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Report

The influence of marital status on the stage at diagnosis, treatment, and survival of older women with breast cancer

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Summary

Research indicates an association between marital status and health but this link has not been thoroughly explored. Our goal was to examine the association of marital status on the diagnosis, treatment, and survival of older women with breast cancer and the potential role socioeconomic status, education level, and comorbidities may play in explaining these associations. Retrospective cohort study using linked Medicare and National Cancer Institute Surveillance, Epidemiology, and End Results cancer registry. The sample consisted of 32,268 women aged 65 years and older who received a diagnosis of breast cancer from 1991 to 1995. Information available through 1998 allowed for 3 years of follow-up. Results showed that unmarried women were more likely to be diagnosed with breast cancer stage II–IV versus stage I and *in situ* (OR 1.17; CI_{95} 1.12, 1.23). Unmarried women diagnosed with stage I or II breast cancer were less likely to receive definitive therapy (OR 1.24; CI_{95} 1.17, 1.31). Even after controlling for cancer stage and size at diagnosis and treatment received, unmarried women were at an increased risk of death from breast cancer (HR 1.25; CI_{95} 1.14, 1.37). Socioeconomic variables and comorbidity had little impact on the relationship between marital status and survival. Older married women were at decreased risk for mortality after a diagnosis of breast cancer. Many of the health benefits enjoyed by married women are likely derived from increased social support and social networks.

Introduction

Married persons enjoy overall better health and increased life expectancy compared with the unmarried (divorced, separated, never married) [1–5]. Research also indicates a survival advantage for married persons living with a chronic disease such as cancer [6–9]. Kravdal [6], for example, found married men and women with cancer to have a 15% reduced risk of death compared with unmarried men and women.

The survival advantage among married persons is poorly understood. Married persons typically enjoy higher socioeconomic status than unmarried persons, which may translate into better access to healthcare. Marriage may also reflect a healthy selection bias, such that those with psychiatric or physical impairments may be less likely to marry [3]. Marriage may also influence lifestyle behaviors such as health screenings, diet, and exercise, all of which may be mediating factors of better health [6]. Additionally, marriage may offer a protective benefit [7–9] through increased social support networks [10]. While loneliness or social isolation has a negative impact on health, positive relationships including marriage have shown a consistent protective effect against declining health and survival post acute illness [10–14]. For example, structural support, described as the interrelationship between a person and community, is associated with survival [11–13]. Other forms of social support including emotional, informational (help with researching a problem), and tangible or instrumental (i.e. reminding spouse to undergo screening exams, driving spouse to doctor appointments, or helping with physical care of spouse) may also be responsible for a survival advantage [10, 14].

For the present study, we investigated the association between marital status and diagnosis, treatment and survival for 32,268 women aged 65 or older with breast cancer. Data are from the Surveillance, Epidemiology, and End Results (SEER) tumor registries, merged with Medicare data for the years 1991 through 1995. This study extends previous research by including information on sociodemographics, comorbidity, and stage and tumor biologic characteristics of subjects.

Methods

Data sources

We used the merged SEER-Medicare database for women who received a diagnosis of breast cancer during the period of 1991 through 1995. The SEER program, supported by the National Cancer Institute, includes population-based tumor registries in selected geographic areas: the metropolitan areas of Detroit, San Francisco/Oakland, Atlanta, Seattle, Los Angeles and San Jose/Monterey; and the States of Connecticut, Iowa, New Mexico, Utah and Hawaii. These areas represent approximately 14% of the United States population [15]. The registries gather all newly diagnosed (incident) breast cancer cases from multiple reporting sources including hospitals; out patient clinics; laboratories; private medical practitioners; nursing homes; convalescent homes; hospices; autopsy reports and death certificates [16]. Information includes tumor location, size, American Joint Committee on Cancer stage (AJCC), axillary node status, estrogen receptor status; demographic characteristics such as age, sex, race, and marital status; and types of treatment provided within 4 months after the date of diagnosis [16].

The Medicare program is administered by the Centers for Medicare & Medicaid Services (CMS). The program covers hospital, physician, and other medical services for more than 97% of persons ≥65 years of age [17]. The Medicare claims data used in the study includes the following three files [18]: (1) Medicare Provider Analysis Review File, which contains inpatient hospital claims; (2) the Hospital Outpatient Standard Analytic File, which contains the claims for outpatient facility services; and (3) the 100% physician/supplier file, which contains the claims for physicians and other professional services. These data are available for all beneficiaries starting in 1991 and their Medicare claims are available through 1998.

