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ORIGINAL REPORT

Use and Costs of Disease Monitoring in Women With Metastatic Breast Cancer

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ABSTRACT

Purpose

The optimal frequency of monitoring patients with metastatic breast cancer (MBC) is unknown; however, data suggest that intensive monitoring does not improve outcomes. We performed a population-based analysis to evaluate patterns and predictors of extreme use of disease-monitoring tests (serum tumor markers [STMs] and radiographic imaging) among women with MBC.

Methods

The SEER-Medicare database was used to identify women with MBC diagnosed from 2002 to 2011 who underwent disease monitoring. Billing dates of STMs (carcinoembryonic antigen and/or cancer antigen 15-3/ cancer antigen 27.29) and imaging tests (computed tomography and/or positron emission tomography) were recorded; if more than one STM or imaging test were completed on the same day, they were counted once. We defined extreme use as > 12 STM and/or more than four radiographic imaging tests in a 12-month period. Multivariable analysis was used to identify factors associated with extreme use. In extreme users, total health care costs and end-of-life health care utilization were compared with the rest of the study population.

Results

We identified 2,460 eligible patients. Of these, 924 (37.6%) were extreme users of disease-monitoring tests. Factors significantly associated with extreme use were hormone receptor–negative MBC (odds ratio [OR], 1.63; 95% CI, 1.27 to 2.08), history of a positron emission tomography scan (OR, 2.92; 95% CI, 2.40 to 3.55), and more frequent oncology office visits (OR, 3.14; 95% CI, 2.49 to 3.96). Medical costs per year were 59.2% higher in extreme users. Extreme users were more likely to use emergency department and hospice services at the end of life.

Conclusion

Despite an unknown clinical benefit, approximately one third of elderly women with MBC were extreme users of disease-monitoring tests. Higher use of disease-monitoring tests was associated with higher total health care costs. Efforts to understand the optimal frequency of monitoring are needed to inform clinical practice.

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INTRODUCTION

The distribution of health care expenditures in the United States is skewed, with a small proportion of patients consuming a disproportionately high proportion of health care resources. In 2010, 1% of the total population accounted for > 20% of total health care costs, and the top 50% accounted for 97.2% of overall health care expenditures.[1] In the Medicare population, diagnostic testing, including radiographic imaging, is the most rapidly growing sector of reimbursed services and represents almost one quarter of ambulatory health care costs.[2] Among Medicare beneficiaries with cancer, imaging costs have risen at a rate that outpaces total health care costs.[3] A population-based study of Medicare patients with metastatic cancer demonstrated a > 50% increase in imaging tests per patient per month from 1995 to 2006.[4] This is particularly salient because cancer care costs are rising rapidly and are highest in patients with advanced cancer.[5]

In patients with advanced cancer, the optimal frequency and modality of disease monitoring are unknown. A potential advantage of more frequent testing may be earlier detection of disease progression that would result in a switch to alternate

therapies. Clinical guidelines, such as those of the National Comprehensive Cancer Center Network, suggest that patients with metastatic disease should be monitored routinely while undergoing systemic therapy to continue treatments that control disease while avoiding toxicities from nonefficacious therapies. These guidelines do not specify the optimal frequency or the modality (radiographic imaging, serum tumor markers [STMs]).[6] Although no prospective studies have evaluated whether frequent testing is associated with better outcomes, some data have suggested that earlier detection of disease progression is not associated with improved outcomes.[7] Disease monitoring contributes significantly to health care costs for patients with metastatic breast cancer (MBC).[8-14]

A subset of the general population uses a disproportionately high percentage of health care services.[15] Previous reports have shown that higher use of imaging studies is associated with patient age, ethnicity, and socioeconomic status.[16,17] The objectives of this study were to identify patterns and predictors of use and extreme use of disease-monitoring tests (ie, STMs, radiographic imaging studies) among women with MBC.

METHODS

Data Source

Data from the SEER-Medicare database were analyzed.[18] SEER data provide tumor characteristics and represent 28% of the US population.[19] Linkage with the Medicare database allows longitudinal evaluation of cancer care and characterizes inpatient, outpatient, and physician-billed services, including diagnoses and health care costs.[20]

Cohort Selection

We identified all women age ≥ 65 years with pathologically confirmed breast cancer diagnosed between January 1, 2002, and December 31, 2011. To evaluate patients monitored with both STMs and imaging, the study population was restricted to patients with stage IV breast cancer who had at least two claims for STM tests and at least two claims for a computed tomography (CT) and/or positron emission tomography (PET) scan after the date of diagnosis.

