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Association of the severity of diabetes-related complications with stage of breast cancer at diagnosis among elderly women with pre-existing diabetes

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Abstract

Purpose—This study assessed the association between the severity of diabetes complications using diabetes complications severity index (DCSI) and stage of breast cancer (BC) at diagnosis among elderly women with pre-existing diabetes and incident BC.

Methods—Using Surveillance, Epidemiology and End Results-Medicare data, we identified women with incident BC during 2004–2011 and pre-existing diabetes ($N = 7729$). Chi-square tests were used to test for group differences in stage of BC at diagnosis. Multinomial logistic regression was used to examine the associations between the severity of diabetes complications and stage of BC at diagnosis.

Results—Overall, women with a DCSI = 2 and a DCSI ≥ 3 were more likely to be diagnosed at advanced stages as compared to those with no diabetes complications. In full adjusted association (after adding BC screening to the analysis model), the severity of diabetes complications was no longer an independent predictor of advanced stages at diagnosis. However, women with a DCSI = 2 were 26% more likely to be diagnosed at stage I (versus stage 0) of BC at diagnosis as compared to those without diabetes complications (OR 1.26, 95% CI 1.03–1.53).

Conclusion—The increased likelihood of having advanced-stage BC at diagnosis associated with severity of diabetes-related complications appears to be mediated by lower rates of breast cancer screening among elderly women with pre-existing diabetes complications. Therefore, reducing disparity in receiving breast cancer screening among elderly women with diabetes may reduce the risk of advanced-stage breast cancer diagnosis.

Keywords

Diabetes complications; Breast cancer; Stage at diagnosis; Elderly; Mammography

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Introduction

Several previous studies have found that women with diabetes were more likely to be diagnosed in advanced stages of breast cancer (BC) as compared to those without diabetes mellitus (DM), and this may contribute to their higher mortality after cancer diagnosis [1–4]. Many reasons have been put forward to possibly account for later stage diagnosis of BC among women with diabetes. Studies have showed that women with diabetes are more likely to be diagnosed with metastatic and larger tumors as compared to those without diabetes [5]. Lower rates of screening mammography among women with diabetes could also account for later stage diagnosis of BC, although women with diabetes have more frequent primary health care visits than women without diabetes [6]. This lower rates of BC screening could play a role in the association between diabetes and risk of advanced stages of BC at diagnosis.

Age and age-related changes also play a crucial role in the association between diabetes and advanced-stage diagnosis of BC. Elderly women with diabetes are more likely to be diagnosed at advanced stages of breast cancer [7–9], with more frequent pre-existing diabetes-related complications as compared to younger population [9].

Since elderly women with DM have a higher likelihood of complications and advanced stage BC, it is important to determine how the severity of these complications contributes to advanced-stage BC at diagnosis. Thus, the aim of this study is to determine the association between the severity of diabetes complications and stage of BC at diagnosis in women with incident BC and pre-existing diabetes. We hypothesized that stage of BC at diagnosis is associated with severity of diabetes complications in elderly women with incident BC and pre-existing diabetes.

Methods

Study design and data source

This was a retrospective observational study in a cohort of elderly women with incident BC diagnosis and pre-existing diabetes. The cohort was followed retrospectively for 24 months prior to the BC diagnosis to assess the association between the severity of diabetes complications and stage of BC at diagnosis.

We used the US Surveillance Epidemiology and End Results (SEER)-Medicare data. Information of individuals in the SEER database who have been matched with Medicare enrollment records is in a customized file known as the Patient Entitlement and Diagnosis Summary File (PEDSF) [10]. The linked claims database consists of Medicare Provider Analysis and Review (MEDPAR), the Carrier Claims (old name Physician/Supplier (NCH)), Outpatient (OUTPT), Home Health Agencies (HHA), Hospice, Durable Medical Equipment (DME) and Part D Event (PDE) files [10]. These files in Medicare data have been linked with PEDSF file of cancer cases from SEER using an algorithm, and based on the linkage, a common identification number is given to each enrollee in PEDSF and claims files [11, 12].

We also linked the Area Resource File (ARF) [13] to the SEER-Medicare dataset using the state and county Federal Information Processing Standards code for each beneficiary to extract the county level information on the availability of mammography facilities.

Study cohort

Our cohort consisted of elderly women aged 67 years or older with the first primary diagnosis of incident BC between January 1, 2004 and December 31, 2011 who had pre-existing diabetes. Women must have at least 24 months of continuous enrollment in Medicare part A and B prior to the BC diagnosis and must have no enrollment in a health maintenance organization (HMO) at any time during the study period. Diabetes was determined on the basis of either a single inpatient claim or at least two outpatient claim diagnoses with International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis code of 250.xx during the 12 months that preceded BC diagnosis [14]. Women who were diagnosed with BC via death certificate or autopsy, or were with any previous cancer diagnosis, unknown, or missing BC stage information were excluded from the study cohort (Fig. 1).

