

Delay in Surgical Treatment and Survival After Breast Cancer Diagnosis in Young Women by Race/Ethnicity

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Importance: Breast cancer in women between the ages of 15 and 39 years (adolescents and young adults [AYAs]) constitutes 5% to 6% of all breast cancer cases in the United States. Breast cancer in AYA women has a worse prognosis than in older women. Five-year survival rates are lowest for AYA women, and only a few studies have examined the impact of delay in treatment, race/ethnicity, and other socioeconomic factors on survival in AYA women.

Objective: To examine the impact of treatment delay time (TDT), race/ethnicity, socioeconomic status, insurance status, cancer stage, and age on the survival from breast cancer among AYA women.

Design, Setting, and Participants: This is a retrospective case-only study of 8860 AYA breast cancer cases diagnosed from 1997 to 2006 using the California Cancer Registry database.

Exposure: Treatment delay time was defined as the number of weeks between the date of diagnosis and date of definitive treatment. Kaplan-Meier estimation was used to generate survival curves, and a multivariate Cox proportional hazards regression model was performed to assess the association of TDT with survival while accounting for covariates (age, race/ethnicity, socioeconomic status, insurance status, cancer stage [American Joint Committee on Cancer], tumor markers, and treatment).

Main Outcomes and Measures: Five-year survival rates for breast cancer as influenced by host factors, tumor factors, and TDT.

Results: Treatment delay time more than 6 weeks after diagnosis was significantly different ($P < .001$) between racial/ethnic groups (Hispanic, 15.3% and African American, 15.3% compared with non-Hispanic white, 8.1%). Women with public or no insurance (17.8%) compared with those with private insurance (9.5%) and women with low socioeconomic status (17.5%) compared with those with high socioeconomic status (7.7%) were shown to have TDT more than 6 weeks. The 5-year survival in women who were treated by surgery and had TDT more than 6 weeks was 80% compared with 90% ($P = .005$) in those with TDT less than 2 weeks. In multivariate analysis, longer TDT, estrogen receptor negative status, having public or no insurance, and late cancer stage were significant risk factors for shorter survival.

Conclusions and Relevance: Young women with breast cancer with a longer TDT have significantly decreased survival time compared with those with a shorter TDT. This adverse impact on survival was more pronounced in African American women, those with public or no insurance, and those with low SES.

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THE AMERICAN CANCER Society reported that approximately 203 500 women in the United States were diagnosed with invasive breast cancer and nearly 39 500 died of breast cancer in 2011. Although the majority of breast cancers occur among women 50 years and older, 11 300 were diagnosed among women younger than 40 years and nearly 1200 died of breast cancer in 2011 in that age group.¹

Although 5% to 6% of all breast cancers occur in adolescents and young adults (AYAs) (aged 15-39 years),² the disease is considered to be more aggressive with worse prognosis than in older

women.³⁻⁵ Five-year survival rates for breast cancer are lowest for AYA women, attributed to the aggressive biologic and pathologic characteristics of tumors.⁶ Few studies have examined the impact of treatment delay time (TDT), race/

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ethnicity, and socioeconomic factors on survival after breast cancer in AYA women. Our research objective was to examine the impact of TDT, race/ethnicity, socioeconomic status (SES), insurance status, cancer stage, and age on the survival after breast cancer diagnosis among AYA women.

STUDY POPULATION

We performed a retrospective case-only observational study of AYA breast cancer cases diagnosed in California from 1997 to 2006 using the California Cancer Registry database. The California Cancer Registry is part of the National Cancer Institute Surveillance, Epidemiology, and End Results program, with standardized data collection and quality control protocols since 1988.⁷⁻¹⁰ Both case reporting and follow-up completion rates are more than 95% for the entire state of California.¹¹ After data are abstracted from medical and laboratory records by trained tumor registrars, tumor site, histologic diagnosis, cancer stage, and tumor receptor status are coded according to the World Health Organization criteria (*International Classification of Diseases for Oncology*, third edition).¹²

There were 12 189 incident breast cancer cases in AYA women diagnosed from 1997 to 2006. We included breast cancer defined by morphology codes 8500 to 8543 using *International Classification of Diseases for Oncology*, third edition. We included infiltrating ductal, infiltrating lobular, intraductal, and lobular carcinomas, inflammatory adenocarcinoma, and Paget disease. We excluded patients with in situ (n=1620) and other histologic diagnoses (n=940), unknown American Joint Committee on Cancer stage (n=524), incomplete chemotherapy information (n=221), incomplete date of diagnosis (n=18), and incomplete date of surgery (n=6). Thus, our sample size was 8860 AYA patients with breast cancer who had complete information necessary for the analyses (eFigure 1, <http://www.jamasurg.com>).

DEFINITION OF TDT

Treatment delay time was based on the number of weeks between date of diagnosis and date of definitive treatment. The date of diagnosis was the date of pathologic diagnosis. The date of definitive treatment was the date of (1) earliest definitive surgery (partial mastectomy including lumpectomy, subcutaneous mastectomy, total [simple] mastectomy, modified radical mastectomy, radical mastectomy, extended radical mastectomy, and mastectomy not otherwise specified; we classified patients who had surgery into 3 groups [partial, simple, and modified radical mastectomy]) or (2) definitive chemotherapy given as the first course of treatment (including neoadjuvant chemotherapy followed by surgery). The patients were divided into 3 groups: surgery only, neoadjuvant chemotherapy followed by surgery, and surgery followed by chemotherapy. The TDT was classified into 4 groups: less than 2 weeks, 2 to 4 weeks, 4 to 6 weeks, and more than 6 weeks.

