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Breast conserving surgery versus mastectomy: the influence of comorbidities on choice of surgical operation in the Department of Defense health care system

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Abstract

BACKGROUND: Studies on the effect of comorbidities on breast cancer operation have been limited and inconsistent. This study investigated whether pre-existing comorbidities influenced breast cancer surgical operation in an equal access health care system.

METHODS: This study was based on linked Department of Defense cancer registry and medical claims data. The study subjects were patients diagnosed with stage I to III breast cancer during 2001 to 2007. Logistic regression was used to determine if comorbidity was associated with operation type and time between diagnosis and operation.

RESULTS: Breast cancer patients with comorbidities were more likely to receive mastectomy (odds ratio [OR] = 1.27; 95% confidence interval [CI], 1.14 to 1.42) than breast conserving surgery plus radiation. Patients with comorbidities were also more likely to delay having operation than those without comorbidities (OR = 1.27; 95% CI, 1.14 to 1.41).

CONCLUSIONS: In an equal access health care system, comorbidity was associated with having a mastectomy and with a delay in undergoing operation.

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Breast cancer is the most common occurring cancer and the second leading cause of cancer mortality among US women.[1] In 2012, it was estimated that 226,870 new breast cancer cases would be diagnosed with 39,510 deaths due to breast cancer.[1] Effective treatment reduces the mortality of the disease.[2] The local treatment for nonmetastatic breast cancer is either mastectomy or breast conserving surgery (BCS) followed by radiation.[3] Various factors can influence whether women receive BCS or mastectomy.[4,5] Comorbidity, the coexistence of chronic diseases or acute illnesses in addition to the index disease, may influence the selection and timing of treatment.

Studies of the effect of comorbidities on treatment decisions have been limited and inconsistent. Several studies have shown that comorbidities present at the time of cancer diagnosis influence treatment choice.[6–10] For example, Mandelblatt et al[9] found that women with high levels of comorbidity were more likely to receive a mastectomy (odds ratio [OR] = 3.33; 95% confidence interval [CI], 1.23 to 9.00) or BCS alone (OR = 16.6; 95% CI, 4.87 to 56.5) than BCS and radiation compared with women who have low levels of comorbidity. Thompson et al[10] also reported that the likelihood of having a mastectomy was higher among women who had anemia or heart failure. On the other hand, an association between comorbidities and cancer therapy was not identified in other studies.[11,12] Furthermore, few studies have assessed whether comorbidities are associated with delayed breast cancer operation,[13,14] although the presence of comorbidities was shown to increase the waiting time for breast cancer operation.[13]

Many previous studies were based on cancer patients with medical insurance.[13,15,16] People with certain pre-existing conditions and with low socioeconomic status, however, may not be able to obtain insurance and thus were not included in these studies. Due to the selectiveness, the study participants might differ from those excluded based on pre-existing conditions and low socioeconomic status. Therefore, study results on comorbidities might have been affected.

The Department of Defense (DoD) military health care system provides universal medical care to its beneficiaries, including active duty members, retirees, and their family members. Because there are no financial incentives to physicians and cost prohibitions for patients within the system, a study based on this system provides a unique opportunity to identify factors that may influence treatment decisions while minimizing the effects of socioeconomic factors. The objective of this study was to investigate whether pre-existing comorbidities were associated with the selection of initial breast cancer surgical operation, using linked DoD cancer registry and medical claims data. In addition, the study assessed whether comorbidities were associated with delayed surgical operation.

Methods

Data sources and study subjects

This study was based on linked data from the DoD Central Cancer Registry (CCR) and the Military Health System Data Repository (MDR). The CCR was initiated in 1998 and contains tumor-specific (eg, site, histology, stage, and treatment) and person-specific (eg, sex, race, and age at diagnosis) information on those diagnosed or treated at military treatment facilities. The MDR includes administrative and medical claims' information for all DoD beneficiaries, including information on clinical diagnoses, diagnostic procedures, treatments including operation type, medical conditions including comorbidities, prescription medications, and related costs. The data linkage was approved by the National Naval Medical Center institutional review board (IRB), the Armed Forces Institute of Pathology IRB, the National Cancer Institute IRB, and TRICARE Management Activity, which manages the DoD's health care program.

The subjects eligible for this study were 5,548 female breast cancer patients with histologically confirmed, first primary malignant breast tumors diagnosed from 2001 to 2007. Only patients with stages I to III, defined by the American Joint Committee on Cancer staging system,[17] were included because surgical operation often applies to them as a therapeutic procedure. There was only 1 woman diagnosed during the study period who had missing operation information and she was, therefore, excluded from the study.

