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Temporal and Geographic Variation in the Use of Hematopoietic Growth Factors in Older Women Receiving Breast Cancer Chemotherapy: Findings From a Large Population-Based Cohort

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Abstract

Purpose—Hematopoietic growth factors have played a major role in preventing infection and shortening the duration of neutropenia in patients receiving cancer chemotherapy. Little information is available on how these growth factors are used in patients with cancer outside the clinical trial setting. We performed descriptive and exploratory analyses on the patterns and correlates of the use of hematopoietic growth factors in community-dwelling elderly patients.

Patients and Methods—We identified 5,843 women from the Surveillance, Epidemiology, and End Results (SEER)–Medicare-linked data cohorts who were diagnosed with breast cancer at age 65 or older in 1992 to 1999 from the 11 SEER areas and received chemotherapy.

Results—Overall, 17.3% of the elderly women with breast cancer chemotherapy received filgrastim and 6.8% received epoetin. The use of the growth factors increased significantly over time from 1992 to 1999 ($P < .001$ for trend). Compared with patients diagnosed in 1992 to 1994, patients diagnosed in 1998 to 1999 were more than five times and 65 times more likely to receive filgrastim and epoetin, respectively, after controlling for other factors such as age and comorbidity. There also was substantial geographic variation in the use of hematopoietic growth factors, ranging from 10.6% in Seattle to 22.9% in Atlanta. Significant predictors of growth factors included patient age, race, tumor stage, and comorbidity.

Conclusion—There were substantial temporal and geographic variations in the use of hematopoietic growth factors among patients receiving chemotherapy for breast cancer. The nationwide and population-based Medicare claims provide potential for examining the effectiveness, medical costs, and cost effectiveness of hematopoietic growth factors in the community.

Introduction

Patients with cancer who receive chemotherapy often have adverse effects such as nausea, vomiting, anemia, and neutropenia.¹⁻³ Neutropenia is the most serious hematologic toxicity of cancer chemotherapy. Neutrophils are the first line of defense against infection, but chemotherapy predisposes patients with cancer to infections by suppressing the production of neutrophils and by cytotoxic effects on the cells. Because of the high risk of death from rapidly

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This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibilities of the authors.

spreading infection, patients with neutropenic fever must be treated aggressively, typically with intravenous antibiotics and hospitalization.^{1,3} More recently, hematopoietic growth factors have played a major role in preventing infection in cancer patients and shortening the duration of neutropenia in patients receiving chemotherapy.⁴⁻¹⁹ As a result, patients can better tolerate the standard chemotherapy regimens and may be able to tolerate the higher doses of chemotherapeutic agents, thereby improving therapeutic outcomes.^{3,9-11}

During the last decade, numerous clinical trials and meta-analyses have demonstrated the efficacy of colony-stimulating factors (CSFs) in reducing neutropenia and shortening duration of hospitalization among patients with various cancers and all age groups.⁴⁻¹⁹ However, the evidence on the role of CSFs in reducing infection-related mortality and increasing survival has been inconsistent and inconclusive.^{20,21} On the basis of these findings, the American Society of Clinical Oncology issued guidelines in 1994 on the use of CSFs, recommending their use in some situations, such as when the expected incidence of febrile neutropenia is $\geq 40\%$.²² The most commonly used CSF is filgrastim, which increases the number of granulocytes, particularly neutrophils. Filgrastim is often administered intravenously or subcutaneously starting 24 hours after chemotherapy administration and continuing until the absolute neutrophils count exceeds $10,000/\mu\text{L}$.³ Another hematopoietic growth factor, epoetin, is a biosynthetic form of erythropoietin, which stimulates RBC production. Numerous studies examined its potential usefulness as an alternative to transfusion in the management of anemia for patients with cancer. The evidence-based clinical practice guidelines of the American Society of Clinical Oncology and the American Society of Hematology were recently published in 2001²³ and recommend the use of epoetin as a treatment option for patients with chemotherapy-associated anemia with a hemoglobin less than 12 g/dL but never less than 10 g/dL.