Measures

The dependent variable was cancer staging based on the American Joint Committee on Cancer's staging system. Stage at diagnosis (0–IV) of the cancer/tumor was taken from PEDSF file. For the study purpose, we grouped our cohort into four categories: elderly women with stage 0, stage I, stage II, and advanced stage (III & IV) at BC diagnosis.

The key independent variable was the severity of diabetes-related complications which was identified during the 12 months that preceded the BC diagnosis. The severity of diabetes-related complications was measured using the diabetes comorbidity severity index (DCSI) [15–17]. The DCSI was first developed by Young and colleagues to include seven categories of diabetes complications: cardiovascular disease, nephropathy, retinopathy, peripheral vascular disease, cerebrovascular, neuropathy, and metabolic complications. Theses complications were identified using ICD-9-CM diagnosis code [15]. The index for each complication was categorized into 2 or 3 levels (no abnormality = 0, some abnormality = 1, and severe abnormality = 2), based on the presence and severity of the complication, and the indices of all complications were added together to get the DCSI which is a 13-point scale with a range of 0–13 [15, 16]. The study cohort was divided into 4 subgroups consisting of DCSI = 0, DCSI = 1, DCSI = 2, and DCSI ≥ 3.

Other independent variables included biological factors, non-biological factors, and mammography screening use. The biological factors were age at diagnosis, race, hormone receptor status (HR), and other comorbid conditions. Age at BC diagnosis and race were decided using the SEER PEDSF file. Age at diagnosis was categorized as follows (in years): 67–70, 71–74, 75–79, and 80 or older. Race was categorized based into "White," "African-American," or "Other". The HR was categorized into positive, negative, and borderline/unknown. The pre-existing comorbid conditions were measured as the presence or absence of the following chronic conditions: thyroid syndrome, arthritis, asthma, Chronic Obstructive Pulmonary Disorder (COPD), dementia, hyperlipidemia, hypertension,

osteoporosis, anxiety, and depression. These comorbid conditions were identified using ICD-9 diagnosis codes in the Medicare inpatient and outpatient claims.

The non-biological factors included access to health care (primary care providers (PCP) visits, endocrinologist visits, and availability of BC screening facilities in county of women's residence) and community-related factors (census tract median annual household income, census tract-level education, geographic region of residence, and metropolitan status). We defined PCP as providers who had the following specialties: general practice, family medicine, primary care internal medicine, geriatric medicine, and obstetrics and gynecology. PCPs visits and endocrinologist visits were measured during the 12 months prior to BC diagnosis and was categorized into a dichotomous group: yes (having at least one visit during the year that preceded BC diagnosis) or none. The availability of BC screening facilities in the county of women's residence was derived from the ARF file and dichotomized into a yes or no variable. Education percentage was measured by the census tract survey of percent of people age >25 with at least 4 years of college education. Census tract education percentage was categorized into 0–13.29, 13.30–22.83, 22.84–38.55, and >38.55%. Income was measured by census tract survey of median annual income and was divided into <$25,000, $25,001–50,000, $50,001–75,000, and >$75,000. Breast cancer screening was identified during the 24 months that preceded the BC diagnosis using Healthcare Common Procedure Coding System (HCPCS) codes: 76085, 76092, 77052, 77057, 77063, G0202, and G0203, and ICD-9-CM diagnosis code: V7612 which are assigned for screening mammography. Women must have had at least one mammography screening during the past 24 months to be grouped into those who had BC screening; otherwise, they were considered as not having BC screening.

Statistical analysis

Descriptive statistics were obtained using frequencies and percentages for all included factors. Chi-square tests were used to test for significant differences among the four groups based on BC stage at diagnosis (0, I, II, and III/IV). The level of statistical significance was defined at a p value ≤ 0.05. To examine the associations between stage of BC at diagnosis and the severity of diabetes-related complications using DCSI, we used three multinomial logistic regression models. The first model assessed the unadjusted association between stage of BC at diagnosis and the severity of diabetes-related complications. The second model was used to partially adjust for biological and non-biological factors (except mammography screening use) while the third model assessed the full adjusted association after controlling for all covariates: biological factors, non-biological factors and screening mammography use. In all models, "stage 0," was the reference group. The results are presented as odds ratios with their corresponding 95% confidence intervals (95% CI). All analyses were conducted using SAS 9.4 (SAS® version 9.4, SAS Institute Inc., Cary, NC, USA). Statistical significance was defined as a p-value ≤ 0.05.