Study population

The study population includes female patients aged 65 years or older who were diagnosed with breast cancer in 1991 through 1995, and were followed over a 3-year period (n = 32,268). Excluded were women who did not have full coverage of both Medicare Part A and Part B, or who were members of Health Maintenance Organizations (HMO), because claims from these organizations may not be complete.

Chemotherapy

Information concerning chemotherapy administration was obtained from the Medicare data using methods described in detail elsewhere [19, 20]. For the present study, we searched Medicare claims for chemotherapy administration made within 6 months of a breast cancer diagnosis.

Surgery and radiation therapy

Cancer-directed surgery was defined as either mastectomy, which includes total/subcutaneous/radical/modified radical mastectomy, or breast-conserving surgery (BCS), which includes segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified. Definitive surgical intervention for stage I or II breast cancer was defined as modified radical mastectomy or BCS plus axillary lymph node dissection followed by radiation therapy [19].

Analytic variables

Patient and tumor characteristics included age, race, marital status, income, education, comorbidity, tumor stage, tumor size, tumor grade, and receptor status. Age was categorized as 65–69, 70–74, 75–79, and ≥80. Race was categorized as white, black, and other. Marital status at diagnosis was coded as married, single (never married), separated, divorced, widowed, or unknown. For this study, we excluded women with unknown marital status, and recoded marital status as: married and unmarried. Household income at the census tract level was categorized into approximate quartiles: less than $27,669, $27,670–34,464, $34,465–43,974, and ≥$43,974. Education at the census tract level was categorized into approximate quartiles as the percentage of women having more than 12 years of formal education ((18.1%, 18.1–25.6%, 25.7–33.2%, and >33.2%). Those without information on income or education were categorized as missing.

Comorbidity was ascertained from Medicare claims data through diagnoses or procedures made in the two years prior to the diagnosis of breast cancer. We used the comorbidity index created by Charleson et al. [21] and later adapted by Romano et al. [22] using the ICD-9-CM diagnosis and procedure codes. Both the Medicare inpatient and outpatient claims were searched for comorbid conditions, not including breast cancer diagnosis codes (ICD-9-CM codes of 174x). Patients who had no inpatient or outpatient Medicare claims during this period were coded as a separate category. The comorbidity index was categorized as no comorbidity (score = 0), 1, 2, or 3 or more comorbidities. Because tumor stage and size are independent risk factors of breast cancer survival both variables were entered into the model. Tumor stage was categorized into five groups including *in-situ*, and stages I through IV. Tumor size, in centimeters, was categorized as (1, 1–1.9, 2–2.9, 3–3.9, and ≥4. Tumor grade included four categories: well differentiated, moderately differentiated, poorly differentiated, and undetermined. Estrogen receptor status was categorized as positive, negative, and unknown.

Analyses

Bivariate associations between marital status and other factors were tested using χ^2 statistics. We used multivariate logistic regression analyses to generate odds ratios (OR) of having late stage breast cancer diagnosis and of receiving non-definitive surgical intervention in unmarried women with breast cancer compared with married women. The models adjusted for age, race, comorbidity level, household income and education at census tract level, cancer stage, tumor size, tumor grade, estrogen receptor status, and SEER area.

Cox proportional hazard models were used to examine 3-year breast cancer survival rates adjusting for age, race, cancer stage, tumor size, SEER area, comorbidity scores, and breast cancer therapies (i.e. surgery and chemotherapy). Cox proportional hazard models also tested interaction effects. Breast cancer-specific death was defined if patients died of breast cancer as an underlying cause of death. Information on months of survival from the date of diagnosis was provided in SEER. The last date of the follow-up for this cohort was December 31, 1998. This allowed for analyses on the 3-year survival in women diagnosed with breast cancer in 1991–1995, with all subjects censored after 3 years. All analyses were estimated in SAS (SAS Institute, Cary, NC) [23].

Results

Table 1 presents the distribution of characteristics of women with breast cancer stratified by marital status. The majority of women were white (91.1%). Most of the married women were less than 75 years of age (68.2%) whereas the most of the unmarried women were 75 years of age or older (57.3%). Unmarried women had, on average, more medical conditions than married women.

Unmarried women had larger primary tumors ($p < 0.0001$), less well differentiated tumors ($p < 0.0001$) and were more likely to present with advanced stage disease ($p < 0.0001$). There was no difference between the two groups for estrogen receptor status ($p = 0.43$). Unmarried women were more likely to receive no cancer directed surgery and were less likely to be given chemotherapy than married women ($p < 0.0001$). Unmarried women who received breast conserving surgery were also less likely than married women to receive adjuvant radiotherapy (25.7% versus 42.1%, $p < 0.0001$).