We excluded patients who were enrolled in a non-Medicare health maintenance organization or who were not continuously enrolled by Medicare Parts A and B for a period of 12 months before diagnosis through death or end of the study period. Patients who were enrolled in Medicare due to end-stage renal disease as well as patients with other primary cancers were excluded.

Disease-Monitoring Testing and Extreme Use

Breast cancer STM tests included carcinoembryonic antigen (CEA), cancer antigen (CA) 27.29, and CA 15-3.[21-23] CEA testing (Healthcare Common Procedure Coding System [HCPCS] code 82378) was identified uniquely; however, CA 15-3 and CA 27.29 testing could not be separated because one code is used for both tests (HCPCS 86300).[24] The date of each STM test was recorded from the time of diagnosis until death or end of the study period. To avoid overcounting, each CEA and CA 27.29/15-3 claim was counted as a single STM test if performed on the same day.

Claims for imaging tests were identified with HCPCS, International Classification of Diseases, Ninth Revision (ICD-9), and Current Procedural Terminology (CPT) codes.[4] CT scans of the chest, abdomen, and pelvis performed on the same day were counted as one imaging test. Each PET-CT scan (claims for PET and CT scans on the same day) was counted as one PET claim. We eliminated duplicate claims within each file by matching patient identifier, date of procedure, CPT, HCPCS, or ICD-9 code. Because outpatient claims often do not include date of service and may be submitted according to a billing cycle rather than to the date of service, we extended the date criteria for this match to 7 days; > 98% of matches occurred on the same day.[4] For duplicate claims, we preferentially retained the claim billed with CPT or HCPCS codes over ICD-9 codes.[4] To avoid duplicate counting, a cap of two imaging tests per week was applied.

On the basis of our prior work and monitoring patterns in clinical trials, we defined extreme users of disease-monitoring testing as any patients who had > 12 STMs and/or more than four radiographic imaging tests in any 1-year interval from diagnosis until death or end of the study period.[9,25,26]

Covariates

Demographic covariates included age at diagnosis (65 to 69, 70 to 74, 75 to 79, ≥ 80 years), year of diagnosis, marital status (married, single, unknown), ethnicity (white, other), geographic area classified (metropolitan, other), region, Charlson comorbidity score (0, 1, ≥ 2), and socioeconomic status. Tumors were categorized as hormone receptor (estrogen receptor [ER] and/or progesterone receptor [PR]) positive, negative, or unknown.

Other covariates were history of PET scan after diagnosis of breast cancer (yes, no), maximum number of imaging tests in any 1-year period (two or fewer, three, four, five or more), and maximum number of medical oncology office visits in a 1-year time frame (low, medium, high). To define medical oncology office visits, physician files were used to determine provider specialty and date of office visit. Medical oncologists were identified as physicians with a listed specialty of medical oncology or hematology/oncology. Visits were identified through HCPCS codes for office new visits, office established visits, and office consultations.

Costs of Care

Costs of care were calculated from Medicare reimbursement claims from physician, hospital, outpatient, durable medical equipment, and hospice filings between the date of diagnosis and the date of death or end of the study period. Costs were categorized as total costs in the first year, total costs in the last year of life, and total costs per year alive.

End-of-Life Care

To further understand the relationship between disease monitoring and health care costs at the end of life, end-of-life quality-of-care indicators were evaluated in the last month of life.[27,28] Quality-of-care indicators evaluated in the last month of life were more than one emergency department visit, more than one hospital admission, more than 14 days hospitalized, admission to the intensive care unit (ICU), and admission to hospice within 3 days before death.[27,28] ICU admissions in the last month of life were identified by using ICD-9 codes (96.7x) and diagnosis-related group codes (475 or 483) for mechanical ventilation and the ICU indicator variable in the Medicare inpatient file.[29,30] Hospice admissions were identified through billing claims for hospice in the Medicare hospice files during the last month of life.