Results

Table 1 describes the study cohort of 7729 elderly women with pre-existing diabetes, aged 67 years and older, diagnosed with a first primary incident BC in 2004–2011. About 57% of

the study cohort had at least one screening mammography during the last 24 months. A majority of the women were white (75.1%), resided in metro areas (79.3%), had at least one PCP visit during the 12 months prior to the BC diagnosis (94.5%), had no endocrinologist visits in the year that preceded BC diagnosis (88.1%), and had positive progesterone & estrogen HR (62.6% & 74%). For the most common comorbid chronic conditions, 70.4% had hyperlipidemia, 89.7% had hypertension, 28.3% had arthritis, and 15.8% had depression.

With respect to DCSI, 38.4% had no diabetes-related complications, 13.1% had a DCSI = 1, 23% had a DCSI = 2, and 25.4% had a DCSI ≥ 3. The most frequent diabetes-related complications were cardiovascular complications (45.2%), nephropathy (19.5%), and neuropathy (13.6%) (non-tabulated). Compared with women who had no diabetes complications, those with a DCSI ≥ 3 were older, more likely to have had an endocrinologist visit, less likely to have had screening mammography, and more likely to have other comorbid conditions (arthritis, thyroid syndrome, COPD, dementia, hypertension, and depression).

Table 2 shows the group differences in all the independent variables by stage of BC at diagnosis. About 15% of the cohort were diagnosed at stage 0, 38.4% stage I, 29.1% stage II, and 17.7% were diagnosed at advanced stages (stage III or stage IV). The biological factors that have significant bivariate associations with stage of BC at diagnosis were DCSI, age, race, progesterone HS, estrogen HS, thyroid disease, arthritis, COPD, dementia, hyperlipidemia, osteoporosis, and depression. The non-biological factors that were statistically significant in the Chi-square analyses were mammography screening, PCP visits, endocrinologist visits, availability of BC screening centers, census tract education, and census tract annual household income.

Elderly women who were diagnosed with advanced stages (stage III/IV) BC were more likely to have had a DCSI ≥ 3 (29.9%) and less likely to have had screening mammography as compared to those women who were diagnosed with stage 0 (21.7%).

Regarding other factors, elderly women who were diagnosed with advanced stages (stage III/IV) BC were less likely to have positive progesterone HR, more likely to have COPD, arthritis, and dementia as compared to women who were diagnosed with stage 0 of BC.

The results from the multinomial logistic regressions are reported in Table 3. Model 1 presents the unadjusted association between the severity of diabetes complications using DCSI and stage of BC at diagnosis. In this model, the severity of diabetes complications was significantly associated with BC stage at diagnosis. Women with a DCSI = 2 were 30%, 45%, and 57% more likely to be diagnosed at stages I (OR 1.30, 95% CI 1.08–1.56), stage II (OR 1.45, 95% CI 1.20–1.76), and advanced stage (III/IV) (OR 1.57, 95% CI 1.27–1.93), respectively, as compared to those with no diabetes complications. Women with a DCSI ≥ 3 were 20%, 50%, and 77% more likely to be diagnosed at stage I (OR 1.20, 95% CI 1.00–1.43), stage II (OR 1.50, 95% CI 1.25–1.81), and advanced stage (III/IV) (OR 1.77, 95% CI 1.45–2.17), respectively, as compared to those women with no diabetes complications. In the partial adjusted association between severity of diabetes complications and stage of BC at

diagnosis, controlling for biological and non-biological factors in model 2, we found that the severity of diabetes complication (a DCSI = 2 and a DCSI ≥ 3) continue to be significantly associated with stage of BC at diagnosis.

Model 3 shows the fully adjusted association between BC stage at diagnosis and severity of diabetes complications after controlling for biological factors, non-biological factors, and use of screening mammogram. Women with a DCSI = 2 were 26% more likely to be diagnosed at stage I (OR 1.26, 95% CI 1.03–1.53) while having a DCSI ≥ 3 was no longer an independent predictor of BC stage at diagnosis. Women who had at least one screening mammography during the two year that preceded BC diagnosis were 44%, 81%, and 91% less likely to be diagnosed with stage I (OR 0.56, 95% CI 0.47–0.67), stage II (OR 0.19, 95% CI 0.16–0.23), and advanced stages (III/IV) (OR 0.09, 95% CI 0.08–0.11), respectively, as compared to women who did not received any screening mammography.

