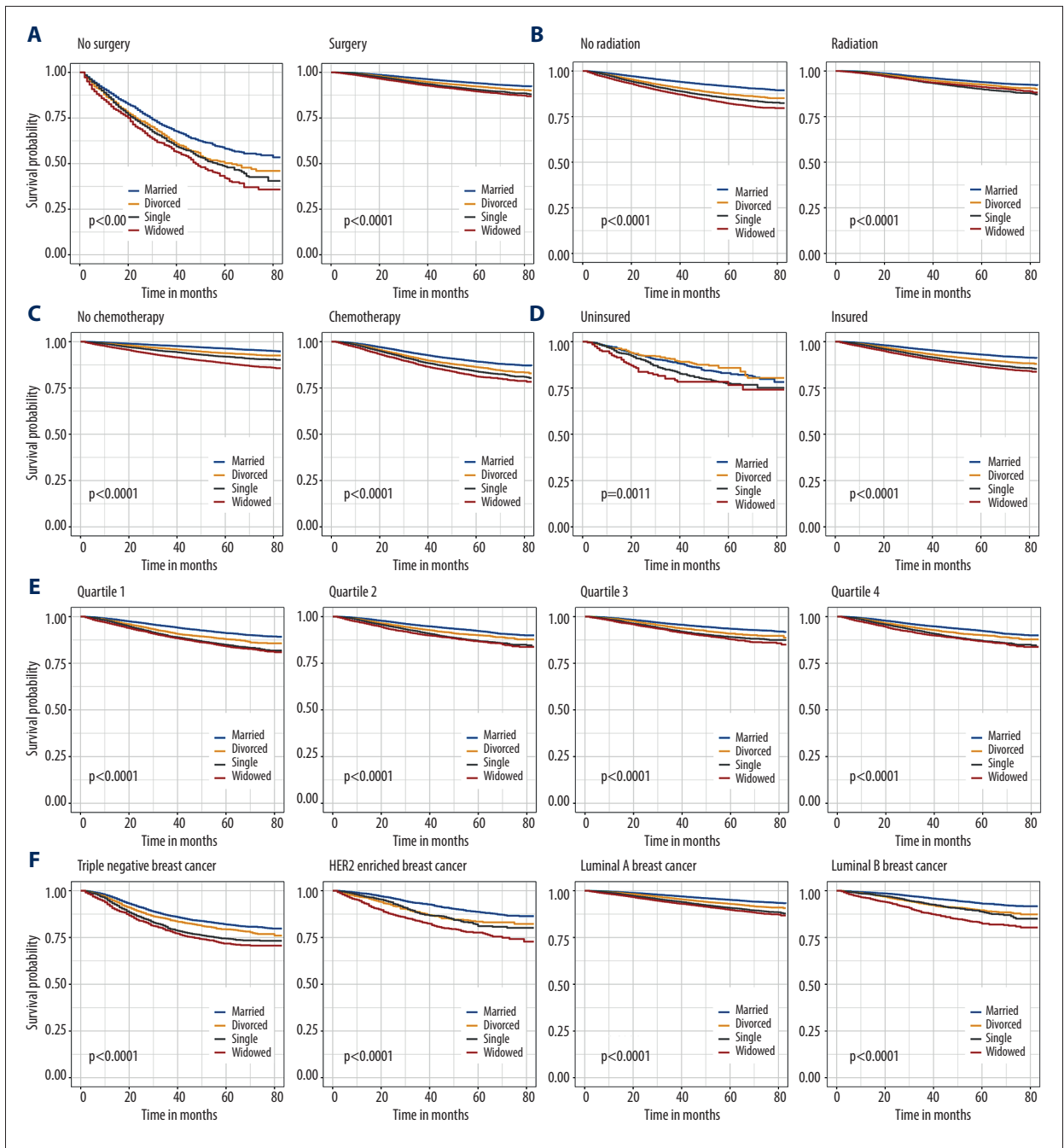


Figure 3. Breast cancer-specific survival curves in subgroups stratified by surgery (A), radiation (B), chemotherapy (C), insurance status (D), median household income (E), and subtype (F).