PREDICTOR VARIABLES

Patient demographics included age (15-29 and 30-39 years), SES, race/ethnicity (white, African American, Hispanic, and Asian), and insurance status. The SES variable used in this study was a single index created from statewide census data measures of education, income, and occupation. The variable was created from a principle component analysis of census block group-level data, including median educational attainment, median household income, proportion below 200% of the federal poverty level, median house value, median rent, percentage employed, and proportion of the population with blue-collar employment.¹³ Each patient was assigned an SES quintile based on the SES distribution in the study population; more details about the SES score can be found in Yost et al.¹³ For the Cox proportional hazards regression analysis, SES was divided into

3 categories: the first quintile in one group, second to fourth quintiles in a second group, and fifth quintile into a third group.

Insurance status was grouped into public insurance including Medicaid (US government program for low-income or medically needy individuals) and other government-assisted programs; private insurance including health maintenance organization, preferred provider organization, managed care not otherwise specified, and military care; uninsured including individuals with self-pay; and unknown insurance status. Patients who were uninsured or self-pay were grouped with patients with public insurance.

Clinical variables include American Joint Committee on Cancer stage (I, II, III, and IV), tumor markers (estrogen, progesterone, and Her2New receptor status), lymph node status (positive, negative, and unknown), and type of surgery as defined earlier.

OUTCOME VARIABLE

The outcome variable was survival defined as the interval between the date of diagnosis and the date of death or study end point. Last date of follow-up was either the date of death or the last date of contact.

STATISTICS

Patients' demographic and clinical characteristics, such as age, race/ethnicity, stage, grade, SES, and treatment, were analyzed with the χ^2 test or Fisher exact test for categorical variables. Kaplan-Meier estimation was used to generate group-specific survival curves. The log-rank test was conducted to evaluate the relationship between categorical predictor variables and survival. After verifying the proportionality assumption, a Cox proportional hazards regression model was performed for multivariate analysis to produce hazard ratios (HRs) and 95% confidence intervals. Cox regression using forward stepwise selection of covariates was accomplished to assess the association of TDT with survival, accounting for covariates including race, insurance status, SES, age group, cancer stage, tumor markers, and tumor characteristics. A 2-tailed *P* value of less than .05 was considered significant.

RESULTS

Descriptive results are shown in **Table 1**. Our study population consisted of 8860 cases of breast cancer in AYA women, predominantly non-Hispanic white (49.8%) and Hispanic (27.7%). Overall, 28.3% of cases had stage I breast cancer and 18.2% had stages III to IV breast cancer (Table 1). The mean TDT for all cases was 2.7 weeks. Among patients with TDT more than 6 weeks, the greatest proportion were Hispanic and African American. This was statistically significant (*P* < .001) (Table 1). More young women with low SES had TDT more than 6 weeks than those with high SES (17.5% vs 7.7%, respectively) (*P* < .001); in addition, more women with public or no insurance had TDT more than 6 weeks compared with those with private insurance (17.8% vs 9.5%, respectively) (*P* < .001). As expected, more women with stage III breast cancer (14.6%), or stage IV (12.7%), had a TDT more than 6 weeks compared with those with stage I breast cancer (9.7%) (*P* < .001).

Figure 1 shows the 5-year survival by TDT and treatment modality. Patients with TDT more than 6 weeks

Table 1. Baseline Characteristics of Patients With Breast Cancer, Diagnosed 1997 to 2006 in California