Discussion

In this study, we examined the relationship between severity of diabetes-related complications and stage of BC at diagnosis in a large sample of elderly women with pre-existing diabetes and an incident BC. Overall, severity of diabetes-related complications was associated with stage of BC at diagnosis. Adjustment for other biological and non-biological factors did not attenuate the association between severity of diabetes complications and BC stage at diagnosis. Our findings showed that among elderly women with pre-existing diabetes, the likelihood of being diagnosed with advanced stages of BC increased from 46% in women with a moderate severity of diabetes-related complications (a DCSI = 2) to 62% in women with highest severity of diabetes-relates complications (a DCSI ≥ 3), as compared to women with no diabetes complications.

After adjustment for BC screening in Model 3, a moderate severity of diabetes complications (a DCSI = 2) continued to be associated with 20% increase in the likelihood of being diagnosed at stage I versus stage 0 as compared to women without diabetes complications. For the association between the likelihood of being diagnosed at advanced stages (III/IV) of BC and the severity of diabetes complications, estimates were attenuated and confidence limits did not reach statistical significance. However, the range of these estimates stays consistently in the range of 1.16–1.26 which suggest that more severe diabetes may have a modest impact on breast cancer stage. Also, It is evident from the results that BC screening may mediate the association between the severity of diabetes-related complications and likelihood of having advanced-stage BC at diagnosis. It is possible that as severity of diabetes complications increases, screening mammography use decreases which may lead to delayed diagnosis of BC. Thus, more advanced diabetes-related care is required to deal with the complexity of diabetes disease among elderly women to avoid the risk of serious comorbid condition, such as cancer in advanced stages which burden the disease management. One good example of such care is Medicare’s chronic care management that provide a comprehensive care coordination for elderly with multiple chronic conditions to facilitate access to care and receiving preventive care along with disease management [18].

Although previous research found that diabetes was an independent predictor of the risk of advanced stage (III/IV) BC at diagnosis as compared to women without diabetes after accounting for BC screening mammography [2, 3], we found that the severity of diabetes-related complications is associated with this risk indirectly through its negative impact on BC screening.

However, our study has several potential limitations that should be mentioned. Although we controlled for many biological and non-biological variables that could be associated with BC stage at diagnosis, we lacked data on other factors, such as obesity and family history of BC which could have residual confounding effect. Second, exclusions, such as 6% of BC cases with missing stage of BC may have affected the generalizability of our findings. Third, since we used claims database instead of medical records to measure DSCI, the index was measured without laboratory results. However, a study by Chang et al. found that the DCSI without laboratory results performs similar to the DCSI with laboratory information [19].

Despite the limitations, our study included modeling a comprehensive list of biological factors (e.g., comorbid conditions and hormone receptor status) and non-biological factors (e.g., access to health care and community-related factors). To assess the severity of diabetes-related complications, we used DCSI which captures both count and severity of complications while a simple count of complications does not take the severity of each complication into account [15]. In addition to its use as a measure of diabetes severity, a study by Young et al. found that this index may be considered as a proxy measure for diabetes duration since severity index of diabetes complications was highly correlated with diabetes duration [15]. Because diabetes may remain undiagnosed for years, using DCSI as a severity measure of long-term complications probably demonstrate the consequences of biologic markers of diabetes duration [20].

In conclusion, our study provides evidence that the severity of diabetes-related complications is associated with stage of BC at diagnosis and has an indirect association with the risk of advanced stages diagnosis of BC among women with pre-existing diabetes. The increased likelihood of advanced-stage BC diagnosis that is associated with the severity of diabetes-related complications may be mainly driven by lower rates of BC screening among those with diabetes complications.