Table 4. Patient baseline characteristics after PSM.

Characteristic	Divorced	Married	P value	Single	Married	P value	Widowed	Married	P value
	(%)	(%)		(%)	(%)		(%)	(%)	
	22754	22754		19148	19148		19148	19148	
Age									
18–49	4653 (20.4)	4734 (20.8)	0.744	440 (2.3)	440 (2.3)	0.958	440 (2.3)	440 (2.3)	0.958
50–59	6625 (29.1)	6642 (29.2)		1718 (9.0)	1728 (9.0)		1718 (9.0)	1728 (9.0)	
60–69	7093 (31.2)	7093 (31.2)		5265 (27.5)	5251 (27.4)		5265 (27.5)	5251 (27.4)	
70–79	3425 (15.1)	3335 (14.7)		7597 (39.7)	7656 (40.0)		7597 (39.7)	7656 (40.0)	
≥80	958 (4.2)	950 (4.2)		4128 (21.6)	4073 (21.3)		4128 (21.6)	4073 (21.3)	
Race									
White	17685 (77.7)	17605 (77.4)	0.826	15575 (81.3)	15434 (80.6)	0.084	15575 (81.3)	15434 (80.6)	0.084
Black	3530 (15.5)	3582 (15.7)		1957 (10.2)	2081 (10.9)		1957 (10.2)	2081 (10.9)	
API	1380 (6.1)	1410 (6.2)		1492 (7.8)	1529 (8.0)		1492 (7.8)	1529 (8.0)	
AI	159 (0.7)	157 (0.7)		124 (0.6)	104 (0.5)		124 (0.6)	104 (0.5)	
Gender									
Male	113 (0.5)	112 (0.5)	1.000	83 (0.4)	74 (0.4)	0.522	83 (0.4)	74 (0.4)	0.522
Female	22641 (99.5)	22642 (99.5)		19065 (99.6)	19074 (99.6)		19065 (99.6)	19074 (99.6)	
Median household income									
Quartile 1	6606 (29.0)	6592 (29.0)	0.989	5905 (30.8)	5887 (30.7)	0.195	5905 (30.8)	5887 (30.7)	0.195
Quartile 2	5534 (24.3)	5512 (24.2)		4628 (24.2)	4590 (24.0)		4628 (24.2)	4590 (24.0)	
Quartile 3	5623 (24.7)	5638 (24.8)		4493 (23.5)	4385 (22.9)		4493 (23.5)	4385 (22.9)	
Quartile 4	4991 (21.9)	5012 (22.0)		4122 (21.5)	4286 (22.4)		4122 (21.5)	4286 (22.4)	
Insurance									
Uninsured	500 (2.2)	501 (2.2)	1.000	180 (0.9)	185 (1.0)	0.833	180 (0.9)	185 (1.0)	0.833
Insured	22254 (97.8)	22253 (97.8)		18968 (99.1)	18963 (99.0)		18968 (99.1)	18963 (99.0)	
Grade									
I	4634 (20.4)	4602 (20.2)	0.917	4350 (22.7)	4300 (22.5)	0.144	4350 (22.7)	4300 (22.5)	0.144
II	9265 (40.7)	9264 (40.7)		8514 (44.5)	8383 (43.8)		8514 (44.5)	8383 (43.8)	
III	8855 (38.9)	8888 (39.1)		6284 (32.8)	6465 (33.8)		6284 (32.8)	6465 (33.8)	

Table 4 continued. Patient baseline characteristics after PSM.