Category	Total, No. (%) (N = 8860)	P Value	TDT, No. (%)			
			≤2 wk (n = 4268)	2-4 wk (n = 2413)	4-6 wk (n = 1183)	>6 wk (n = 996)
Race						
White	4410 (49.8)	<.001	2301 (52.2)	1222 (27.7)	530 (12.0)	357 (8.1)
African American	720 (8.1)		307 (42.6)	193 (26.8)	110 (15.3)	110 (15.3)
Hispanic	2458 (27.7)		1051 (42.8)	658 (26.8)	374 (15.2)	375 (15.3)
Asian	1219 (13.8)		588 (48.2)	327 (26.8)	161 (13.2)	143 (11.7)
Other	53 (0.6)		21 (39.6)	13 (24.5)	8 (15.1)	11 (20.8)
Age group, y						
15-29	705 (8.0)	.10	371 (52.6)	173 (24.5)	86 (12.2)	75 (10.6)
30-39	8155 (92.0)		3897 (47.8)	2240 (27.5)	1097 (13.5)	921 (11.3)
SES						
1st Quintile (lowest)	1263 (14.3)	<.001	557 (44.1)	311 (24.6)	174 (13.8)	221 (17.5)
2nd-4th Quintiles	5394 (60.9)		2559 (47.4)	1500 (27.8)	729 (13.5)	606 (11.2)
5th Quintile (highest)	2203 (24.9)		1152 (52.3)	602 (27.3)	280 (12.7)	169 (7.7)
Insurance status						
No insurance/public insurance	1496 (16.9)	<.001	651 (43.5)	337 (22.5)	242 (16.2)	266 (17.8)
Private/military insurance	6925 (78.2)		3393 (49.0)	1994 (28.8)	883 (12.8)	655 (9.5)
Unknown	439 (5.0)		224 (51.0)	82 (18.7)	58 (13.2)	75 (17.1)
AJCC stage						
I	2503 (28.3)	<.001	1346 (53.8)	608 (24.3)	306 (12.2)	243 (9.7)
II	4737 (53.5)		2262 (47.8)	1340 (28.3)	614 (13.0)	521 (11.0)
III	1368 (15.4)		542 (39.6)	396 (28.9)	230 (16.8)	200 (14.6)
IV	252 (2.8)		118 (46.8)	69 (27.4)	33 (13.1)	32 (12.7)
Estrogen receptor status						
Positive	4536 (51.2)	<.001	2106 (46.4)	1259 (27.8)	616 (13.6)	555 (12.2)
Negative	2897 (32.7)		1497 (51.7)	807 (27.9)	352 (12.2)	241 (8.3)
Unknown	1427 (16.1)		665 (46.6)	347 (24.3)	215 (15.1)	200 (14.0)
Progesterone receptor status						
Positive	4033 (45.5)	<.001	1931 (47.9)	1084 (26.9)	545 (13.5)	473 (11.7)
Negative	3233 (36.5)		1593 (49.3)	931 (28.8)	403 (12.5)	306 (9.5)
Unknown	1594 (18.0)		744 (46.7)	398 (25.0)	235 (14.7)	217 (13.6)
Her2New status						
Positive	1669 (18.8)	<.001	694 (41.6)	473 (28.3)	280 (16.8)	222 (13.3)
Negative	3556 (40.1)		1599 (45.0)	1030 (29.0)	494 (13.9)	433 (12.2)
Unknown	3635 (41.0)		1975 (54.3)	910 (25.0)	409 (11.3)	341 (9.4)
Positive lymph nodes						
No	4207 (47.5)	<.001	2105 (50.0)	1130 (26.9)	550 (13.1)	422 (10.0)
Yes	4388 (49.5)		2025 (46.1)	1228 (28.0)	599 (13.7)	536 (12.2)
Unknown	265 (3.0)		138 (52.1)	55 (20.8)	34 (12.8)	38 (14.3)
Treatment						
Surgery only	2320 (26.2)	<.001	1211 (52.2)	527 (22.7)	281 (12.1)	301 (13.0)
Surgery and chemotherapy	6540 (73.8)		3057 (46.7)	1886 (28.8)	902 (13.8)	695 (10.6)
Type of surgery						
Partial mastectomy	2384 (26.9)	<.001	1254 (52.6)	539 (22.6)	288 (12.1)	303 (12.7)
Simple mastectomy	994 (11.2)		276 (27.8)	322 (32.4)	216 (21.7)	180 (18.1)
Modified radical mastectomy	5482 (61.9)		2738 (49.9)	1552 (28.3)	679 (12.4)	513 (9.4)
Treatment						
Surgery only	4143 (46.8)	<.001	2089 (50.4)	1165 (28.1)	513 (12.4)	376 (9.1)
Surgery and chemotherapy neoadjuvant	949 (10.7)		355 (37.4)	284 (29.9)	159 (16.8)	151 (15.9)
Surgery and chemotherapy	3768 (42.5)		1824 (48.4)	964 (25.6)	511 (13.6)	469 (12.4)

Abbreviations: AJCC, American Joint Committee on Cancer; SES, socioeconomic status; TDT, treatment delay time.

had the worst 5-year survival (78%) compared with patients with TDT less than 2 weeks and 2 to 4 weeks (84% and 83%, respectively) ($P = .005$ using the log-rank test) (Figure 1A). When stratified by treatment modality, TDT was significantly different among patients who received surgery only ($P = .002$) (Figure 1B).

African American and Hispanic patients had worse 5-year survival compared with white and Asian patients (73% and 78%, compared with 85% and 86%, respectively) (**Table 2**). There was a statistically significant

heterogeneity in the 5-year survival across the different racial/ethnic groups (log-rank, $P < .001$); patients with public or no insurance had worse 5-year survival compared with those with private insurance (69% vs 86%; $P < .001$). In addition, patients who had low SES had worse 5-year survival than those with high SES (72% and 89%, respectively; $P < .001$). Lastly, patients who were 30 to 39 years old had a statistically significant better survival than patients who were 15 to 29 years old (83% and 76%; $P < .001$) (eFigure 2).