However, little information is available on how these expensive growth factors are used in patients with cancer outside clinical trial settings.^{24,25} Surveys were conducted on how physicians prescribed these agents for patients with cancer and found a substantial variation in the use of CSFs among physicians.²⁴ Another study reported the use of growth factors for cancer patients in oncology clinic-based settings with a small number of cancer patients and found that 18% of women with breast cancer received a CSF.²⁵ Therefore, the aims of this study were to perform descriptive and exploratory analyses on the patterns and correlates of CSF use in older women diagnosed with breast cancer from 1992 to 1999 using nationwide, population-based Medicare data, and to identify significant predictors of CSF use.

Patients and Methods

Data Sources

The Surveillance, Epidemiology, and End Results (SEER) program, supported by the National Cancer Institute, includes population-based tumor registries in 11 selected geographic areas between 1992 and 1999²⁶⁻²⁸: the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, and Seattle; Los Angeles county; the San Jose-Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii.

The Medicare Program covers hospital, physician, and outpatient medical services for more than 97% of persons age 65 years or older.^{29,30} These data were available for all beneficiaries starting in 1991, and their Medicare claims are available through 2001. Patient data reported by the SEER registries from 1992 to 1999 were matched against the Medicare master enrollment file. For persons age 65 years or older appearing in the SEER records, Medicare eligibility could be identified for 94% of these patients. The method of linking these data has been described elsewhere.^{29,30} The Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston approved this study.

Study Population

Our study is based on the analytic SEER-Medicare files that excluded women who did not have full coverage of both Medicare Parts A and B and were members of health maintenance organizations, because claims from these organizations may not be complete. The study population consisted of 5,843 women age 65 years or older who were diagnosed with breast cancer during the period from 1992 to 1999 from the 11 SEER areas, and who received chemotherapy according to the Medicare professional and outpatient claims.^{31,32}

Study Variables

Conceptual framework—Hematopoietic growth factors are supportive care in patients with cancer preparing to receive chemotherapy. The use of supportive care is affected by the social and demographic characteristics of the patients, their tumor characteristics and comorbid conditions, the dosage and frequency of chemotherapy, and the characteristics of the physician and hospital.³⁻²⁵ Figure 1 illustrates the use of hematopoietic growth factors in association with these characteristics. This research measures the patterns of use and explores their association with some of these characteristics.

Chemotherapy—The details of the methods of identification of chemotherapy use through Medicare claims have been described previously.³¹⁻³⁶ In brief, patients with breast cancer were defined as having received chemotherapy if any of the following Medicare procedure codes was present in the physician or outpatient Medicare claims data³⁷⁻⁴⁰: the International Classification of Diseases (9th revision, clinical modification) procedure code 9925 and V codes of V58.1, V66.2, or V67.2³⁷; the common procedure codes of 96400 to 96549, J8530 to J8999, J9000 to J9999, or Q0083 to Q0085^{38,39}; and revenue center codes of 0331, 0332, or 0335.⁴⁰ The dosage and intensity of chemotherapy were not reliably identified through Medicare claims data.

Hematopoietic growth factors—The following common procedure codes were used to identify specific hematopoietic growth factors³⁹: filgrastim (J1440 or J1441), epoetin (Q0136), sargramostim (J2820), and interleukins ([ILs] J9015 for IL-2 or aldesleukin, and J2355 for IL-11 or oprelvekin). Among 5,843 patients with breast cancer receiving chemotherapy, no patient used ILs, and only 94 patients (1.6%) received sargramostim as a granulocyte-macrophage CSF. Therefore, in this study we only reported the results for filgrastim as a granulocyte CSF, and epoetin as a biosynthetic form of erythropoietin.³