Table 2 presents odds ratios (OR) of diagnosis at AJCC stages II–IV (versus stage I or *in situ*) by marital status. In the unadjusted model (Model 1), unmarried women had 1.33 (CI_{95}: 1.27, 1.39) OR of presenting with later stage breast cancer compared with married women. After adjusting for age, race, income, education, and SEER area, unmarried women had 1.21 (CI_{95}: 1.16, 1.27) OR of presenting with later stage breast cancer (Model 2). Similar results were found in Model 3 which added education and household income at the census tract level. In the fully adjusted model (Model 4), which added comorbidity, the odds of presenting with later stage breast cancer for the unmarried was 1.17 (CI_{95}: 1.12, 1.23).

Table 3 shows the odds of receiving a non-definitive treatment for women with stage Table I or II breast cancer as a function of marital status. In the unadjusted model (Model 1), unmarried women were significantly more likely to receive non-definitive treatment than married women (OR 1.59, CI_{95}: 1.51, 1.68). The OR decreased to 1.25 (CI_{95}: 1.18, 1.33) after controlling for age, ethnicity and SEER area. Adding measures of education, income, and comorbidity had little effect on the odds ratio (OR 1.24, CI_{95}: 1.17, 1.31).

Table 4 presents the 3-year breast cancer specific mortality for unmarried women compared with married women. In the fully adjusted model (Model 5), controlling for age, race, stage, receptor status, tumor grade, comorbidity, treatment variables, socioeconomic and educational variables, unmarried women were still at an increased risk of death from breast cancer than married women (HR 1.25, CI_{95}: 1.14, 1.37).

There was a significant interaction in the Cox survival model between marital status and comorbidity ($p < 0.01$) and between marital status and income ($p < 0.05$). Table 5 shows the impact of marital status on the hazard ratio, stratified by comorbidity and also by income. Marital status had a significant impact on mortality for women living in higher income areas (HR 1.45, CI_{95}: 1.17, 1.80), and for women without comorbid illnesses (HR 1.33, CI_{95}: 1.18, 1.48).

Discussion

Findings from this study add to an emerging body of research on the positive influence of marriage on women with breast cancer. Our results indicate unmarried women are more likely to be diagnosed with more advanced disease and are less likely to receive definitive treatment. Unmarried women also had a significantly increased risk of death from breast cancer after controlling for relevant risk factors, including stage at diagnosis and treatment. Socioeconomic factors and comorbidity had little effect on the relationship between marital status and survival. Additionally, significant interactions were found between marital status and income, and marital status and comorbidity. For both interactions, the effect of marital status on survival was stronger in the more advantaged woman; i.e. unmarried women with no comorbidities and those in the highest income quartile were at greatest risk, relative to married women.

Although marriage imparts beneficial effects to older women with breast cancer, the mechanisms are not well understood. Several researchers have proposed that spouses promote positive health behavior (i.e. screening exams, regular doctors visits), which would promote earlier diagnosis [24, 25]. In addition, unmarried women

Table 1. Distribution of women with breast cancer diagnosed in 1991–1995 in SEER, by marital status, in relation to patient and tumor characteristics, comorbidity, and treatment

Characteristics	*N*	Percent		*p* value[a]
		Married (*n* = 14,247)	Unmarried (*n* = 18,021)	
Age				
65–69	8343	35.0	18.6	
70–74	9077	33.2	24.1	
75–79	7080	20.2	23.3	
80+	7768	11.5	34.0	<0.001
Race				
White	29,407	92.4	90.1	
Black	1768	3.4	7.1	
Other	1093	4.2	2.7	<0.001
Comorbidity scores				
0	23,009	75.0	68.4	
1	4465	12.4	15.0	
2	1838	5.0	6.3	
3+	2956	7.6	10.4	<0.001
Household income[b]				
1st quartile (≤ $27,669)	6457	19.3	20.6	
2nd quartile ($27,670–34,464)	6414	20.0	19.8	
3rd quartile ($34,465–43,974)	6477	20.5	19.8	
4th quartile (>$43,974)	6436	21.7	18.6	
Unknown	6484	18.6	21.3	<0.001
Education (percent of subjects having >12 years of education[b]				
1st quartile (<18.1%)	6451	22.3	18.2	
2nd quartile (18.1–25.6%)	6453	21.0	19.2	
3rd quartile (25.7–33.2%)	6458	20.5	19.6	
4th quartile (>33.2%)	6422	17.6	21.7	
Unknown	6484	18.6	21.3	<0.001
Tumor stage				
In-situ	3657	12.9	10.1	
Stage I	15,519	50.3	46.3	
Stage II	10,165	29.4	33.1	
Stage III	1826	4.6	6.5	
Stage IV	1101	2.7	4.0	<0.001
Tumor size (cm)				
<1	6985	24.7	19.2	
1–1.9	11,322	36.0	34.4	
2–2.9	6133	18.1	19.7	
3–3.9	2597	6.9	9.0	
≥4	3230	7.9	11.7	
Unknown	2001	6.5	6.0	<0.001
Tumor grade				
Well differentiated	3806	12.3	11.4	
Moderately differentiated	9404	28.5	29.6	
Poorly differentiated	6802	20.2	21.8	
Undetermined	12,256	38.9	37.2	<0.001
Estrogen receptor status				
Positive	18,928	58.5	58.8	
Negative	3766	11.9	11.5	
Unknown	9574	29.6	29.7	0.4300
Cancer directed therapies				
No cancer-directed surgery	904	2.0	3.4	
BCS only	5531	14.3	19.4	