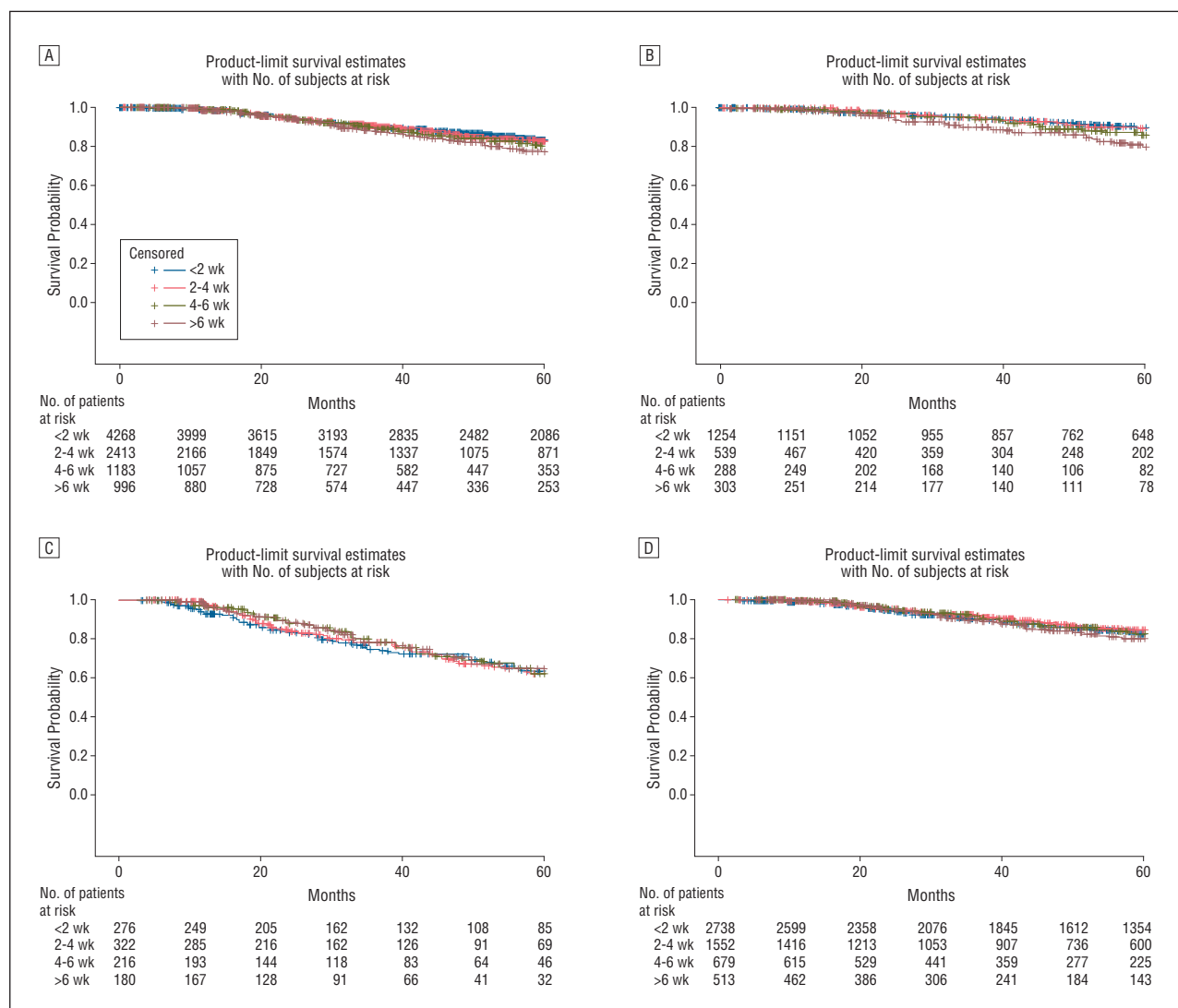


Figure 1. Five-year survival by treatment delay time (TDT) and treatment modality. A, Survival of young women with breast cancer based on TDT, with number of patients at risk (log-rank, $P = .005$). B, Survival of young women with breast cancer who underwent surgery only based on TDT, with number of patients at risk (log-rank, $P = .002$). C, Survival of young women with breast cancer who underwent surgery and neoadjuvant chemotherapy based on TDT, with number of patients at risk (log-rank, $P = .91$). D, Survival of young women with breast cancer who underwent surgery and chemotherapy after surgery based on TDT, with number of patients at risk (log-rank, $P = .30$).

We also examined the 5-year survival by race/ethnicity, insurance status, and SES among patients with TDT more than 6 weeks. A statistically significant difference in survival across the different racial/ethnic groups ($P < .001$) (**Figure 2A**) was observed, with African American patients having the worst 5-year survival compared with other racial/ethnic groups (57% in African American, 74% in Hispanic, 81% in Asian, and 86% in non-Hispanic white patients). Patients with low SES had worse 5-year survival than those with high SES (69% vs 84%, respectively; $P = .003$) (**Figure 2B**). Those with public or no insurance had a statistically significant worse 5-year survival than those with private insurance (65% vs 82%, respectively; $P < .001$) (**Figure 2C**).

Table 2 presents the 5-year survival for all patients stratified by treatment modality, race, age at diagnosis, SES, insurance status, cancer stage, estrogen receptor status, and TDT. We observed a 10% difference in survival

between the patients who received surgery only with TDT less than 2 weeks (90%) compared with those who received surgery only with TDT more than 6 weeks (80%). Overall, the neoadjuvant chemotherapy prior to surgery group had the worst 5-year survival across all characteristics. In addition, the effect of race/ethnicity, SES, and insurance status was expressed in all 3 treatment groups.

Multivariate analysis (**Table 3**) showed that African American patients had significantly shorter survival within the group receiving neoadjuvant chemotherapy (HR, 1.96; 95% CI, 1.28-2.98; $P = .01$) and the group receiving chemotherapy after surgery (HR, 1.46; 95% CI, 1.15-1.85; $P = .006$). Patients with low SES (first quintile and second-fourth quintiles) had shorter survival (HR, 1.66; 95% CI, 1.25-2.20 and HR, 1.31; 95% CI, 1.05-1.64, respectively) compared with those with high SES ($P < .001$). Patients with public or no insurance had shorter survival in all 3 treatment groups compared with those