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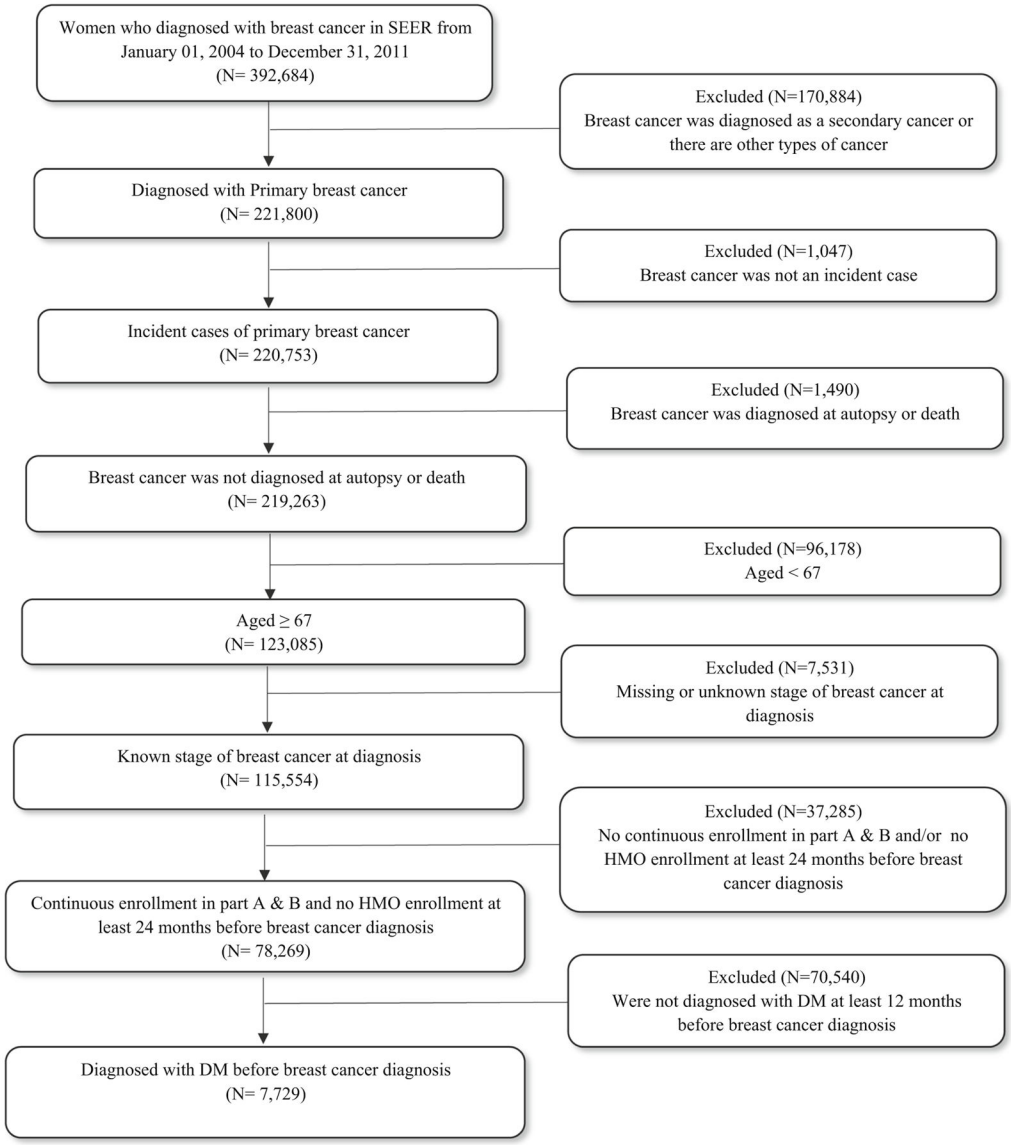

Fig. 1.
Study cohort selection flowchart

Table 1

The baseline characteristics of the study cohort

Characteristic	All women		DCSI = 0		DCSI = 1		DCSI = 2		DCSI ≥ 3	
	N = 7729		*N* = 2968		*N* = 1009		*N* = 1788		*N* = 1964	
	No.	%	No.	%	No.	%	No.	%	No.	%
Mammography screening										
Annual/biennial	4463	57.7	1951	65.7	654	64.8	941	52.6	917	46.7
No screening	3266	42.3	1017	34.3	355	35.2	847	47.4	1047	53.3
Age group										
67–70	1677	21.7	774	26.1	239	23.7	301	16.8	363	18.5
71–74	2075	26.8	858	28.9	278	27.6	477	26.7	462	23.5
75–79	1566	20.3	572	19.3	201	19.9	371	20.7	422	21.5
>= 80	2411	31.2	764	25.7	291	28.8	639	35.7	717	36.5
Race										
White	5804	75.1	2271	76.5	758	75.1	1373	76.8	1402	71.4
African American	1370	17.7	443	14.9	175	17.3	303	16.9	449	22.9
Others	555	7.2	254	8.6	76	7.5	112	6.3	113	5.8
Progesterone receptor status										
Positive	4840	62.6	1888	63.6	658	65.2	1119	62.6	1175	59.8
Negative	1957	25.3	756	25.5	244	24.2	435	24.3	522	26.6
Borderline/Unknown	932	12.1	324	10.9	107	10.6	234	13.1	267	13.6
Estrogen receptor status										
Positive	5718	74.0	2243	75.6	759	75.2	1313	73.4	1403	71.4
Negative	1177	15.2	447	15.1	155	15.4	262	14.7	313	15.9
Borderline/Unknown	834	10.8	278	9.4	95	9.4	213	11.9	248	12.6
Thyroid syndrome										
Yes	1862	24.1	592	19.9	264	26.2	459	25.7	547	27.9
No	5867	75.9	2376	80.1	745	73.8	1329	74.3	1417	72.1
Arthritis										
Yes	2188	28.3	736	24.8	313	31.0	518	29.0	621	31.6