Comorbidity index—Comorbidity was ascertained from Medicare claims through diagnoses or procedures made 1 year before and 1 month after the date of diagnosis of breast cancer. The Medicare inpatient, outpatient, and physician claims were used to create a comorbidity score; the detailed method has been reported elsewhere.^{35,41} The rationale for including diagnoses from the outpatient and physician claims is that many more people visit the outpatient department and see a physician than are hospitalized, thus increasing the possibility of identifying more complete comorbid conditions.⁴² For physician and outpatient claims, a patient's comorbid diagnoses must appear on at least two different claims that are more than 30 days apart. Conditions that do not appear on two different claims are considered to be rule-out diagnoses, and are not counted as comorbid conditions. This comorbidity index reflects the Deyo adaptation of the Charlson comorbidity index,^{43,44} with several procedure codes that reflect the Romano adaptation.⁴⁵ Because cancer is the primary disease of interest under study, it is not included in the comorbid conditions described above. Women diagnosed with breast cancer at age 65 may have a short duration for identifying comorbid conditions in Medicare claims. However, these women had similar comorbidity scores to those age 66 to 69 years, and therefore were included in the analysis.

Other characteristics—Patient and tumor characteristics such as age, race/ethnicity, marital status, tumor stage, tumor size, tumor grade, node positivity status, number of positive nodes, hormone receptor status, surgery, radiotherapy, year of diagnosis, and geographic areas (11 SEER areas) were available from the SEER data. Information on household income at the level of the zip code in the SEER-Medicare database was obtained from the National Census Bureau.

Analyses

The prevalence rate of growth factor use was the percentage of patients with breast cancer who received chemotherapy and also received growth factors (either filgrastim or epoetin; Table 1). The χ^2 statistic was used to test the statistical significance of difference in the prevalence of growth factors use across different strata of patient and tumor characteristics. Multivariable logistic regression analyses were used to assess the odds ratio of receiving growth factors in association with the year of diagnosis and geographic areas while simultaneously controlling for other factors. These analyses were adjusted for race, tumor stage, tumor size, tumor grade, node positivity, number of positive nodes, and comorbidity scores. The significant predictors for receiving growth factors were selected from the stepwise logistic regression models. All computer programming and analyses were completed using the SAS system (version 9.1; SAS Institute, Cary, NC).⁴⁶

Results

Table 1 presents the percentage of women with chemotherapy for breast cancer who received hematopoietic growth factors (filgrastim and epoetin), by patient characteristics. Overall, 17.3% received filgrastim and 6.8% received epoetin. The use of these growth factors was more than 17% in patients age 65 to 79, and 10% in patients age 80 or older. The receipt of filgrastim was lower in black women than in those of another race or ethnicity. The rate did not differ much by marital status, comorbidity, and household incomes (at zip code level). However, the use of these factors increased significantly by the year of diagnosis (test for trend $P < .001$). For example, none of those patients diagnosed in 1992 received filgrastim and only 4% of patients diagnosed in 1993 received it, whereas 27% of patients diagnosed in 1999 received this therapy. The percentage of patients receiving epoetin was much lower, but the trend by the year of diagnosis was significant. The receipt of both filgrastim and epoetin differed significantly across the 11 different geographic areas. For instance, 10.6% of patients in Seattle received filgrastim compared with 22.9% in Atlanta, whereas 2.7% received epoetin in New Mexico compared with 12.8% in San Jose-Monterey area in California.

Table 2 lists the receipt of filgrastim and epoetin by tumor characteristics. The use of filgrastim varied significantly by tumor stage, size, number of positive nodes, and grade, and radiation therapy. For example, 11% in patients with stage I received filgrastim compared with 24% in patients with stage III and 17% in those with stage IV. Patients receiving radiation therapy also had a higher prevalence of using filgrastim. However, the use of filgrastim did not vary by hormone receptor status and the type of surgery.