Statistical Analysis

We calculated the per-patient-per-year STM testing rate and per-patient-per-year radiographic imaging rate. Univariable analyses comparing characteristics of patients and the care they received were performed with t tests for continuous variables and χ^2 tests for categorical variables. We developed logistic regression models to determine the association between clinical, demographic, and treatment factors and extreme use of disease-monitoring testing.[31,32]

A linear regression model was used to estimate the association between extreme use of disease monitoring and total cost of care. Total cost was approximately log-normally distributed, and log-transformed cost of care was analyzed as a continuous response variable. To display results as percent changes in cost of care, parameter estimates from the regression model were exponentiated.[24] We performed a sensitivity analysis by removing the costs of STM and radiographic imaging tests for each subject from the regression models. Costs of each STM and imaging modality were calculated from

Medicare reimbursement rates.[33,34] The effect extreme use of disease monitoring on overall survival (OS) was evaluated by using a Cox proportional hazard model. All analyses were conducted with SAS version 9.4 software (SAS Institute, Cary, NC). All statistical tests were two sided, with $\alpha = .05$.

RESULTS

We identified 6,038 women with de novo MBC between 2002 and 2011 of whom 2,460 (40.7%) were eligible for the analysis. A total of 3,548 (58.8%) were excluded because they were not monitored with STMs. The cohort was predominantly white (85.4%), single (60.3%), and without comorbidities (57.3%; Table 1). The majority (1,784 [72.5%]) had hormone receptor–positive MBC. The majority (85.7%) were alive > 12 months from time of diagnosis during the study period. Among the 2,460 included patients, 924 (37.6%) were classified as extreme users, 222 (9.0%) were extreme users of STM tests, and 807 (32.8%) were extreme users of radiographic imaging. Additionally, the results of a sensitivity analysis of the proportion of

Table 1. Demographics of Study Population and Associations With Extreme Use of Disease-Monitoring Testing

	Total Population		Extreme Users			
	No.	%	No.	%	OR*	95% CI
No. of patients	2,460	100	924	37.6		
Age, years						
65-69	581	23.6	260	28.2	0.97	0.76 to 1.23
70-74	655	26.6	285	30.8		Reference
75-79	550	22.4	205	22.2	0.85	0.68 to 1.12
≥ 80	674	27.4	174	18.8	0.58†	0.45 to 0.75
Diagnosis year						
2002-2004	649	26.4	241	26.1		Reference
2005-2007	796	32.4	316	34.2	0.94	0.74 to 1.19
2008-2011	1,015	41.3	367	39.7	0.75†	0.59 to 0.95
Ethnicity						
White	2,200	85.4	791	85.6		Reference
Other/unknown	360	14.6	133	14.4	1.02	0.79 to 1.33
Marital status						
Married	870	35.4	380	41.1		Reference
Single	1,483	60.3	500	54.1	0.77†	0.63 to 0.93
Geographic area						
Large metropolitan	1,460	59.3	526	56.9	0.83	0.69 to 1.00
Other	1,000	40.7	398	43.1		Reference
Charlson comorbidity score						
0	1,408	57.3	526	57.0		Reference
1	632	25.7	232	25.1	1.15	0.93 to 1.43
≥ 2	417	17.0	165	17.9	1.43†	1.12 to 1.84
Region						
East	757	30.8	273	29.5		Reference
Midwest	832	33.8	327	35.4	1.04	0.83 to 1.32
West	871	35.4	324	35.1	0.89	0.71 to 1.11
Socioeconomic status						
Low	1,112	45.2	417	45.2		Reference
Medium	620	25.2	216	23.4	0.92	0.73 to 1.16
High	726	29.6	289	31.4	1.15	0.92 to 1.45
ER/PR status						
Positive	1,784	72.5	644	69.7		Reference
Negative	335	13.6	170	18.4	1.63†	1.27 to 2.08
Unknown	341	13.9	110	11.9	0.97	0.74 to 1.25
PET use						
No	1,050	42.7	245	26.5		Reference
Yes	1,410	57.3	679	73.5	2.92†	2.40 to 3.55
Maximum oncology office visit volume in any 1 year						
Low	792	32.2	205	22.2		Reference
Medium	799	32.5	277	30.0	1.42†	1.13 to 1.78
High	709	28.8	395	42.7	3.14†	2.49 to 3.96
Maximum No. of imaging tests in any 1 year					1.31	0.88 to 1.95
≤ 2	623	25.3				
3	546	22.2				
4	484	19.7				
≥ 5	807	32.8				
More than 12 STM tests in any 1 year						
Yes	222	9.0				
No	2,238	91.0				