Measures

Extensive procedures were undertaken to evaluate and consolidate the data from the CCR and MDR. Data on operation type, radiation therapy, and chemotherapy were obtained from both the CCR and MDR. In the CCR, Registry Operations and Data Standards (ROADS) or Facility Oncology Registry Data Standards (FORDS) codes were used to identify the type of operation performed.[18] In the MDR, both the *International Classification of Diseases* 9th revision (ICD-9) codes and the Current Procedural Terminology (CPT) codes were used to identify whether patients underwent BCS or mastectomies (including subcutaneous mastectomies, simple mastectomies, radical mastectomies, and modified radical mastectomies). Radiation therapy and chemotherapy were categorized as yes or no according to the documentation in both the CCR and MDR. Hormonal therapy information was obtained only from the CCR because MDR prescription data were not available for the entire study period. Demographic (age at diagnosis, race, marital status, duty status) and tumor (stage, grade, size, and estrogen receptor [ER] status) variables were obtained from the CCR.

Data on the existence of comorbidities were extracted from the MDR using ICD-9 codes. To assess the level of comorbidities, we computed the modified Charlson comorbidity index,[19] which consists of 17 comorbid conditions including cancer; breast cancer was excluded from the calculation. Comorbidities were considered to be present if a diagnosis was recorded during the 1 year prior to surgical operation either 1 time in inpatient data or 3 times in outpatient data. The comorbid conditions present were classified as Charlson index = 0 or Charlson index ≥1. The 2 most common comorbidities were chronic obstructive pulmonary disease and diabetes (data not shown). There was a relatively small proportion of women with a Charlson index ≥1 (n = 473); therefore, further classification of comorbidity level was not explored.

Statistical analysis

The distributions of basic characteristics for those with and without comorbidities were compared using Chi-square tests. The odds ratios and 95% confidence intervals were calculated using multinomial logistic regression to compare the probability of receiving different surgical operations while adjusting for age, race, marital status, military duty status, year of diagnosis, tumor stage, tumor grade, tumor size, estrogen receptor (ER) status, chemotherapy, and hormonal therapy. Treatment selection may vary by tumor and demographic features; therefore, models were then stratified by age, race, marital status, duty status, tumor stage, tumor grade, tumor size, and ER status. The impact of comorbidities on the interval between cancer diagnosis and surgical operation was also examined. Time interval was dichotomized as ≤2 months vs >2 months following breast cancer diagnosis. Analyses were conducted using SAS software (version 9.1; SAS, Cary, NC).

Results

The distributions of selected demographic, diagnostic, and treatment factors by comorbidity status are shown in Table 1. Compared with women without comorbidities, women with at least 1 comorbidity were more likely to be older, not married, non-active duty military, have later stage tumors, and less likely to have received chemotherapy. The distribution of race between the 2 groups was not significantly different. There were also no significant differences in year of diagnosis, tumor grade, tumor size, ER status, and receipt of hormonal therapy between those with and without comorbidities (data not shown).

A comparison of treatment by comorbidity is shown in Table 2. In comparison to patients without comorbidities, patients with comorbidities were more likely to have received a mastectomy (OR = 1.27; 95% CI, 1.14 to 1.42) or mastectomy plus radiation (OR = 1.16; 95% CI, 1.00 to 1.35) than BCS plus radiation. However, patients with comorbid conditions were as likely to have BCS alone as BCS plus radiation (OR = .96; 95% CI, .74 to 1.23) compared with those without comorbidities. Receipt of radiation did not seem to affect the association between

Table 1 Distributions of demographic, diagnostic, and treatment factors by comorbidity status among female Department of Defense beneficiaries diagnosed with breast cancer between 2001 and 2007 (N = 5,548)

	Comorbidity				
	Charlson index = 0		Charlson index ≥ 1		
Factor	N	%	N	%	*P* value*
Age at Diagnosis					
<50	1,914	38	78	16	<.01
≥50	3,161	62	395	84	
Race					
White	3,596	71	339	72	.14
Black	799	16	68	14	
Other†	531	10	59	12	
Unknown	149	3	7	1	
Marital Status					
Single/separated/divorced/widowed	867	17	123	26	<.01
Married	4,078	80	344	73	
Unknown	130	3	6	1	
Duty Status at Diagnosis					
Active duty	289	6	16	3	.03
Non-active duty	4,786	94	457	97	
Tumor Stage					
Stage I	2,570	51	214	45	.02
Stage II	1,938	38	189	40	
Stage III	567	11	70	15	
Chemotherapy					
Yes	2,882	57	218	46	<.01
No	2,193	43	255	54	

*Chi-square test.
†American Indian, Aleutian, Eskimo, Asian, or Pacific Islander.