Table 3 lists the multivariable logistic regression analysis on the odds ratio of receiving hematopoietic growth factors while controlling for other patient and tumor characteristics. Compared with patients diagnosed in 1992 to 1994, those diagnosed in 1995 to 1997 were more than three times more likely to receive filgrastim, and 26 times more likely to receive epoetin, whereas patients diagnosed in more recent years (1998 to 1999) were more than five times and 65 times more likely to receive filgrastim and epoetin, respectively. There also was substantial geographic variation in the use of hematopoietic growth factors. For example, compared with patients diagnosed in Seattle, those diagnosed in three metropolitan areas in

California were more than twice as likely to receive filgrastim, whereas patients diagnosed in Connecticut, Iowa, or New Mexico were significantly less likely to receive epoetin.

Table 4 lists the significant predictors of using filgrastim and epoetin, which were generated from the stepwise logistic regression analysis. Age, race, tumor size, number of lymph nodes, comorbidity score, geographic area of residence, and year of diagnosis were significant predictors for using filgrastim. For example, women who were younger, of white race, with more advanced tumor stage, smaller tumor size, higher number of positive lymph nodes, living in certain geographic areas, and diagnosed in later years were more likely to receive filgrastim, whereas women older than 80 years, black women, women with stage I disease, women with larger tumors, women with few positive nodes, women with greater comorbidity, and women diagnosed between 1992 and 1994 were less likely to receive filgrastim. Women with more advanced tumor stage, with higher number of positive lymph nodes, living in Atlanta and San Jose-Monterey, and diagnosed in later years were more likely to receive epoetin, whereas women living in Iowa, New Mexico, and Utah were less likely to receive epoetin.

Discussion

This study described how hematopoietic growth factors, specifically filgrastim and epoetin, were used in patients with breast cancer who received chemotherapy. Overall, 17% of patients receiving chemotherapy also received filgrastim and 6% received epoetin. The receipt of these growth factors increased significantly over time from 1992 to 1999. There was also substantial geographic variation in the use of both filgrastim and epoetin. Significant predictors for the use of filgrastim were older age, black race, advanced tumor stage, larger tumor size, higher number of positive lymph nodes, higher comorbidity score, geographic areas, and later years of diagnoses. For the use of epoetin, advanced tumor stage, high number of positive lymph nodes, geographic areas, and later years of diagnoses were significant predictors.

Filgrastim, one of the most commonly used CSFs, has been studied extensively in clinical trials for preventing, delaying, or reducing the severity of neutropenia among patients receiving cancer chemotherapy.⁴⁻²² After receiving these growth factors, patients can better tolerate the standard chemotherapy regimens and may be able to tolerate the higher doses of chemotherapeutic agents, thereby improving therapeutic outcomes and control of the disease.^{3,9-11,17-19} These trials led to the first clinical guideline issued by the American Society of Clinical Oncology in 1994 for the use of filgrastim for these purposes.²² The 1997 survey was conducted on what physicians thought about the use of filgrastim after the 1994 guidelines were released.²⁴ In 1994 and 1997, a significant majority (85%) of medical oncologists preferred to use filgrastim, only 2% to 4% preferred to use sargramostim as another colony growth factor, and the remaining 10% to 14% indicated that these two types of CSFs were interchangeable. Only 12% to 14% of medical oncologists indicated that they used filgrastim for primary prophylaxis. However, the survey showed that 30% of physicians would use colony-stimulating growth factors for treating a febrile neutropenia, a practice considered to be overuse because it was not consistent with what was recommended. This percentage remained unchanged in 1997 after the guidelines were published. However, it is unknown whether physician responses differ from what they actually did in the practice. There was a lack of information from the population-based studies on how the patients living in the community with cancer chemotherapy received these growth factors. The only study conducted in the community setting among 1,385 women with breast cancer in 1996 to 1998 showed that 18% received colony stimulating factor,²⁵ which was consistent with what was reported in a large cohort of patients in our study (17.3%).