Abbreviations: ER/PR, estrogen receptor/progesterone receptor; OR, odds ratio; PET, positron emission tomography; STM, serum tumor marker.
*ORs were derived from multivariable analysis, and models were adjusted for all other factors listed in the table.
†$P < .05$.

extreme users with a cap of one imaging test per week were similar. Extreme users were more likely to be younger (age ≥ 80 years, 18.8% *v* 32.6%; $P < .001$), to have ER/PR-negative cancer (18.4% *v* 10.7%; $P < .001$), to have had at least one PET scan (73.5% *v* 47.6%; $P < .001$), and to have more oncology visits (42.8% *v* 20.4%; $P < .001$).

In a multivariable model (Table 1), extreme use of disease-monitoring tests was associated with a Charlson comorbidity score ≥ 2 (odds ratio [OR], 1.43; 95% CI, 1.12 to 1.84), an ER/PR-negative cancer (OR, 1.63; 95% CI, 1.27 to 2.08), and a history of at least one PET scan (OR, 2.92; 95% CI, 2.40 to 3.55). Patients who had a higher number of oncology visits were more likely to have frequent testing (OR, 3.14; 95% CI, 2.49 to 3.96). Patients ≥ 80 years old (OR, 0.58; 95% CI, 0.45 to 0.75), patients diagnosed in later years (2008 to 2011), and patients who were single (OR, 0.77; 95% CI, 0.63 to 0.93) were less likely to be extreme users.

Increased use of STM tests was associated with having a higher socioeconomic status, having at least one PET scan (OR, 2.02; 95% CI, 1.42 to 2.88), and a higher frequency of office visits (OR, 1.72; 95% CI, 1.10 to 2.68; Table 2). Women with ER/PR-negative MBC (OR, 0.59; 95% CI, 0.37 to 0.95) were less likely to be extreme users of STM tests. Similar associations were seen with extreme use of radiographic imaging; however, women with ER/PR-negative MBC had a higher odds of extreme imaging (OR, 1.93; 95% CI, 1.50 to 2.49; Table 2). We found no difference in OS for patients who were extreme users of disease-monitoring testing (hazard ratio, 0.93; 95% CI, 0.86 to 1.02).

Total costs of care were higher for patients categorized as extreme users of disease-monitoring testing (Fig 1). For extreme users in the first year after diagnosis, costs were 50.6% higher (95% CI, 40.7% to 61.1%), and mean cost of care was $56,249 compared with $37,121 for the rest of the study population ($P < .001$). In the last year of life, costs were 68.7% higher (95% CI, 54.2% to 84.6%) in extreme users, and mean cost of care was $63,697 compared with $39,843 in the rest of the study population ($P < .001$). Total costs per year after diagnosis were also 59.2% (95% CI, 49.8% to 69.1%) higher in extreme users, and mean cost per year was $54,211 compared with $35,038 for the rest of the study population ($P < .001$). The results were similar after removing the total costs from disease-monitoring testing. With the exception of ICU admissions, extreme users were more likely to use health care services at the end of life compared with the rest of the study population (Fig 2). Extreme users were also more likely to be admitted to hospice closer to death.

DISCUSSION

The findings suggest that approximately 40% of women older than age 65 years with MBC are monitored with both STMs and radiographic imaging. Of these patients, approximately one third undergo frequent disease monitoring. Women who have more appointments with their medical oncologist are more likely to undergo frequent testing as are those who undergo more expensive imaging tests (ie, PET scans). Total health care costs are approximately 50% higher in patients who have more frequent disease-monitoring testing, even after accounting for the individual costs of the tests. Additionally, extreme users of disease-monitoring testing are more likely to have increased health care service utilization near the end of life. Finally, there seems to be no association between disease monitoring and OS.