Table 2 Multinomial logistic regression analyses assessing the likelihood of operation type among female Department of Defense beneficiaries with breast cancer, 2001 to 2007 (N = 5,548)

	Comorbidity				
	Charlson index = 0		Charlson index ≥ 1		
Surgical operation	N	%	N	%	OR (95% CI)*
BCS + radiation	2,369	47	169	36	Reference
BCS only	254	5	20	4	.96 (.74–1.23)
Mastectomy + radiation	1,003	20	101	21	1.16 (1.00–1.35)†
Mastectomy only	1,449	29	183	39	1.27 (1.14–1.42)†

BCS = breast conserving surgery; CI = confidence interval; OR = odds ratio.

* All models were adjusted for age at diagnosis, race, marital status, duty status at diagnosis, year of diagnosis, tumor stage, tumor grade, tumor size, estrogen receptor status, chemotherapy, and hormonal therapy.

†$P < .05$.

comorbidity and type of operation; therefore, only operation type was considered in further stratified analyses.

Stratified analyses indicated that the association between comorbidity and operation type varied by tumor stage and size (Table 3); significant associations were observed among women with stage II tumors and tumors >2 cm, but not among women with stage I tumors or tumors ≤2 cm. The association was close to the statistical significance level for women with stage III tumors. Women with comorbidities were more likely to receive mastectomy than BCS regardless of their marital and ER statuses (data not shown). Additionally, although the statistical significance of an association between comorbidity and operation type seemed to vary when stratified by age at diagnosis, race, duty status, and tumor grade, the strata-specific confidence intervals overlapped, making it less clear whether the association truly differed across these covariate categories (data not shown).

Table 4 shows the relationship between comorbidity and the time interval from cancer diagnosis to surgical operation. The majority of the operations were performed within 2 months of cancer diagnosis (81% for those without comorbidities and 70% for those with comorbidities). However, patients with comorbidities were more likely to have delayed surgical operation (OR = 1.27; 95% CI, 1.14 to 1.41) than patients without comorbidities. When stratified by operation type, the results indicated that comorbidity was significantly associated with delayed operation for both BCS (OR = 1.26; 95% CI, 1.07 to 1.50) and mastectomy (OR = 1.26; 95% CI, 1.11 to 1.47).

Table 3 Stratified multinomial logistic regression analyses assessing the likelihood of operation type among female Department of Defense beneficiaries with breast cancer, 2001 to 2007 (N = 5,548)

		Comorbidity				
		Charlson index = 0		Charlson index ≥ 1		
Stratum	Surgical operation	N	%	N	%	OR (95% CI)*
Tumor Stage						
Stage I	BCS	1,612	63	122	57	Reference
	Mastectomy	958	37	92	43	.90 (.72–1.14)
Stage II	BCS	894	46	59	31	Reference
	Mastectomy	1,044	54	130	69	1.39 (1.15–1.69)‡
Stage III	BCS	117	21	8	11	Reference
	Mastectomy	450	79	62	89	1.45 (.98–2.16)
Tumor Size (cm)†						
≤2	BCS	2,336	55	175	46	Reference
	Mastectomy	1,897	45	208	54	1.10 (.95–1.27)
>2	BCS	251	35	9	12	Reference
	Mastectomy	476	65	66	88	1.96 (1.32–2.91)‡

BCS = breast conserving surgery; CI = confidence interval; OR = odds ratio.

*Unless stratified by the variable, all models were adjusted for radiation, age at diagnosis, race, marital status, duty status at diagnosis, year of diagnosis, tumor stage, tumor grade, tumor size, estrogen receptor status, chemotherapy, and hormonal therapy.

†Unknown categories are not included; therefore, values for tumor size do not add up to total number of patients.

‡$P < .05$.

Comments

Comorbidity may complicate the selection of surgical operation for breast cancer because these conditions likely affect treatment tolerance and patient survival. The results of this study indicate that breast cancer patients with comorbidities were less likely to receive BCS plus radiation and more likely to receive mastectomy. Stratified analyses indicated that this association existed regardless of marital and ER statuses but could vary by tumor stage and size. Comorbidity was also significantly associated with delayed operation for both BCS and mastectomy.

The primary treatment of non-metastatic breast cancer has changed dramatically during the past 2 decades. The National Institutes of Health Consensus Development Conference established BCS with radiation as an appropriate primary therapy for women with non-metastatic breast cancer in 1990.[20] Randomized trials have also shown that BCS with radiation was as effective as mastectomy in treating breast cancer,[21–24] while body image of patients treated with BCS seems to be better.[25] Thus, BCS has replaced mastectomy as the most common procedure for the treatment of breast cancer without metastasis.[26–28] However, the optimal treatment for patients with comorbidity is still uncertain because patients with pre-existing serious diseases were generally not eligible for those trials.[29]