Table 1. Continued.

Characteristics	*N*	Percent		*p* value[a]
		Married (n = 14,247)	Unmarried (n = 18,021)	
BCS and RT	8032	29.3	21.4	
Mastectomy	17,801	54.4	55.8	<0.001
Chemotherapy				
No	28,864	87.7	90.9	
Yes	3404	12.3	9.1	<0.001
Total	32,268	14,247 (100.0)	18,021 (100.0)	

[a]χ^2-test statistic.
[b]Household income and education were obtained at the level of the census tract.

Table 2. Odds ratio for diagnosis at AJCC stage II–IV versus *in situ* or stage I for unmarried women compared with married women (n = 32,268)

Models	Diagnosis at stage II–IV	
	OR	95% CI
Model 1	1.33	1.27–1.39
Model 2	1.21	1.16–1.27
Model 3	1.20	1.15–1.26
Model 4	1.17	1.12–1.23

- Model 1: marital status only.
- Model 2: adds age (65–69, 70–74, 75–79, 80+), ethnicity (white, black and other), and 9 SEER areas.
- Model 3: adds census tract education level (quartiles of percent subjects having 12 years or more education) and census tract household income in quartiles.
- Model 4: adds comorbidity index scores (scores 0, 1, 2, and 3+).

Sample size (and *in-situ* and stage I) was 14,247 (63.3%) for married and 18,021 (56.4%) for unmarried women, for a total sample size of 32,268 (59.4%).

Table 3. Odds ratio of receiving non-definitive surgical intervention[a] in women with stage I or II breast cancer for unmarried women compared with married women (n = 25,684)[a]

Models	Non-definitive surgical intervention	
	OR	95% CI
Model 1	1.59	1.51–1.68
Model 2	1.25	1.18–1.33
Model 3	1.25	1.18–1.33
Model 4	1.24	1.17–1.31

[a]Definitive surgical intervention was defined for women with stage I or II breast cancer as breast conserving surgery with axillary dissection plus radiation therapy, or mastectomy with axillary dissection.
- Model 1: marital status only.
- Model 2: adds age (65–69, 70–74, 75–79, 80+), ethnicity (white, black and other), and 9 SEER areas.
- Model 3: adds census tract education level (quartiles of percent subjects having 12 years or more education) and census tract household income in quartiles.
- Model 4: adds comorbidity index scores (scores 0, 1, 2, and 3+).

Sample size (and receiving definitive therapy) for stage I or II was 11,363 (74.0%) for married and 14,321 (66.5%) for unmarried women, for a total sample size of 25,684 (69.8%).

Table 4. The 3-year breast cancer specific mortality for unmarried women compared with married women with AJCC stage 0–IV breast cancer from SEER cases in 1991–1995 (n = 32,268)

Models	Three-year mortality	
	HR	95% CI
Model 1	1.63	1.50–1.78
Model 2	1.43	1.30–1.56
Model 3	1.25	1.14–1.37
Model 4	1.27	1.16–1.39
Model 5	1.25	1.14–1.37

- Model 1: marital status only.
- Model 2; adds age (65–69, 70–74, 75–79, 80+), ethnicity (white, black and others), and 9 SEER areas.
- Model 3: adds tumor size (<1, 1–<2, 2–<3, 3–<4, ≥4 cm), tumor stage (AJCC stages 0, 1, 2, 3, 4), tumor grade (well, moderately or poorly differentiated, or undetermined), estrogen receptor status (positive, negative or unknown), and comorbidity index scores (scores 0, 1, 2, and 3+).
- Model 4: adds treatment variables (no cancer directed surgery, BCS alone, BCS plus radiotherapy, mastectomy) and chemotherapy (yes or no).
- Model 5: adds census tract education level (quartiles of percent subjects having ≥12 years of education) and census tract household income in quartiles.