In the United States, an estimated 6% to 10% of new breast cancer cases are initially diagnosed as stage IV, and 20% to 30% of all cases become metastatic over time.[35-37] Clinical guidelines suggest that patients with MBC should be actively monitored for disease progression to continue effective therapies and to avoid toxicities from therapies that are no longer effective.[6] The National Comprehensive Cancer Network guidelines do not specifically recommend which tests to use and at what frequency.[6] Currently in the metastatic setting, there is no evidence to suggest that more frequent testing is associated with better outcomes. A clinical trial in women with MBC with persistently increased circulating tumor cells suggested that changing treatment early was not associated with improvement in survival.[7] Furthermore, in women with early-stage breast cancer, surveillance testing, which can result in earlier treatment initiation, does not affect survival.[38,39]

In addition to cost, frequent disease monitoring can be associated with emotional harm. The prevalence of anxiety and depression among patients with advanced cancers is estimated to be 25% to 65%.[40] Previous work has shown that depression and anxiety can increase over time in patients with metastatic solid tumors and has been attributed to multiple factors, including fear of death and fear of disease progression.[41,42] A study of 154 women with ovarian cancer found that on average, most women were moderately preoccupied with their CA-125 levels and that degree of preoccupation was associated with increased emotional distress.[43] In a study that assessed distress in women during the surveillance period, women with more frequent testing had higher levels of anxiety without survival benefit.[44]

Despite potential emotional harms and unclear benefits, patients with other advanced solid tumors undergo frequent disease monitoring. Recently, we retrospectively evaluated 928 patients with advanced solid tumors and found almost one quarter had three or more individual STM tests within a 1-month period.[9] To determine the rationale for STM evaluation, medical records of the top 10% of STMs were reviewed. Only 2% of patients had a change in treatment as a result of rising STMs after confirmation with radiographic imaging. The majority of oncologists reported that STM tests were ordered by copying the previous order.[9]

In patients with asymptomatic early-stage breast cancer, strong evidence exists against the use of surveillance testing to detect early recurrence.[23,45-47] However, despite this evidence, there are still high rates of testing in this population. Recently, a population-based study demonstrated that 42.0% of elderly patients had STM tests despite guidelines against their use, and this testing was associated with increased Medicare expenditures.[24] Another study demonstrated that 77% of women received at least one tumor marker test and that 57% received at least one nonrecommended imaging test.[48]

Another setting of high health care utilization in patients with cancer is during the end of life. Despite recommendations against aggressive care at the end of life, which represents poor quality of care, a high percentage of patients receive aggressive end-of-life care.[27,28] A population-based study of elderly patients with advanced cancers found that approximately 10% of patients had aggressive use of hospital resources, including the emergency department, hospital admissions, and the ICU, in the last month of life.[27] Also similar was a high proportion of patients admitted

to hospice within the last 3 days of life.[27] The same study found use of health care resources at the end of life is associated with receipt of other aggressive care measures. These results are similar to the present findings that extreme users of disease-monitoring testing were more likely to use other health care services, including more-aggressive end-of-life care.

The changing of physician behavior is challenging. Physicians are motivated by both extrinsic (ie, financial reimbursement) and intrinsic (ie, altruism) factors.[49] Additionally, physicians who profit from monitoring tests should be mindful of potential conflicts of interest. A successful strategy may be to change policy for reimbursement. For example, this approach helped to curb inappropriate use of erythropoiesis-stimulating agents. After initial US Food and Drug Administration approval, uptake was high (27%) in patients with cancer who received chemotherapy.[50-53] After changes in reimbursement, there was a rapid decline in the

Table 2. Demographics and Associations of Extreme Users of STM Tests and Radiographic Imaging