Table 2. Five-Year Survival for All Patients Stratified by Treatment^a

	Hazard Ratio (95% CI)				P Value
	All	Surgery Only	Surgery and Neoadjuvant Chemotherapy	Surgery and Chemotherapy	
Race					
White	0.85 (0.84-0.86)	0.92 (0.90-0.94)	0.68 (0.63-0.73)	0.85 (0.83-0.87)	<.001
African American	0.73 (0.69-0.77)	0.82 (0.75-0.89)	0.50 (0.37-0.63)	0.73 (0.58-0.78)	
Hispanic	0.78 (0.76-0.80)	0.82 (0.78-0.86)	0.62 (0.56-0.68)	0.80 (0.77-0.83)	
Asian	0.86 (0.84-0.89)	0.92 (0.88-0.96)	0.62 (0.51-0.73)	0.87 (0.84-0.90)	
Age group, y					
15-29	0.76 (0.72-0.80)	0.86 (0.78-0.94)	0.56 (0.43-0.69)	0.76 (0.71-0.81)	<.001
30-39	0.83 (0.81-0.85)	0.89 (0.87-0.91)	0.64 (0.60-0.68)	0.84 (0.83-0.85)	
SES					
1st Quintile	0.72 (0.69-0.75)	0.78 (0.73-0.83)	0.52 (0.43-0.61)	0.74 (0.70-0.78)	<.001
2nd-4th Quintiles	0.82 (0.81-0.83)	0.90 (0.88-0.92)	0.62 (0.56-0.68)	0.82 (0.80-0.84)	
5th Quintile	0.89 (0.87-0.91)	0.93 (0.90-0.96)	0.77 (0.71-0.83)	0.89 (0.87-0.91)	
Insurance status					
Private/military insurance	0.86 (0.76-0.96)	0.92 (0.90-0.94)	0.69 (0.65-0.73)	0.85 (0.71-0.98)	<.001
No insurance/public insurance	0.69 (0.66-0.72)	0.74 (0.68-0.80)	0.55 (0.47-0.63)	0.71 (0.67-0.75)	
AJCC stage					
I	0.95 (0.94-0.96)	0.96 (0.95-0.97)	0.85 (0.71-0.99)	0.94 (0.92-0.96)	<.001
II	0.84 (0.83-0.85)	0.86 (0.83-0.89)	0.76 (0.71-0.81)	0.84 (0.83-0.85)	
III	0.59 (0.55-0.63)	0.56 (0.44-0.68)	0.54 (0.48-0.68)	0.62 (0.57-0.67)	
IV	0.37 (0.30-0.44)	0.39 (0.18-0.60)	0.38 (0.26-0.50)	0.37 (0.27-0.47)	
Estrogen receptor status					
Positive	0.87 (0.86-0.88)	0.94 (0.92-0.96)	0.69 (0.64-0.74)	0.87 (0.81-0.85)	<.001
Negative	0.75 (0.73-0.77)	0.82 (0.78-0.86)	0.57 (0.51-0.63)	0.77 (0.75-0.79)	
Unknown	0.82 (0.79-0.85)	0.86 (0.83-0.89)	0.65 (0.57-0.73)	0.83 (0.81-0.85)	
TDT, wk					
<2	0.84 (0.83-0.85)	0.90 (0.88-0.92)	0.64 (0.57-0.71)	0.83 (0.81-0.85)	.005
2-4	0.83 (0.81-0.85)	0.90 (0.87-0.93)	0.63 (0.56-0.70)	0.85 (0.83-0.87)	
4-6	0.80 (0.77-0.83)	0.86 (0.80-0.92)	0.63 (0.54-0.72)	0.83 (0.79-0.87)	
>6	0.78 (0.74-0.82)	0.80 (0.73-0.87)	0.65 (0.56-0.74)	0.80 (0.75-0.85)	

Abbreviations: AJCC, American Joint Committee on Cancer; SES, socioeconomic status; TDT, treatment delay time.

^aP values are based on log-rank tests.

with private insurance (surgery only: HR, 2.47; 95% CI, 1.78-3.44; $P < .001$; neoadjuvant chemotherapy: HR, 1.38; 95% CI, 1.03-1.86; $P = .001$; and chemotherapy after surgery: HR, 1.59; 95% CI, 1.32-1.91; $P < .001$). In addition, women with stage II to IV breast cancer had a significantly shorter survival across all 3 treatment modalities ($P < .001$) when compared with patients with stage I disease. Similarly, women with estrogen receptor–negative tumors had the worst 5-year survival for all 3 treatment modalities compared with patients with estrogen receptor–positive tumors (surgery only: HR, 3.14; 95% CI, 2.18-4.53; $P < .001$; neoadjuvant chemotherapy: HR, 2.19; 95% CI, 1.63-2.94; $P < .001$; and chemotherapy after surgery: HR, 2.26; 95% CI, 1.92-2.66; $P < .001$). Lastly, patients with surgery only and TDT more than 6 weeks had shorter survival at 60 months (HR, 1.82; 95% CI, 1.21-2.74; $P = .03$) compared with patients with TDT less than 2 weeks.

DISCUSSION

The results of this study show that TDT, race/ethnicity, insurance status, and SES have a significant effect on the 5-year

survival after breast cancer diagnosis in AYA women. The data presented herein provide a unique perspective that can be used to improve the outcome of breast cancer in AYA women. Our findings demonstrate that young women with a delay in surgical treatment (>6 weeks) have shorter survival compared with those who had surgery closer to their diagnosis. This adverse impact on survival was more pronounced in African American patients, those with public or without insurance, and those with low SES. In univariate analysis, Hispanic and African American patients with public or no insurance and low SES were more likely to have longer TDT. In multivariate analysis, longer TDT, estrogen receptor negative status, having public or no insurance, and having late-stage disease were significant risk factors for shorter survival.

Since breast cancer is not common in young women, there are very few studies in the literature that have focused on women younger than 40 years. However, a study by Sariego¹⁴ studied 70 437 cases using the American College of Surgeons National Cancer Data Base (1998-2005). He found that in young women with breast cancer 20% were diagnosed with advanced disease (stages III and IV). This is confirmed in our study where 18.2%

of our young breast cancer cases were diagnosed at an advanced stage (stages III and IV). This study did not examine delay in treatment as a factor affecting survival. Our study found that many risk factors, including stage, can influence the survival of young women with breast cancer, in particular, delay in surgical treatment.