Our study demonstrated substantial temporal and geographic variations in the use of hematopoietic growth factors. Given that more evidence has been cumulated over time to

support the use of colony-stimulating factors and the clinical guidelines have evolved from 1994 to the present,^{22,47} the increasing use of these growth factors over time is expected. Because there was no clinical guideline on the use of epoetin until 2001, substantial geographic variation in its use from 1992 to 1999 was also expected. However, we also observed a large geographic variation in the use of filgrastim. Although unexpected, the geographic variation in treatments for breast cancer has been known for decades.^{48,49} This indicates a need for additional research on reasons for this variation and whether it is associated with clinical outcomes.

Our study also identified some important predictors of patients receiving these factors. African American women were less likely to receive growth factors than white women, which was consistent with the reports on racial disparity in health care from the Institute of Medicine⁵⁰ and the American College of Physicians.⁵¹ Age is a known risk factor for less adequate treatment.⁵² In our study, only those women age 80 years or older had a significantly lower use of filgrastim and other age groups had a similar rate, whereas the receipt of epoetin did not vary significantly across different age groups. The reason patients age 80 or older were less likely to receive filgrastim but not epoetin compared with younger women was not clear, but could be related to physician characteristics. Those patients with a comorbidity score of three or higher had a significantly lower percentage of filgrastim use. This was unexpected because higher comorbidity scores were associated with increased neutropenia and other chemotherapy-related toxicities.^{33,35} These patients were expected to be more likely to receive filgrastim to prevent neutropenia. Finally, patients receiving radiation therapy had a higher rate of receiving both filgrastim and epoetin, but radiation was not a significant predictor of these growth factors after controlling for other factors.

This study has a number of strengths. First, this was a large population-based study conducted in patients with breast cancer living in the community in 11 SEER areas, accounting for 14% of the United States population. Furthermore, the nationwide Medicare claims data offered a unique opportunity to study the use of hematopoietic growth factors for patients receiving chemotherapy because chemotherapy and hematopoietic growth factors are among the few drugs that are covered by Medicare program, and thus can be identified by the Medicare claims. In addition, the Medicare claims data cover all services provided regardless of where the patients seek their care throughout the United States, thus ensuring more completeness of the information on growth factors.

This study, however, has several limitations. First, the study findings may only be applied to women diagnosed with breast cancer at age 65 or older who were not health maintenance organization members and had both Medicare Parts A and B coverage. The use of hematopoietic growth factors might be different for women younger than 65 years with breast cancer. Second, although the construct validity (internal consistency) of Medicare claims for growth factors was good, Medicare claims for growth factors have not been validated externally. In addition, this study did not specify whether the growth factors were used for primary prevention of neutropenia or anemia that may be associated with the receipt of chemotherapy, or for treatment of patients with existing conditions of neutropenia or anemia. Furthermore, we did not have data on the dosage and intensity of chemotherapy that could have affected the use of hematopoietic growth factors. Although specific chemotherapy drugs can be identified in Medicare claims data, patients with breast cancer often receive combination chemotherapy regimens, making it difficult to address drug-specific association with the use of hematopoietic growth factors. We also did not have information on physician or hospital characteristics that may be associated with the use of growth factors in preventing and treating chemotherapy-related neutropenia and anemia.

In conclusion, there were substantial temporal and geographic variations in the use of hematopoietic growth factors in patients receiving breast cancer chemotherapy, and the significant predictors included patient age, black race, advanced tumor stage, higher comorbidity score, and later years of diagnoses. The findings suggest the need for additional research on why geographic variation exists and whether the variation has any impact on the reduction of neutropenia infection. More studies would be needed to address the effectiveness of hematopoietic growth factors in preventing and/or treating neutropenia and anemia, and medical costs and cost effectiveness of these agents. Such research would also need to address if the use of hematopoietic growth factors might affect all-cause or breast cancer specific survival. It would be ideal to have randomized clinical trials or prospective cohort studies to document the efficacy and effectiveness of hematopoietic growth factor. However, the nationwide, population-based Medicare claims provide great potential for examining these issues related to hematopoietic growth factors in patients living in the community who were diagnosed with breast as well as other cancers.

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Fig 1.
Conceptual framework for the association between the use of hematopoietic growth factors and related characteristics.