Characteristic	All women		DCSI = 0		DCSI = 1		DCSI = 2		DCSI ≥ 3	
	N = 7729		*N* = 2968		*N* = 1009		*N* = 1788		*N* = 1964	
	No.	%	No.	%	No.	%	No.	%	No.	%
No	5541	71.7	2232	75.2	696	69.0	1270	71.0	1343	68.4
Asthma										
Yes	624	8.1	170	5.7	73	7.2	195	10.9	186	9.5
No	7105	91.9	2798	94.3	936	92.8	1593	89.1	1778	90.5
COPD										
Yes	1222	15.8	239	8.1	118	11.7	380	21.3	485	24.7
No	6507	84.2	2729	91.9	891	88.3	1408	78.7	1479	75.3
Dementia										
Yes	625	8.1	148	5.0	66	6.5	162	9.1	249	12.7
No	7104	91.9	2820	95.0	943	93.5	1626	90.9	1715	87.3
Hyperlipidemia										
Yes	5443	70.4	2046	68.9	754	74.7	1242	69.5	1401	71.3
No	2286	29.6	922	31.1	255	25.3	546	30.5	563	28.7
Hypertension										
Yes	6936	89.7	2489	83.9	919	91.1	1648	92.2	1880	95.7
No	793	10.3	479	16.1	90	8.9	140	7.8	84	4.3
Osteoporosis										
Yes	626	8.1	219	7.4	79	7.8	172	9.6	156	7.9
No	7103	91.9	2749	92.6	930	92.2	1616	90.4	1808	92.1
Anxiety										
Yes	767	9.9	217	7.3	115	11.4	200	11.2	235	12.0
No	6962	90.1	2751	92.7	894	88.6	1588	88.8	1729	88.0
Depression										
Yes	1221	15.8	340	11.5	172	17.0	311	17.4	398	20.3
No	6508	84.2	2628	88.5	837	83.0	1477	82.6	1566	79.7
PCP visit										
Yes	7301	94.5	2743	92.4	958	94.9	1714	95.9	1886	96.0
No	428	5.5	225	7.6	51	5.1	74	4.1	78	4.0

Characteristic	All women		DCSI = 0		DCSI = 1		DCSI = 2		DCSI ≥ 3	
	N = 7729		*N* = 2968		*N* = 1009		*N* = 1788		*N* = 1964	
	No.	%	No.	%	No.	%	No.	%	No.	%
Endocrinologists visit										
Yes	919	11.9	252	8.5	143	14.2	198	11.1	326	16.6
No	6810	88.1	2716	91.5	866	85.8	1590	88.9	1638	83.4
Availability of BC screening centers										
Yes	3661	47.4	1408	47.4	470	46.6	856	47.9	927	47.2
No	4068	52.6	1560	52.6	539	53.4	932	52.1	1037	52.8
Census tract education percentage										
0–13.29%	1614	20.9	589	19.8	206	20.4	387	21.6	432	22.0
13.30–22.83%	1773	22.9	703	23.7	215	21.3	387	21.6	468	23.8
22.84–38.55%	1499	19.4	587	19.8	205	20.3	343	19.2	364	18.5
>38.55%	1251	16.2	502	16.9	168	16.7	298	16.7	283	14.4
Missing	1592	20.6	587	19.8	215	21.3	373	20.9	417	21.2
Census tract household median income										
<$25,000	488	6.4	178	6.0	62	6.2	106	6.0	142	7.3
$25,001–50,000	3327	43.3	1245	42.2	446	44.7	751	42.2	885	45.4
$50,001–75,000	2447	31.9	974	33.0	314	31.5	555	31.2	604	31.0
>$75,000	1413	18.4	553	18.7	175	17.6	366	20.6	319	16.4
SEER region										
Northeast	1336	17.3	494	16.6	174	17.2	344	19.2	324	16.5
South	2346	30.4	835	28.1	288	28.5	561	31.4	662	33.7
North-central	1332	17.2	527	17.8	188	18.6	283	15.8	334	17.0
West	2715	35.1	1112	37.5	359	35.6	600	33.6	644	32.8
Metropolitan status										
Metro	6131	79.3	2315	78.0	821	81.4	1420	79.4	1575	80.2
Urban	1391	18.0	573	19.3	161	16.0	324	18.1	333	17.0
Rural	205	2.7	79	2.7	27	2.7	44	2.5	55	2.8

A cohort of 7729 elderly women with incident breast cancer and pre-existing DM using SEER-Medicare dataset 2004–2011 *COPD* chronic obstructive pulmonary disorder; *SEER* surveillance, epidemiology, and end results; *BC* breast cancer