Shavers et al¹⁵ examined a population of younger patients with breast cancer and demonstrated that both African American and Hispanic women present with later-stage disease and more adverse prognostic indicators compared with white women, resulting in poorer overall survival. We confirmed these findings and added the value of time to treatment as a factor that influences survival. However, Bradley et al¹⁶ found that African American women did not have a higher likelihood of death in comparison with white women after controlling for Medicaid enrollment and poverty. Although the majority of our patient population was white or Hispanic, with only 8% being African American,¹⁷ we demonstrated that African American young women with breast cancer have the highest likelihood of death, after controlling for SES and insurance status.

Fedewa et al¹⁸ examined 3 levels of treatment delay, greater than 30, 60, and 90 days after biopsy, and found that African American and Hispanic patients had higher risks of treatment delay compared with white patients, independent of health insurance status, cancer stage at diagnosis, and age. Another study by Bilimoria et al¹⁹ demonstrated that African American and Hispanic patients with breast cancer were more likely to have more prolonged wait times (>30 days) for surgery. Lastly, Halpern et al²⁰ also found that African American and Hispanic women were more likely to present with advanced-stage breast cancer. The difference in survival between racial/ethnic groups among patients with prolonged TDT (>6 weeks) was significant (Figure 2A). Additionally, we showed that African American women have the highest likelihood of death from breast cancer independent of age, SES, insurance status, cancer stage, and TDT (Table 2). Moreover, when we defined the treatment delay as less than 2 weeks, 2 to 4 weeks, 4 to 8 weeks, 8 to 12 weeks, and more than 12 weeks we observed similar results in both univariate and multivariate analyses (eFigure 3).

In addition to the significant impact of race/ethnicity, few previous studies have examined the effect of delay in treatment on breast cancer survival. Brazda et al,²¹ after controlling for cancer stage, found that delays in time to treatment had no effect on survival. Machiavelli et al²² reported no significant difference in survival by treatment delay within each stage. An earlier study by Charlson²³ demonstrated that patients with delays of 3 months or more had a more advanced clinical disease stage than those with shorter delays (<3 months); however, within each disease stage, prognosis was not affected by the delay, and progression of disease did not invariably occur among patients with longer delays. In contrast, the current study examined only women younger than 40 years with breast cancer. The earlier-mentioned studies examined women with breast cancer of all ages.

Jung et al²⁴ demonstrated that delays of more than 12 weeks in receiving treatment for metastatic breast cancer were related to adverse survival outcomes. Additionally, Af-

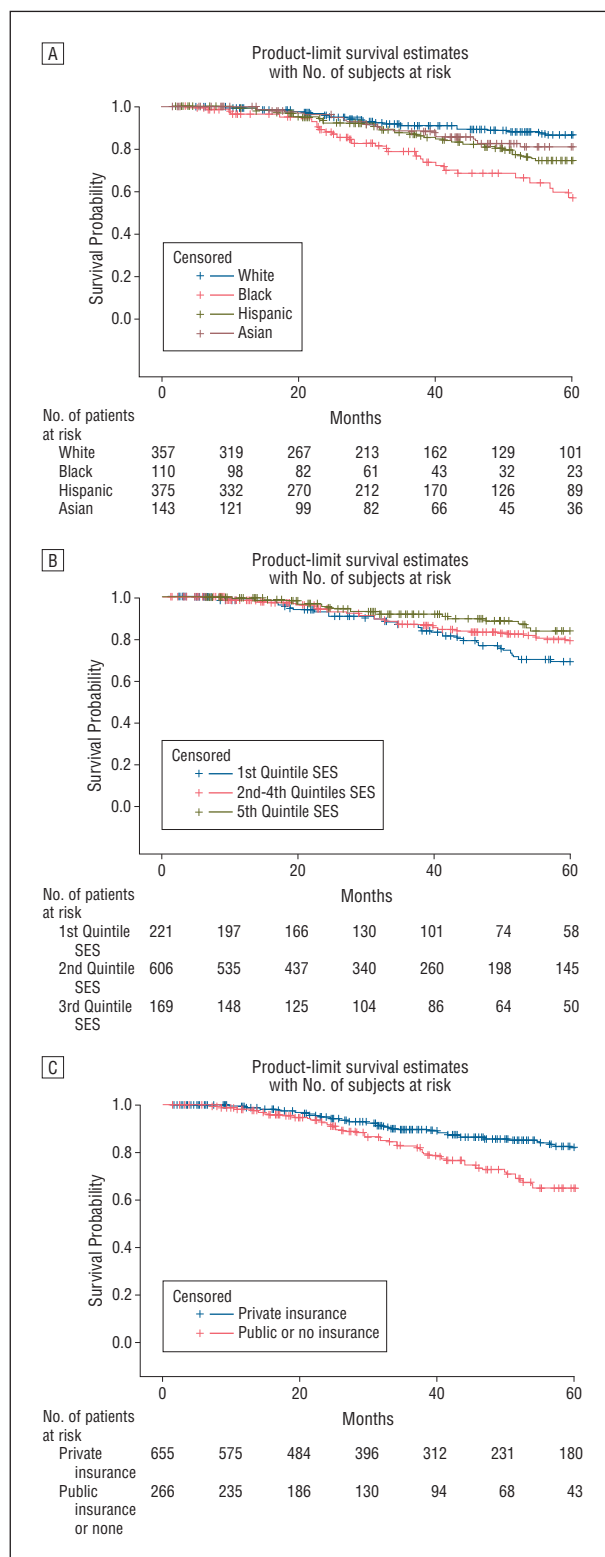


Figure 2. Five-year survival by race/ethnicity, insurance status, and socioeconomic (SES) status among patients with treatment delay time (TDT) more than 6 weeks. A, Survival of young women with breast cancer with TDT more than 6 weeks based on race, with number of patients at risk (log-rank, $P < .001$). B, Survival of young women with breast cancer with TDT more than 6 weeks based on SES, with number of patients at risk (log-rank, $P < .001$). C, Survival of young women with breast cancer with TDT more than 6 weeks based on insurance, with number of patients at risk (log-rank, $P = .03$).