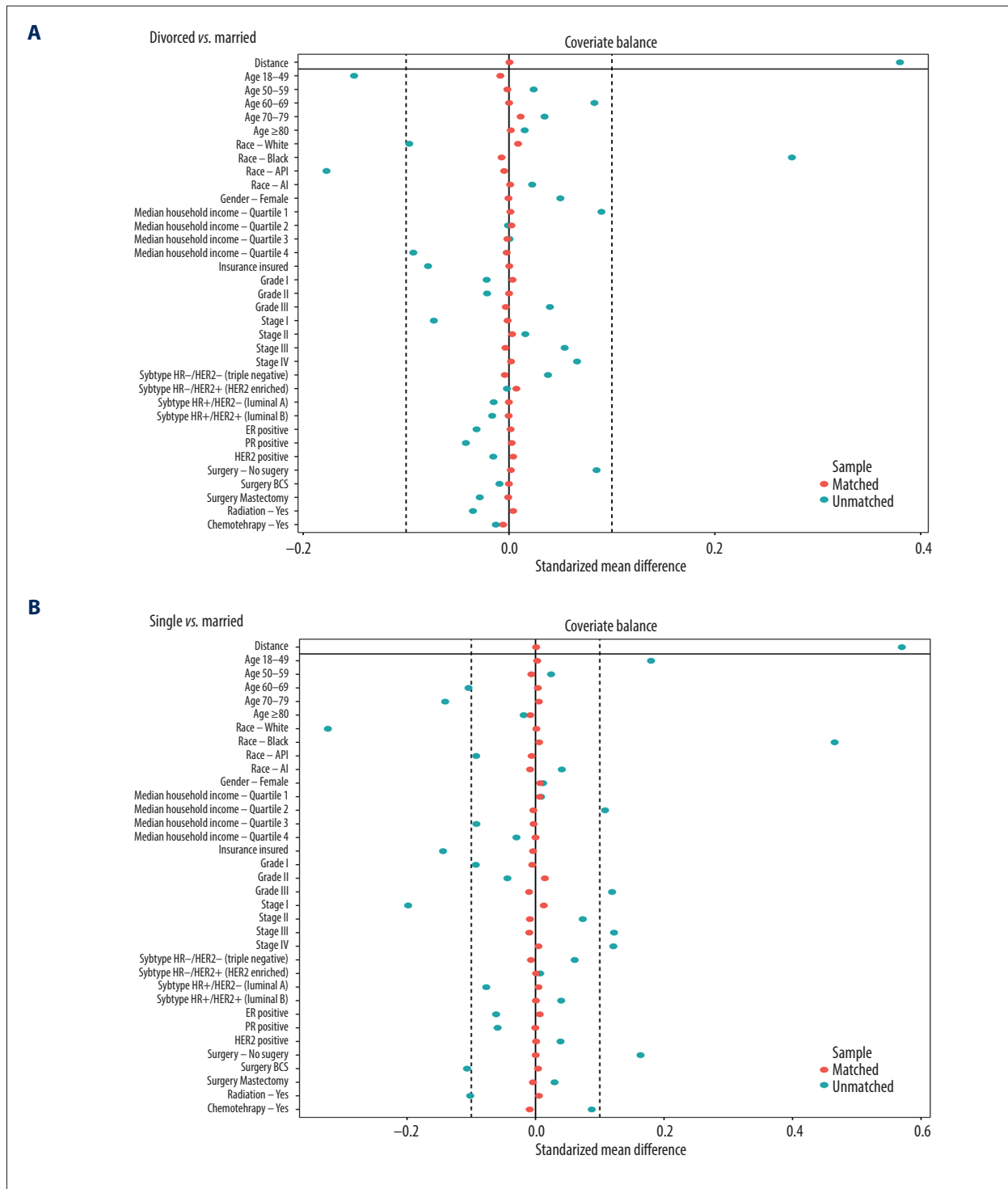
Characteristic	Divorced (%)	Married (%)	P value	Single (%)	Married (%)	P value	Widowed (%)	Married (%)	P value
	22754	22754		19148	19148		19148	19148	
Stage									
I	11345 (49.9)	11360 (49.9)	0.973	10544 (55.1)	10561 (55.2)	0.944	10544 (55.1)	10561 (55.2)	0.944
II	7853 (34.5)	7821 (34.4)		6021 (31.4)	5978 (31.2)		6021 (31.4)	5978 (31.2)	
III	2634 (11.6)	2659 (11.7)		1830 (9.6)	1858 (9.7)		1830 (9.6)	1858 (9.7)	
IV	922 (4.1)	914 (4.0)		753 (3.9)	751 (3.9)		753 (3.9)	751 (3.9)	
Subtype									
HR-/HER2- (triple negative)	3079 (13.5)	3111 (13.7)	0.871	2177 (11.4)	2256 (11.8)	0.151	2177 (11.4)	2256 (11.8)	0.151
HR-/HER2+ (HER2 enriched)	1214 (5.3)	1178 (5.2)		902 (4.7)	925 (4.8)		902 (4.7)	925 (4.8)	
HR+/HER2- (Luminal A)	15769 (69.3)	15771 (69.3)		14259 (74.5)	14065 (73.5)		14259 (74.5)	14065 (73.5)	