Sample size (and 3 year cancer-specific survival) for all stages was 14,247 (94.4%) for married and 18,021 (91.4%) for unmarried women, for a total sample size of 32,268 (92.7%).

may be more likely to decline therapy such as axillary dissection and radiotherapy once diagnosed with breast cancer because of concerns about who might be able to help them with postoperative care or transportation [26]. Silliman et al. [26] found that older unmarried women had more concerns about being able to cope with out of pocket expenses related to treatment, which may contribute to a higher risk of receiving non-definitive treatment. Physicians may also harbor some of these same concerns, which may in turn mean that definitive therapy might be offered to or discussed less frequently with older unmarried women.

Since unmarried women are at increased risk of diagnosis at a later stage of disease and of receiving non-definitive therapy, it is then not surprising that they are at increased risk of mortality when compared with their

Table 5. Three-year mortality for unmarried compared with married women from SEER cases in 1991–1995, stratified by income and comorbidity (n = 32,268)

Stratified by factors that had significant interaction with marital status	Three-year mortality	
	HR	95% CI
Household income[a]		
1st quartile (≤27,669)	1.11	0.92–1.34
2nd quartile (27,670–34,464)	1.25	1.02–1.53
3rd quartile (34,465–43,974)	1.24	1.00–1.53
4th quartile (<43,974)	1.45	1.17–1.80
Comorbidity scores[a]		
0	1.33	1.18–1.48
≥1	1.13	0.97–1.31

[a]Household income and comorbidity models adjusted for variables in Table 4 (Model 5).
Note: Interaction term between marital status and household income was significant for breast cancer-specific mortality ($p < 0.05$); and interaction term between marital status and comorbidity scores was also significant for breast cancer-specific mortality ($p < 0.01$) in the proportional hazard models shown in Table 4.

married counterparts. However, the excess tumor-specific mortality remained after controlling for size and stage at diagnosis, and treatment received.

One striking finding is that unmarried women with no known comorbidities, i.e. those who would be expected to be the ''healthiest'', and unmarried women from the highest economic quartile, i.e. those with the greatest economic advantage, were at the greatest risk as compared with married women, suggesting that married women are not merely enjoying an increased selective (i.e. healthier women are *selected* into marriage, leaving an unhealthier umarried population) [3], or economic advantage, but that there may be something intrinsic to marriage itself that offers a certain protective effect. This benefit may center on varying levels of social support and influence. For example, relatively healthy and financially self-sufficient unmarried women may live relatively autonomous lives. In contrast, unmarried women with multiple health problems may have already had to ''rally'' social support in the form of other family members or social services in order to cope with their health conditions. In short, women who are unmarried, healthy and financially independent may be at risk for increased social isolation and thus experience an increased risk of mortality [10].

The benefits imparted by marital status likely represent an interplay of previously discussed aspects of structural support and functional support, including informational support, instrumental support and emotional support. However, the importance of a given variable may have more or less impact depending on the phase of the disease process. For example, informational and instrumental support may play a larger role in support of breast cancer screening and aiding in receiving definitive therapy [10, 14], whereas the role of emotional support may be the greatest aid in coping with disease, relapse or progressive disease [27, 28].

The results of this study must be interpreted in the light of certain limitations. There is potential for misclassification of marital status. We did not take into account changes of marital status that may have occurred during the follow-up period, which may have influenced outcomes. Thus, our findings may underestimate the protective effect marriage has on breast cancer outcome. Also, we placed divorcees, widows and never married women into a single category; however, studies have shown that while there may be some variation among groups of unmarried women (i.e. never married, divorced and widowed), they all fare worse than their married counterparts [2–5]. Additionally, this study only studied women with both Medicare parts A and B and does not include women with Medicare HMOs. Also, in terms of treatments received, we had no information on the use of Tamoxifen.

In conclusion, older unmarried women are at an increased risk for presentation at a later stage of breast cancer and for greater breast cancer mortality than are married women. Our results suggest that much of the benefit enjoyed by married women is derived from intrinsic social support and social networks. The value of this finding is that social support may well be amenable to intervention and may lead to improved outcomes [12, 29, 30].

Health care providers should recognize that the older unmarried woman is at particular risk with respect to diagnosis and treatment of, and survival from breast cancer. These women may require more counseling regarding the benefits of screening and early detection. Additionally, once a diagnosis of breast cancer has been made, these women may be lacking significant social resources and benefit most from a multidisciplinary approach, which includes comprehensive case management.

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