	STM Test				Radiographic Imaging			
	No.	%	OR*	95% CI	No.	%	OR*	95% CI
No. of patients	222	9.0			807	32.8		
Age, years								
65-69	66	29.7	0.98	0.68 to 1.42	232	28.7	1.07	0.84 to 1.37
70-74	75	33.8		Reference	239	29.6		Reference
75-79	48	21.6	0.84	0.56 to 1.25	182	22.6	0.99	0.77 to 1.28
≥ 80	33	14.9	0.57†	0.37 to 0.90	154	19.1	0.67†	0.52 to 0.87
Diagnosis year								
2002-2004	68	30.6		Reference	198	24.5		Reference
2005-2007	74	33.3	0.83	0.56 to 1.21	275	34.1	1.01	0.79 to 1.29
2008-2011	80	36.1	0.67†	0.46 to 0.98	334	41.4	0.89	0.70 to 1.13
Ethnicity								
White	202	91.0		Reference	683	84.6		Reference
Other/unknown	20	9.0	0.69	0.42 to 1.14	124	15.4	1.11	0.85 to 1.45
Marital status								
Married	100	45.1		Reference	334	41.4		Reference
Single	112	50.4	0.80	0.59 to 1.08	437	54.1	0.76†	0.63 to 0.93
Geographic location								
Large metropolitan	134	60.4	0.85	0.62 to 1.16	458	56.7	0.88	0.72 to 1.06
Other	88	39.6		Reference	349	43.3		Reference
Charlson comorbidity score								
0	142	64.0		Reference	447	55.5		Reference
1	52	23.4	1.00	0.70 to 1.42	204	25.3	1.19	0.96 to 1.48
≥ 2	28	12.6	0.87	0.56 to 1.36	155	19.2	1.61†	1.25 to 2.08
Region								
East	70	31.5		Reference	237	29.4		Reference
Midwest	42	18.9	0.58†	0.38 to 0.89	305	37.8	1.16	0.91 to 1.48
West	110	49.6	1.51†	1.07 to 2.13	265	32.8	0.77†	0.61 to 0.97
Socioeconomic status								
Low	71	32.0		Reference	382	47.4		Reference
Medium	67	30.2	1.53†	1.05 to 2.23	184	22.9	0.84	0.66 to 1.06
High	84	37.8	1.56†	1.07 to 2.27	239	29.7	0.98	0.77 to 1.24
ER/PR status								
Positive	174	77.0		Reference	557	69.0		Reference
Negative	23	10.2	0.59†	0.37 to 0.95	159	19.7	1.93†	1.50 to 2.49
Unknown	29	12.8	1.02	0.65 to 1.59	91	11.3	0.95	0.72 to 1.26
PET use								
No	53	23.9		Reference	208	25.8		Reference
Yes	169	76.1	2.02†	1.42 to 2.88	599	74.2	2.77†	2.26 to 3.39
Maximum oncology office visit volume in any 1 year								
Low	43	19.4		Reference	177	21.9		Reference
Medium	52	23.4	1.06	0.70 to 1.63	245	30.4	1.46†	1.15 to 1.85
High	121	54.5	2.58†	1.75 to 3.80	343	42.5	2.84†	2.23 to 3.61
Maximum No. of imaging tests in any 1 year								
≤ 2	33	14.9		Reference				
3	32	14.4	0.95	0.57 to 1.59				
4	52	23.4	1.60	0.99 to 2.59				
≥ 5	105	47.3	1.72†	1.10 to 2.68				
More than 12 STM tests in any 1 year					105	13.0		
No					702	87.0		Reference
Yes					105	13.0	1.44†	1.06 to 1.96

Abbreviations: ER/PR, estrogen receptor/progesterone receptor; OR, odds ratio; PET, positron emission tomography; STM, serum tumor marker.
*ORs were derived from multivariable analysis, and models were adjusted for all other factors listed in the table.
†$P < .05$.

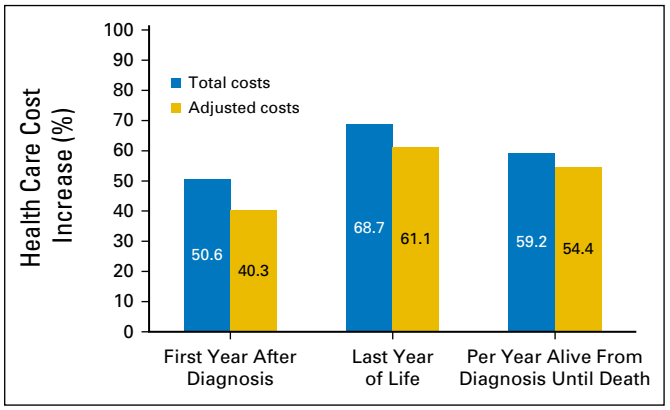

Fig 1. Percentage increase in total and adjusted costs of care from breast cancer diagnosis until death for extreme users of disease-monitoring testing. Adjusted for costs of disease-monitoring testing, including serum tumor-marker tests and radiographic imaging and analyzed by using natural log transformation by multivariable linear regression adjusted for characteristics displayed in Table 1 (20 participants not included due to no cost data). $P < .001$ for all values.

proportion of patients with cancer patients treated with these agents,[54] which demonstrates that changes in reimbursement policy could curb overuse.