HR+/HER2+ (Luminal B)	2692 (11.8)	2694 (11.8)		1810 (9.5)	1902 (9.9)		1810 (9.5)	1902 (9.9)	
Surgery									
No surgery	1303 (5.7)	1294 (5.7)	0.983	1227 (6.4)	1186 (6.2)	0.197	1227 (6.4)	1186 (6.2)	0.197
BCS	12814 (56.3)	12815 (56.3)		11428 (59.7)	11598 (60.6)		11428 (59.7)	11598 (60.6)	
Mastectomy	8637 (38.0)	8645 (38.0)		6493 (33.9)	6364 (33.2)		6493 (33.9)	6364 (33.2)	
Radiation									
None/unknown	10237 (45.0)	10282 (45.2)	0.678	9507 (49.7)	9593 (50.1)	0.385	9507 (49.7)	9593 (50.1)	0.385
Yes	12517 (55.0)	12472 (54.8)		9641 (50.3)	9555 (49.9)		9641 (50.3)	9555 (49.9)	
Chemotherapy									
No/unknown	12022 (52.8)	11956 (52.5)	0.542	13528 (70.6)	13479 (70.4)	0.591	13528 (70.6)	13479 (70.4)	0.591
Yes	10732 (47.2)	10798 (47.5)		5620 (29.4)	5669 (29.6)		5620 (29.4)	5669 (29.6)	