Although this study suggests that women with comorbidities are more likely to undergo mastectomy than BCS, the underlying reasons for this choice are not clear. Indeed, these findings are somewhat paradoxical, because mastectomy is a more time-consuming operation with higher complication rates and morbidity than BCS,[30] and one might expect that women with comorbidities would choose the least invasive procedure (BCS). It is likely that patients with comorbidities and their doctors may choose mastectomy over BCS to avoid the possibility of a 2nd operation (usually mastectomy) if cancer recurs.[31] Patients with comorbidities and their physicians may also choose mastectomy to avoid the need for radiotherapy because it has been associated with life-threatening conditions, including vascular disease (although radiotherapy may now also be recommended after mastectomy for patients with node-positive or large tumors).[32–35] On the other hand, in comparison to women with comorbidities, women without comorbidities may be more likely to receive neoadjuvant chemotherapy before local treatment to reduce the size of the tumor, which in turn may make them more likely to undergo the less invasive BCS.[36] However, the low frequencies of chemotherapy prior to surgical operation in this study's data suggest that this might not be a main reason for the identified association (data not shown). Research has also shown that undergoing mastectomy is associated with greater patient involvement in the treatment decision-making process.[37] However, whether patients with comorbidities are more likely to be involved in making their treatment decisions is unknown.

Our stratified analysis showed an association between comorbidities and operation type among patients with stage II or large (>2 cm) tumors, but not those with stage I or small (≤2 cm) tumors. It is not clear why the association between operation type and comorbidity would vary by tumor stage or size. As stated above, patients with comorbidities and their doctors may choose mastectomy over BCS to avoid the possibility of a 2nd operation or radiation therapy. This possibility may make it more sensible for patients with larger, advanced stage tumors that are more likely to recur[38] to receive the more aggressive mastectomy.

In agreement with our studies, Simunovic et al[13] reported that comorbidities were associated with longer delays for breast cancer surgical operation in Ontario, Canada. The treatment decisions for patients with comorbidities are likely more complicated than those without, and physicians may need more time to evaluate patients' health status and make decisions, which may result in

Table 4 Multinomial logistic regression analyses assessing the effects of comorbidity on the interval between breast cancer diagnosis and surgical operation among female Department of Defense beneficiaries, 2001 to 2007

		Comorbidity				
		Charlson index = 0		Charlson index ≥ 1		
Surgical operation	Time interval*	N	%	N	%	OR (95% CI)†
Any	Within 2 months‡	4,098	81	332	70	Reference
	More than 2 months	976	19	141	30	1.27 (1.14–1.41)§
BCS	Within 2 months‡	2,164	83	138	73	Reference
	More than 2 months	458	18	51	27	1.26 (1.07–1.50)§
Mastectomy	Within 2 months‡	1,934	79	194	68	Reference
	More than 2 months	518	21	90	32	1.26 (1.11–1.47)§

BCS = breast conserving surgery; CI = confidence interval; OR = odds ratio.

*One patient with missing time interval information was not included in this analysis.

†Adjusted for radiation, age at diagnosis, race, marital status, duty status at diagnosis, year of diagnosis, tumor stage, tumor grade, tumor size, estrogen receptor status, chemotherapy, and hormonal therapy.

‡Initial breast surgery performed within 1–2 month of the breast cancer diagnosis.

§$P < .05$.

longer waiting time before surgical operations for patients with comorbidities.

There are several potential limitations to this study. First, information from administrative claims' data may be incomplete or inaccurate. For example, the comorbid conditions from the outpatient data might not be accurate. However, we tried to minimize the inaccuracies by requiring 3 outpatient occurrences of a diagnostic code instead of 1. Given that the stricter criterion was applied, we cannot exclude the possibility that comorbidity was underestimated. However, this might only dilute the true differences between those with and without comorbidity in receiving different surgical operations. Second, some patients, especially military dependants and retirees, might have other medical insurance; therefore, some information about their treatment and medical conditions might not have been included. Third, according to the IRB-approved procedures, the data contained only month and year of cancer diagnosis or operation and not the exact date. Therefore, some patients with an operation performed >2 months after diagnosis might have had it within 1 to 2 months following the diagnosis. However, this misclassification would tend to underestimate, rather than overestimate, the true association of the time interval between diagnosis and mastectomy. Finally, as there were relatively small numbers of patients with comorbidities, we were not able to evaluate the impact of the severity of the pre-existing comorbidity or specific comorbid conditions on the treatment choice of breast cancer patients.

Although BCS is generally regarded as the preferred surgical operation for primary breast cancer, it may not be as accepted for patients with certain comorbidities. The results of our study highlight the need to establish treatment standards for patients with pre-existing conditions. It is not known whether patients' perceptions of their physicians' treatment preferences and patient–provider communication contribute to the choice of treatment.[39,40] Treatment standards for patients with comorbidities should guide physicians' recommendations and discussions with patients. Patients with comorbidities should be fully informed about the possible treatment choices, thus allowing them to make informed decisions.[41] Also, comorbidities appear to be associated with surgical operation delay, and this needs to be further studied because it could adversely affect long-term outcomes.

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