Table 3. Adjusted Hazard Ratio of the Likelihood of Death by Treatment for Young Women With Breast Cancer in California, 1997 to 2006, Using a Multivariate Cox Proportional Hazards Regression Model^a

	Hazard Ratio (95% CI)		
	Surgery Only	Surgery and Neoadjuvant Chemotherapy	Surgery and Chemotherapy
Race			
White		1 [Reference]	1 [Reference]
African American		1.96 (1.28-2.98)	1.46 (1.15-1.85)
Hispanic		1.04 (0.76-1.42)	0.98 (0.81-1.19)
Asian		1.26 (0.82-1.95)	0.88 (0.67-1.15)
P value		.01	.006
Age group, y			
15-29			1.43 (1.13-1.80)
30-39			1 [Reference]
P value			.001
SES			
1st Quintile			1.66 (1.25-2.20)
2nd-4th Quintiles			1.31 (1.05-1.64)
5th Quintile			1 [Reference]
P value			<.001
Year of diagnosis			0.94 (0.91-0.97)
P value			<.001
Insurance status			
Private/military insurance	1 [Reference]	1 [Reference]	1 [Reference]
No insurance/public insurance	2.47 (1.78-3.44)	1.38 (1.03-1.86)	1.59 (1.32-1.91)
Unknown	1.77 (1.09-2.86)	2.20 (1.37-3.54)	0.94 (0.66-1.34)
P value	<.001	.001	<.001
AJCC stage			
I	1 [Reference]	1 [Reference]	1 [Reference]
II	3.14 (2.08-4.76)	1.95 (0.61-6.20)	2.79 (2.09-3.72)
III	10.23 (6.27-16.68)	4.28 (1.36-13.49)	8.24 (6.05-11.23)
IV	24.51 (13.26-45.28)	7.95 (2.45-25.79)	22.67 (15.88-32.93)
P value	<.001	<.001	<.001
Estrogen receptor status			
Positive	1 [Reference]	1 [Reference]	1 [Reference]
Negative	3.14 (2.18-4.53)	2.19 (1.63-2.94)	2.26 (1.92-2.66)
Unknown	1.89 (1.28-2.81)	1.46 (1.00-2.14)	1.24 (0.95-1.61)
P value	<.001	<.001	<.001
TDT, wk			
<2	1 [Reference]		
2-4	0.96 (0.65-1.42)		
4-6	1.11 (0.69-1.78)		
>6	1.82 (1.21-2.74)		
P value	.03		

Abbreviations: AJCC, American Joint Committee on Cancer; SES, socioeconomic status; TDT, treatment delay time.

^aP values are based on score χ^2 tests.

zelius et al²⁵ studied patient and doctor delay (0-14 days), intermediate (15-60 days) and long (>60 days). They found that long patient delay was associated with an unfavorable outcome, but the prognosis was superior for patients with long doctor delay as compared with those with short doctor delay. In contrast, our study shows that delay in surgical treatment that can be classified mainly as a doctor delay significantly influenced survival.

Although it is of utmost importance for young women with breast cancer to have surgery soon after diagnosis, economic barriers such as SES and insurance status may prevent them from having surgery in a timely manner. Similar to our findings, Bilimoria et al¹⁹ found that patients who were uninsured or with Medicaid insurance were more likely to have more prolonged wait times for surgery. A study by DeSantis et al²⁶ demonstrated that

uninsured women were more likely to have metastasis and larger tumors than privately insured women. Halpern et al²⁰ found that patients without health insurance or with Medicaid coverage were more likely to present with advanced-stage breast cancer. Lastly, Bradley et al¹⁶ found that low SES was associated with late-stage breast cancer at diagnosis, type of treatment received, and death.

To our knowledge, our study is the first to examine the impact of race/ethnicity, cancer stage at diagnosis, age, insurance type, SES, and delay in surgical intervention on survival of women with breast cancer. In contrast to some of the previous studies, we focused only on women younger than 40 years, where breast cancer is rare but mortality is high mainly because of aggressive biologic and pathologic characteristics of tumors specific to this age group. In our study, surgical delay time was a sig-

nificant risk factor for reduced survival after breast cancer diagnosis independent of race/ethnicity, cancer stage at diagnosis, age, insurance type, and SES. After a diagnosis of breast cancer is established, it may be difficult for a physician to make arrangements for surgery because of barriers such as a patient's lack of insurance or pending public insurance due to unemployment, which can be directly associated with low SES. Consequently, although surgical delay time is seen mostly as a physician-related delay, it can be affected by other patient-related factors such as insurance status and SES.

Limitations of this study include the challenges that are inherent in using a registry as a source of data. There were patients excluded because of missing information including cancer stage and dates of diagnosis and surgery. Also, this study focused on young women who are in their reproductive years, and if the diagnosis of breast cancer was made during pregnancy, treatment may have been delayed until after the birth of the baby. This may account for a few women who had a delay in surgical treatment; however, pregnancy status is not available in the California Cancer Registry.