PSM – propensity score matching.

Discussion

This is the first study to investigate the influence of marital status on IDC prognosis using PSM in the SEER database. In comparison to previous SEER-based studies, we particularly assessed significant covariates, including molecular subtype, household income, and insurance. We found that 4 marital subgroups showed different survival outcomes for OS and

BCSS. In multivariate Cox analysis encompassing an integrated range of variables, we demonstrated that marriage was an independent prognostic and protective factor for OS and BCSS, and widowed patients were the most likely to die of IDC. After PSM, we further confirmed that those who married showed better OS and BCSS compared to the divorced, single or widowed patients.



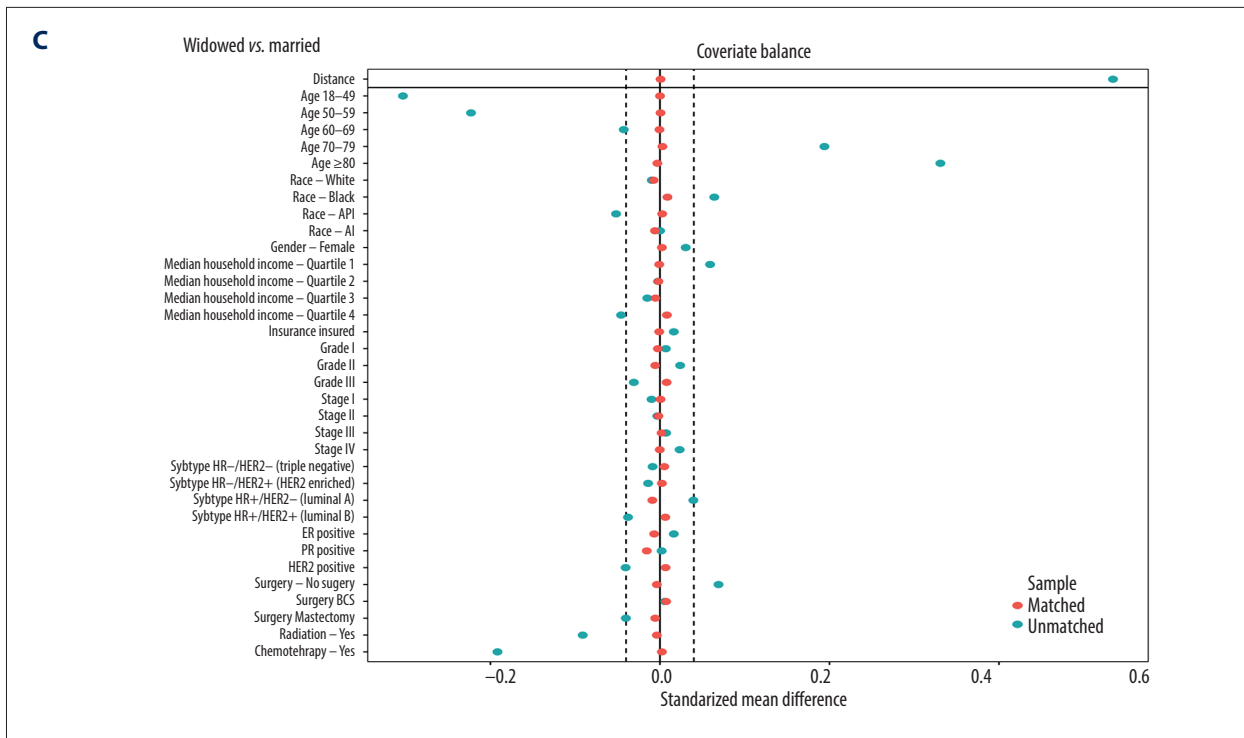


Figure 4. (A) The mean difference in all variables before and after PSM between divorced and married groups. (B) The mean difference between single and married groups. (C) The mean difference between widowed and married groups.

These findings raise the intriguing question of why married patients showed better clinical outcomes. One hypothesis is the higher likelihood for early diagnosis in those who are married. Studies have shown that delayed diagnosis can lead to poor survival of unmarried patients [17,23,24]. In the present study, widowed patients tended to be older than married patients. The incidence of metastasis was lower in the married group (2.9%) compared to the divorced (4.2%), single (5.3%), and widowed (4.0%) groups. Spouses might facilitate early IDC diagnosis, leading to better prognosis.

Secondly, married patients tended to have more financial resources and better access to effective treatment [25,26]. Spouses and their children may provide financial assistance that is unavailable to single, divorced, or widowed patients [27]. Our research indicated that compared with married patients, those who were widowed, single, or divorced tended to be undertreated, which may have contributed to their worse prognosis [28].

Thirdly, married patients might obtain extra psychological and emotional support from their spouse and children, which can improve disease outcomes [29]. A cancer diagnosis was reported to cause higher levels of psychological distress than that of other chronic diseases [30]. In addition, compared to married patients, the single, divorced, and widowed patients were more likely to have depression and anxiety after a diagnosis of

cancer [31]. Stress and depression combined had an association with immune dysfunction, nonadherence to medical advice, and tumor progression [32,33]. Emotional assistance can improve the quality of life, thereby preventing disease-associated decline in breast cancer patients [34,35]. Therefore, the benefits of psychosocial support should not be underestimated for single, divorced, and widowed populations. It is vital that physicians screen for such distress and provide psychosocial support interventions as required.

Fourthly, it was reported that married people have healthier lifestyle behaviors [36]. The single, divorced, and widowed patients were more likely have unhealthy lifestyles, such as heavy drinking and smoking, which can adversely affect overall survival of breast cancer patients [37,38]. This may partly explain the better prognosis in those who are married.

Some limitations of the present study should be discussed. Firstly, reproductive history and comorbidities were not included in the SEER database. These missing factors associated with prognosis may lead to potential bias. Secondly, the SEER database records marital status at diagnosis, but we lacked detailed information on the quality of marriage, the subsequent changes in marital status, and other marital statuses, including gay, lesbian, bisexual, and transgender. Finally, given the retrospective nature of our analysis, further prospective studies are required.