Table 1

Use of Hematopoietic Growth Factors for Patients With Breast Cancer in Association With Patient Characteristics, Year of Diagnosis, and Geographic Areas

Patient and Tumor Characteristic	No. of Patients With Breast Cancer Who Received Chemotherapy	Percentage of Patients Receiving Filgrastim	Percentage of Patients Receiving Epoetin
Age, years			
65-69	2,780	17.5	6.9
70-74	1,623	18.9	7.2
75-79	944	17.9	6.6
≥ 80	496	9.7	5.2
Race			
White	5,169	17.6	6.7
Black	470	13.0	7.2
Other	204	20.1	7.8
Marital status			
Married	2,776	18.3	7.0
Unmarried	2,918	16.5	6.6
Unknown	149	14.8	7.4
Comorbidity scores			
0	3,838	17.9	6.7
1	1,287	17.2	7.0
2	463	16.2	6.5
≥ 3	255	10.6	8.2
Household income			
1st quartile (< \$38,237)	1,405	14.7	6.2
2nd quartile (\$38,237-\$47,459)	1,397	17.1	5.4
3rd quartile (\$47,460-\$60,582)	1,403	18.9	8.1
4th quartile (> \$60,582)	1,400	18.1	7.8
Unknown/missing	238	18.9	5.0
SEER registry areas			
San Francisco, CA	389	21.1	6.9
Connecticut	901	13.5	5.7
Detroit, MI	1,020	19.6	7.1
Hawaii	87	11.5	4.6
Iowa	645	13.8	3.1
New Mexico	219	13.2	2.7
Seattle, WA	498	10.6	8.6
Utah	322	16.2	4.0
Atlanta, GA	455	22.9	11.9
San Jose-Monterey, CA	337	20.5	12.8
Los Angeles, CA	970	20.6	6.6
Year of diagnosis			
1992	629	0	0
1993	560	3.9	0
1994	599	16.5	0.8
1995	658	17.3	5.2
1996	654	20.3	6.7
1997	849	19.4	7.5
1998	909	23.0	9.1
1999	985	27.2	17.0
Total	5,843	17.3	6.8

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.

Table 2

Percentage of Patients Receiving Hematopoietic Growth Factors by Tumor Characteristics, Surgery, and Radiation Therapy

Patient and Tumor Characteristic	No. of Patients With Breast Cancer Who Received Chemotherapy	Percentage of Women Receiving Filgrastim	Percentage of Women Receiving Epoetin
Tumor stage			
I	974	11.2	3.3
II	3,069	17.8	6.4
III	899	24.0	9.9
IV	619	17.1	10.0
Unknown/missing	282	12.1	6.0
Tumor size, cm			
< 1.0	338	14.2	3.3
1.0 to < 2.0	1,442	16.4	6.2
2.0 to < 3.0	1,318	18.4	5.9
3.0 to < 4.0	731	13.3	7.1
4.0 +	1,380	20.9	8.8
Unknown	634	15.5	7.3
No. of positive nodes			
0 (node negative)	1,552	12.8	4.5
1	763	19.0	7.9
2-3	790	18.6	6.2
4-5	422	19.0	7.8
6-9	480	21.7	9.6
10-51	694	25.7	9.2
Unknown	1,142	13.8	6.7
Tumor grade			
Well differentiated	385	20.0	6.8
Moderately differentiated	1,633	17.8	7.5
Poorly differentiated	2,580	18.5	7.3
Unknown	1,073	12.4	4.5
Hormone receptor status			
Positive	3,082	17.3	6.5
Negative	1,566	16.9	6.4
Unknown	1,195	17.9	8.1
Surgery			
No cancer-directed surgery	543	14.7	9.2
Breast-conserving surgery	1,782	17.4	6.6
Mastectomy	3,518	17.6	6.5
Radiation therapy			
No	3,632	15.2	5.7
Yes	2,211	20.7	8.6
Total	5,843	17.3	6.8