The present work has several important limitations. The SEER-Medicare database only includes patients who are 65 years or older with Medicare insurance and may not be generalizable to all patient populations. Almost 50% of women with MBC were excluded from the analysis due to having fewer than two claims for STM tests likely because of normal STM values. Because the analysis was done by using claims data, we do not know the reason for the diagnostic tests. Patients in clinical trials may undergo more frequent evaluation, and we were unable to account for that; however, < 2% of patients with cancer participate in trials, and rates are significantly lower in elderly patients, so we believe that this did not have a significant impact on the findings.[55] The cost estimates did not include costs associated with oral therapies and, therefore, may be an underestimate of total cancer costs. Because there are no prospective studies about optimal frequency and modality of disease-monitoring testing, it is currently unknown whether patients who have more frequent disease-monitoring testing have better clinical outcomes; however, we found no association of frequent monitoring with OS. In the absence of prospective studies, our definition of extreme use is conservative on the basis of clinical practice and not defined by specific guidelines; future studies are necessary to define optimal timing of disease-monitoring testing.

In summary, we found that approximately one third of elderly women with MBC monitored with both STMs and imaging were extreme users of disease-monitoring testing despite its unproven benefit and higher health care costs. Extreme use may reflect both patient and physician factors, and these should be targeted for interventions to curb spending, including potential health policy changes. In addition, better evidence is needed with regard to the benefits and harms of frequent disease-monitoring testing to inform guidelines. Future research should determine the most cost-effective strategy to monitor patients with MBC.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

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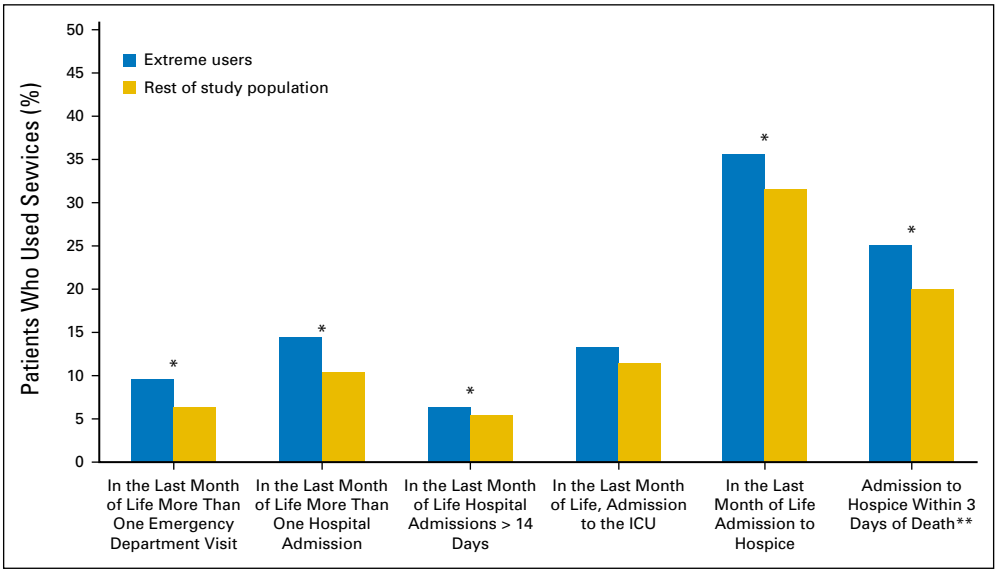

Fig 2. Relationship between aggressive end-of-life care and extreme use of disease-monitoring testing. *$P < .03$. **Percentage of patients admitted to hospice. ICU, intensive care unit.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Use and Costs of Disease Monitoring in Women With Metastatic Breast Cancer

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