Table 2

Description of elderly women with incident breast cancer and pre-existing diabetes mellitus by stage at diagnosis, SEER-medicare 2004–2011 cases

Variables	Stage 0		Stage I		Stage II		Stage III/IV		*P**
	N = 1161		*N* = 2968		*N* = 2246		*N* = 1354		
	N	%	*N*	%	*N*	%	*N*	%	
DCSI									< 0.001
DCSI = 0	510	43.9	1173	39.5	818	36.4	467	34.5	
DCSI = 1	168	14.5	413	13.9	274	12.2	154	11.4	
DCSI = 2	231	19.9	688	23.2	541	24.1	328	24.2	
DCSI ≥ 3	252	21.7	694	23.4	613	27.3	405	29.9	
Mammography screening									< 0.001
Annual/biennial	956	82.3	2133	71.9	1005	44.7	369	27.3	
No screening	205	17.7	835	28.1	1241	55.3	985	72.7	
Age group									< 0.001
67–70	317	27.3	666	22.4	448	19.9	246	18.2	
71–74	367	31.6	803	27.1	565	25.2	340	25.1	
75–79	213	18.3	629	21.2	457	20.3	267	19.7	
> =80	264	22.7	870	29.3	776	34.6	501	37.0	
Race									< 0.001
White	809	69.7	2339	78.8	1683	74.9	973	71.9	
African American	265	22.8	423	14.3	400	17.8	282	20.8	
Others	87	7.5	206	6.9	163	7.3	99	7.3	
Progesterone receptor status									< 0.001
Positive	586	50.5	2121	71.5	1440	64.1	693	51.2	
Negative	221	19.0	635	21.4	647	28.8	454	33.5	
Borderline/unknown	354	30.5	212	7.1	159	7.1	207	15.3	
Estrogen receptor status									< 0.001
Positive	707	60.9	2453	82.6	1704	75.9	854	63.1	
Negative	142	12.2	329	11.1	401	17.9	305	22.5	
Borderline/Unknown	312	26.9	186	6.3	141	6.3	195	14.4	

Variables	Stage 0		Stage I		Stage II		Stage III/IV		P^*
	N = 1161		N = 2968		N = 2246		N = 1354		
	N	%	N	%	N	%	N	%	
Thyroid									< 0.001
Yes	281	24.2	768	25.9	548	24.4	265	19.6	
No	880	75.8	2200	74.1	1698	75.6	1089	80.4	
Arthritis									0.027
Yes	287	24.7	854	28.8	645	28.7	402	29.7	
No	874	75.3	2114	71.2	1601	71.3	952	70.3	
Asthma									0.089
Yes	93	8.0	257	8.7	187	8.3	87	6.4	
No	1068	92.0	2711	91.3	2059	91.7	1267	93.6	
COPD									< 0.001
Yes	150	12.9	440	14.8	365	16.3	267	19.7	
No	1011	87.1	2528	85.2	1881	83.7	1087	80.3	
Dementia									< 0.001
Yes	56	4.8	150	5.1	233	10.4	186	13.7	
No	1105	95.2	2818	94.9	2013	89.6	1168	86.3	
Hyperlipidemia									< 0.001
Yes	890	76.7	2214	74.6	1507	67.1	832	61.4	
No	271	23.3	754	25.4	739	32.9	522	38.6	
Hypertension									0.471
Yes	1044	89.9	2671	90.0	2022	90.0	1199	88.6	
No	117	10.1	297	10.0	224	10.0	155	11.4	
Osteoporosis									0.035
Yes	99	8.5	266	9.0	152	6.8	109	8.1	
No	1062	91.5	2702	91.0	2094	93.2	1245	91.9	
Anxiety									0.361
Yes	104	9.0	288	9.7	242	10.8	133	9.8	
No	1057	91.0	2680	90.3	2004	89.2	1221	90.2	
Depression									0.471