Our study examined surgical delay time, which is a physician-related delay, after the diagnosis of breast cancer was established; however, it would also be important to examine physician-related delay prior to the diagnosis of breast cancer since there are many anecdotal stories of young women who presented to their primary care physicians on numerous occasions prior to being diagnosed with breast cancer. From our literature search, we did not find any studies examining physician-related delay prior to the diagnosis of breast cancer in a large cohort of young women. In conclusion, it is crucial to prevent further physician-related delays before and after the diagnosis of breast cancer is established to maximize the survival of these young women who are in the most productive time of their life.

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REFERENCES

1. American Cancer Society. *Breast Cancer Facts and Figures, 2011-2012*. Atlanta, GA: American Cancer Society Inc; 2011.
2. Bland KI, Menck HR, Scott-Conner CE, Morrow M, Winchester DJ, Winchester DP. The National Cancer Data Base 10-year survey of breast carcinoma treatment at hospitals in the United States. *Cancer*. 1998;83(6):1262-1273.
3. Bonnier P, Romain S, Charpin C, et al. Age as a prognostic factor in breast cancer: relationship to pathologic and biologic features. *Int J Cancer*. 1995;62(2):138-144.
4. Gajdos C, Tartter PI, Bleiweiss IJ, Bodian C, Brower ST. Stage 0 to stage III breast cancer in young women. *J Am Coll Surg*. 2000;190(5):523-529.
5. Fisher CJ, Egan MK, Smith P, Wicks K, Millis RR, Fentiman IS. Histopathology of breast cancer in relation to age. *Br J Cancer*. 1997;75(4):593-596.
6. Bleyer A, O'Leary M, Barr R, Ries LAG. *Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000*. Bethesda, MD: National Cancer Institute; 2006:116. NIH Pub. No. 06-5767.
7. Cancer Surveillance Section. *Cancer Reporting in California: Standards for Automated Reporting. California Cancer Reporting System Standards*. Vol 2. Sacramento: California Department of Health Services, Cancer Surveillance Section; 1997.
8. Cancer Surveillance Section. *Cancer Reporting in California: Data Standard for Localized/Regional Registries and California Cancer Registry. California Cancer Reporting System Standards*. Vol 3. Sacramento: California Department of Health Services, Cancer Surveillance Section; 1997.
9. Cancer Surveillance Section. *Abstract and Coding Procedures for Hospitals. California Cancer Reporting System Standards*. Vol 1. Sacramento: California Department of Health Services, Cancer Surveillance Section; 1997.
10. Cancer Surveillance Section. *Reporting Procedures for Physicians. California Cancer Reporting System Standards*. Vol 4. Sacramento: California Department of Health Services, Cancer Surveillance Section; 1997.
11. How complete are California Cancer Registry Data? California Cancer Registry website. http://www.ccrca.org/Inside_CCR/FAQ.shtml. Accessed March 22, 2012.
12. Flitz A, Percy C, Jack A. *International Classification of Diseases for Oncology*. 3rd ed. Geneva, Switzerland: World Health Organization; 2000.
13. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control*. 2001;12(8):703-711.
14. Sarrago J. Breast cancer in the young patient. *Am Surg*. 2010;76(12):1397-1400.
15. Shavers VL, Harlan LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients under age 35. *Cancer*. 2003;97(1):134-147.
16. Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. *J Natl Cancer Inst*. 2002;94(7):490-496.
17. Bleyer A, O'Leary M, Barr R, Ries LAG. *Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000*. Bethesda, MD: National Cancer Institute; 2006:114. NIH Pub. No. 06-5767.
18. Fedewa SA, Edge SB, Stewart AK, Halpern MT, Marlow NM, Ward EM. Race and ethnicity are associated with delays in breast cancer treatment (2003-2006). *J Health Care Poor Underserved*. 2011;22(1):128-141.
19. Bilimoria KY, Ko CY, Tomlinson JS, et al. Wait times for cancer surgery in the United States: trends and predictors of delays. *Ann Surg*. 2011;253(4):779-785.
20. Halpern MT, Bian J, Ward EM, Schrag NM, Chen AY. Insurance status and stage of cancer at diagnosis among women with breast cancer. *Cancer*. 2007;110(2):403-411.
21. Brazda A, Estroff J, Euhus D, et al. Delays in time to treatment and survival impact in breast cancer. *Ann Surg Oncol*. 2010;17(suppl 3):291-296.
22. Machiavelli M, Leone B, Romero A, et al. Relation between delay and survival in 596 patients with breast cancer. *Oncology*. 1989;46(2):78-82.
23. Charlson ME. Delay in the treatment of carcinoma of the breast. *Surg Gynecol Obstet*. 1985;160(5):393-399.
24. Jung SY, Sereika SM, Linkov F, Brufsky A, Weissfeld JL, Rosenzweig M. The effect of delays in treatment for breast cancer metastasis on survival. *Breast Cancer Res Treat*. 2011;130(3):953-964.
25. Afzelius P, Zedeler K, Sommer H, Mouridsen HT, Blichert-Toft M. Patient's and doctor's delay in primary breast cancer: prognostic implications. *Acta Oncol*. 1994;33(4):345-351.
26. DeSantis C, Jemal A, Ward EM. Disparities in breast cancer prognostic factors by race, insurance status, and education. *Cancer Causes Control*. 2010;21(9):1445-1450.