Table 3

Odds Ratio of Receiving Hematopoietic Growth Factors for Patients With Breast Cancer by the Year of Diagnosis and Geographic Areas
Patients Receiving Growth Factor

Patient and Tumor Characteristic	No. of Patients Receiving Chemotherapy (n = 5,843)	Filgrastim		Epoetin	
		OR	95% CI	OR	95% CI
Year of diagnosis					
1992-1994	1,788	1.00 (reference)			
1995-1997	2,161	3.37	2.71 to 4.20	1.00 (reference)	10.68 to 64.28
1998-1999	1,894	5.26	4.20 to 6.57	65.44	26.79 to 159.83
SEER registry areas					
Seattle, WA	498	1.00 (reference)		1.00 (reference)	
San Francisco, CA	389	2.87	1.92 to 4.30	0.89	0.51 to 1.54
Connecticut	901	1.37	0.95 to 1.97	0.62	0.40 to 0.98
Detroit, MI	1,020	2.21	1.56 to 3.11	0.70	0.45 to 1.07
Hawaii	87	0.94	0.43 to 2.06	0.46	0.15 to 1.47
Iowa	645	1.23	0.84 to 1.79	0.27	0.15 to 0.48
New Mexico	219	1.15	0.69 to 1.91	0.21	0.08 to 0.52
Utah	322	1.29	0.84 to 1.98	0.32	0.16 to 0.62
Atlanta, GA	455	2.74	1.87 to 4.03	1.38	0.86 to 2.20
San Jose-Monterey, CA	337	2.41	1.59 to 3.66	1.64	0.99 to 2.71
Los Angeles, CA	970	2.32	1.65 to 3.28	0.66	0.43 to 1.02

Abbreviations: OR, odds ratio; SEER, Surveillance, Epidemiology, and End Results.

* OR was generated from logistic regression analyses, adjusted for patient and tumor characteristics as listed in Tables 1 and 2

Table 4

Significant Predictors of Hematopoietic Growth Factors in Patients With Breast Cancer Who Received Chemotherapy
Patients Receiving Growth Factor

Significant Predictor	Filgrastim		Epoetin	
	OR	95% CI	OR	95% CI
Age, years				
≥ 80 (v 65-69)	0.47	0.34 to 0.64	—	
Race/ethnicity (v white)				
Black	0.55	0.41 to 0.73	—	
Tumor stage (v stage I)				
II	1.74	1.41 to 2.15	2.15	1.46 to 3.17
III	2.45	1.90 to 3.15	3.47	2.24 to 5.39
IV	1.88	1.41 to 2.49	4.26	2.71 to 6.70
Unstaged	—		2.27	1.22 to 4.23
Tumor size, cm (v < 1.0)				
3.0 to < 4.0	0.64	0.50 to 0.81	—	
No. of positive nodes (v negative nodes)				
5-9	1.32	1.03 to 1.69	1.55	1.09 to 2.21
10-43	1.81	1.48 to 2.23	1.55	1.13 to 2.11
Comorbidity scores (v 0)				
≥ 3	0.44	0.25 to 0.77	—	
SEER registry areas (v Seattle)				
San Francisco, CA	2.23	1.68 to 2.95	—	
Detroit, MI	1.78	1.46 to 2.18	—	
Iowa	—		0.37	0.23 to 0.59
New Mexico	—		0.31	0.13 to 0.71
Utah	—		0.43	0.24 to 0.77
Atlanta, GA	2.21	1.70 to 2.87	1.81	1.30 to 2.51
San Jose-Monterey, CA	1.89	1.40 to 2.56	2.09	1.45 to 3.01
Los Angeles, CA	1.86	1.52 to 2.27	—	
Year of diagnosis (v 1992-1994)				
1995-1997	3.44	2.77 to 4.27	26.65	10.89 to 65.23
1998-1999	5.26	4.24 to 6.54	66.22	27.20 to 161.23

Abbreviations: OR, odds ratio; SEER, Surveillance, Epidemiology, and End Results.