Variables	Stage 0		Stage I		Stage II		Stage III/IV		*P**
	N = 1161		*N* = 2968		*N* = 2246		*N* = 1354		
	N	%	*N*	%	*N*	%	*N*	%	
Yes	160	13.8	427	14.4	399	17.8	235	17.4	
No	1001	86.2	2541	85.6	1847	82.2	1119	82.6	
PCP visit									0.024
Yes	1109	95.5	2820	95.0	2110	93.9	1262	93.2	
No	52	4.5	148	5.0	136	6.1	92	6.8	
Endocrinologists visit									0.017
Yes	162	14.0	370	12.5	243	10.8	144	10.6	
No	999	86.0	2598	87.5	2003	89.2	1210	89.4	
Availability of BC screening centers									< 0.001
Yes	536	46.2	1490	50.2	1034	46.0	601	44.4	
No	625	53.8	1478	49.8	1212	54.0	753	55.6	
Census tract education									0.008
0–13.29%	236	20.3	573	19.3	494	22.0	311	23.0	
13.30–22.83%	262	22.6	705	23.8	495	22.0	311	23.0	
22.84–38.55%	230	19.8	612	20.6	410	18.3	247	18.2	
> 38.55%	208	17.9	494	16.6	364	16.2	185	13.7	
Missing	225	19.4	584	19.7	483	21.5	300	22.2	
Census tract household income									0.042
< $25,000	72	6.3	174	5.9	142	6.4	100	7.5	
$25,001–50,000	490	42.5	1245	42.2	977	43.7	615	45.9	
$50,001–75,000	360	31.3	953	32.3	716	32.0	418	31.2	
> $75,000	230	20.0	576	19.5	400	17.9	207	15.4	
SEER region									0.139
Northeast	194	16.7	492	16.6	393	17.5	257	19.0	
South	338	29.1	897	30.2	679	30.2	432	31.9	
North-central	225	19.4	503	16.9	374	16.7	230	17.0	
West	404	34.8	1076	36.3	800	35.6	435	32.1	
Metropolitan status									0.428

Variables	Stage 0		Stage I		Stage II		Stage III/IV		*P**
	N = 1161		*N* = 2968		*N* = 2246		*N* = 1354		
	N	%	*N*	%	*N*	%	*N*	%	
Metro	940	81.0	2321	78.2	1782	79.3	1088	80.4	
Urban	195	16.8	562	18.9	400	17.8	234	17.3	
Rural	26	2.2	84	2.8	64	2.8	31	2.3	

DCSI diabetes complications severity index; *PCP* primary care providers; *COPD* chronic obstructive pulmonary disorder; *SEER* surveillance, epidemiology, and end results; *BC* breast cancer

* Chi-square test

Table 3

Association of Diabetes Complication Severity Index with Breast Cancer Stage at Diagnosis among Elderly women with pre-existing Diabetes

Variables	Stage I			Stage II			Stage III/IV		
	OR	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Model 1									
DCSI									
DCSI = 0	Ref								
DCSI = 1	1.06	[0.86, 1.30]	0.598	1.01	[0.81, 1.26]	0.947	0.99	[0.77, 1.28]	0.967
DCSI = 2	1.30	[1.08, 1.56]	0.005	1.45	[1.20, 1.76]	< 0.001	1.57	[1.27, 1.93]	<0.001
DCSI ≥ 3	1.20	[1.00, 1.43]	0.047	1.50	[1.25, 1.81]	< 0.001	1.77	[1.45, 2.17]	<0.001
Model 2									
DCSI									
DCSI = 0	Ref								
DCSI = 1	1.05	[0.84, 1.31]	0.661	0.99	[0.79, 1.25]	0.954	1.00	[0.77, 1.30]	0.975
DCSI = 2	1.32	[1.09, 1.61]	0.005	1.42	[1.16, 1.74]	< 0.001	1.46	[1.17, 1.83]	<0.001
DCSI ≥ 3	1.27	[1.05, 1.54]	0.016	1.47	[1.20, 1.80]	< 0.001	1.62	[1.30, 2.01]	<0.001
Model 3									
DCSI									
DCSI = 0	Ref								
DCSI = 1	1.05	[0.84, 1.31]	0.680	0.98	[0.77, 1.25]	0.870	0.97	[0.74, 1.29]	0.856
DCSI = 2	1.26	[1.03, 1.53]	0.023	1.22	[0.99, 1.51]	0.059	1.17	[0.93, 1.48]	0.187
DCSI ≥ 3	1.18	[0.97, 1.44]	0.096	1.17	[0.95, 1.44]	0.136	1.16	[0.92, 1.46]	0.211
Mammography screening									
Annual/biennial	0.56	[0.47, 0.67]	<0.001	0.19	[0.16, 0.23]	< 0.001	0.09	[0.08, 0.11]	<0.001
No screening	Ref								

Model 1 contains DCSI only. Model 2 contains DCSI plus age, race. progesterone receptor status, estrogen receptor status, other comorbid conditions, PCP visit, endocrinologist visit, availability of mammography screening centers, census tract education, and census tract household income. Model 3 contains Model 2 plus mammography screening. Odds ratios and 95% CI from the multinomial logistic regression models *DCSI* Diabetes complications severity index; *BC* breast cancer; *OR* odds ratio; *AOR* adjusted odds ratio; *CI* confidence interval