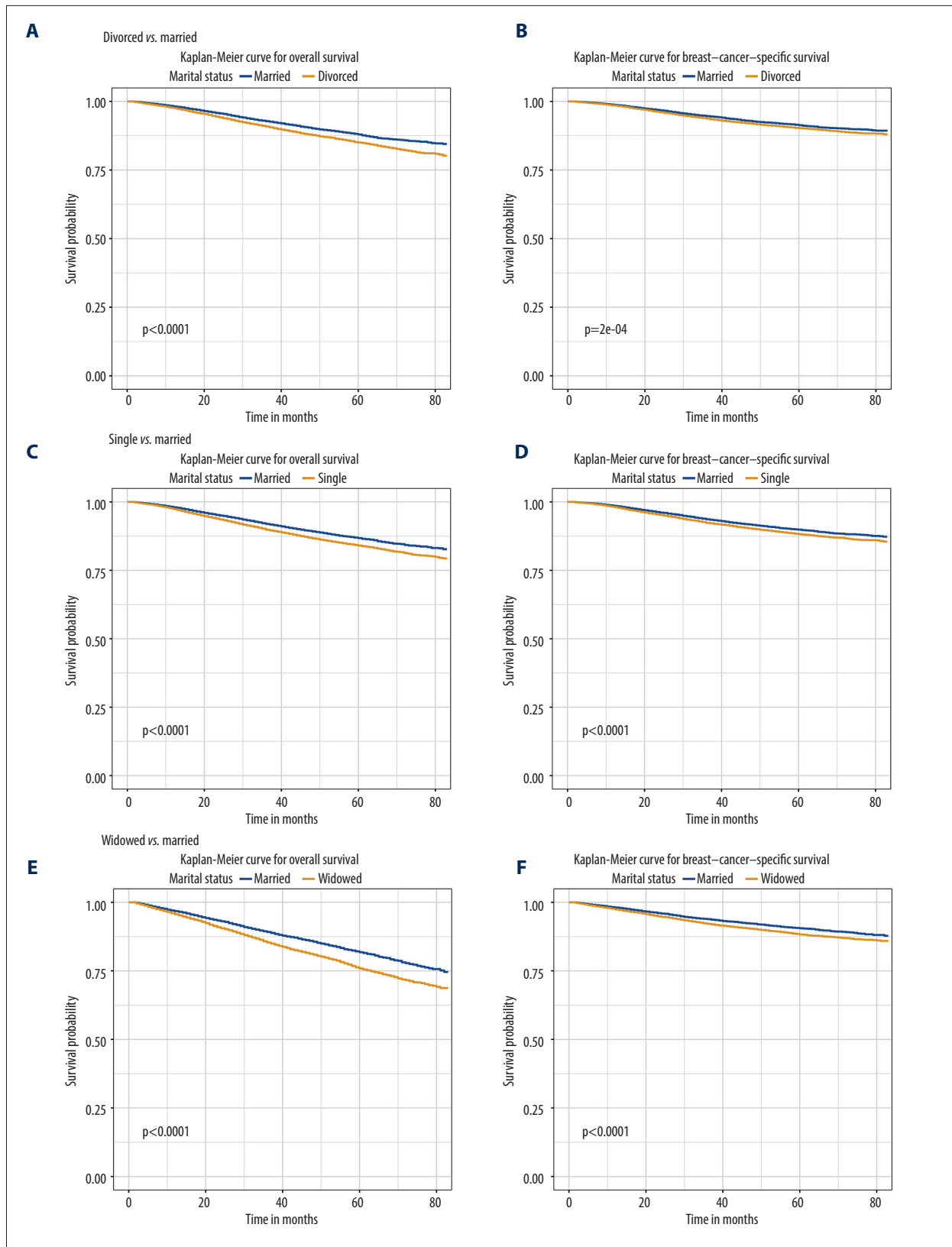


Figure 5. The overall survival (A, C, E) and breast cancer-caused special survival (B, D, F) of patients with breast cancer according to marital status after PSM.

Conclusions

This study, which had a large sample and used ingenious statistical analyses, found that married status was a protective prognostic factor for IDC patients. The single, divorced, and widowed patients were at higher risk of undertreatment, metastasis, and poor outcomes. Widowed patients had the highest mortality rates. Targeted psychosocial support should now be provided to these IDC patient subsets.

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Conflict of interests

None.

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