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Hospitalizations in Older Adults With Advanced Cancer: The Role of Chemotherapy

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CONTEXT AND QUESTION ASKED: In patients with metastatic cancer, chemotherapy may provide symptom control, prevent complications, prolong life, or improve quality of life. Except in rare cases, however, patients with metastatic disease will not be cured. In older patients with metastatic cancer, hospitalization for treatment toxicity may reduce the quality of an already limited life expectancy. We evaluated the association between chemotherapy for metastatic cancer and risk of hospitalization.

MAIN CONCLUSION: Hospitalizations are common in patients with incurable advanced malignancies and are more likely among those who receive chemotherapy.

APPROACH: In the linked SEER-Medicare dataset, we identified Medicare beneficiaries aged 66 years or older with a primary diagnosis of metastatic breast, colorectal, ovarian, bladder, lung, pancreas, esophageal, stomach, or prostate cancer between 2001 and 2009 who died by the end of 2010. Chemotherapy recipients and nonrecipients were pair-matched by age, sex, race, comorbidity, geographic region and survival duration. The primary endpoint was hospital admission, identified in inpatient claims between cancer diagnosis and the first of hospice admission or death. We also identified the subset of admissions associated with a primary or secondary diagnosis code suggestive of an adverse effect of chemotherapy. The association between chemotherapy and hospitalization was estimated in separate multivariable Cox proportional-hazards regression models for each cancer site, accounting for the matched-pairs design and controlling for unmatched demographic and disease characteristics.

RESULTS: Of 18,486 patients who received chemotherapy for metastatic cancer, 92% were hospitalized at least once for any reason, including 51% hospitalized for a likely toxicity. The corresponding rates among matched non-recipients were 83% and 34% (Figure). In nearly all cancers, chemotherapy recipients had a greater risk of hospitalization for a likely toxicity or for any cause. Chemotherapy recipients had substantially higher hospitalization for infection or fever (21% *v* 15%), hematologic complications (11% *v* 3%), dehydration (13% *v* 6%), and PE or DVT (9% *v* 4%) compared with nonrecepients. Chemotherapy was associated with a significantly increased risk of likely toxicity-related hospitalization in nearly all cancers, controlling for socio-demographic characteristics and other treatment. The association was greatest in patients with metastatic esophageal cancer (adjusted hazard ratio, 2.00; 95% CI, 1.11 to 3.60) and smallest in patients with metastatic prostate cancer (adjusted hazard ratio, 1.22; 95% CI, 1.01 to 1.47).

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INTERPRETATION: Older patients receiving chemotherapy for incurable advanced cancers are at high risk of hospitalization, of which a non-negligible proportion is likely attributable to adverse effects of treatment. Infection, fever, dehydration, and hematologic complications constitute a large proportion of these events, some of which may be preventable through evidence-based patient management, prophylactic interventions, and effective outpatient care. Our findings might be limited to older patients with advanced cancer who have a generally poor prognosis or limited expected survival.

SIGNIFICANCE OF FINDINGS: Understanding the common reasons for hospital admissions and developing toxicity management programs and educational resources may help patients and their families make informed treatment decisions, minimize adverse effects and reduce hospitalizations in this population with limited life expectancy. JOP

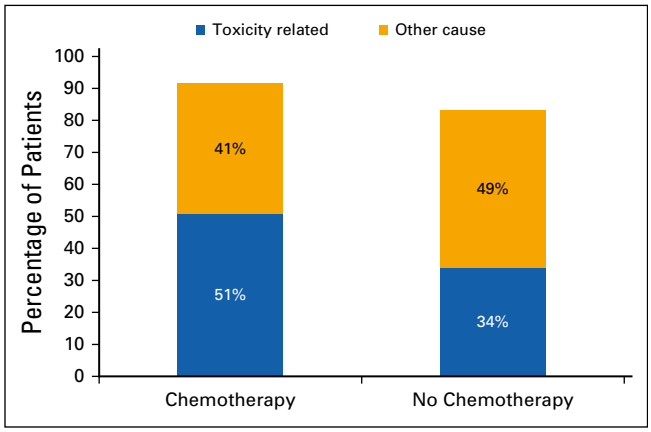

FIG 1. Hospitalization by cause and receipt of chemotherapy.

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Abstract

Purpose

In older patients with metastatic cancer, hospitalization for treatment toxicity may reduce the quality of an already limited life expectancy. We evaluated the association between chemotherapy for metastatic cancer and risk of hospitalization.

Methods

In the population-based SEER-Medicare dataset, we identified patients 66 years or older diagnosed with metastatic cancer of the bladder, breast, prostate, colon or rectum, esophagus, pancreas, stomach, ovaries, or lung in 2001 to 2009 who died by December 31, 2010. Chemotherapy recipients were matched to nonrecipients by age, sex, race, geographic region, comorbidity, and survival duration. We identified hospitalizations for any cause and for likely chemotherapy-related toxicity, comparing chemotherapy recipients with their matched peers.

Results

Of 18,486 patients who received chemotherapy for metastatic cancer, 92% were hospitalized at least once for any reason, including 51% hospitalized for a likely toxicity. The corresponding rates among matched nonrecipients were 83% and 34%. Chemotherapy was associated with a significantly increased risk of likely toxicity-related hospitalization in nearly all cancers, controlling for sociodemographic characteristics and other treatment. The association was greatest in patients with metastatic esophageal cancer (adjusted hazard ratio, 2.00; 95% CI, 1.11 to 3.60) and smallest in patients with metastatic prostate cancer (adjusted hazard ratio, 1.22; 95% CI, 1.01 to 1.47).

Conclusion

Hospitalizations are common in patients with incurable advanced malignancies and more likely among those who receive chemotherapy. Understanding common reasons for these events may help reduce adverse effects of chemotherapy for metastatic cancer and help patients and their families make informed treatment decisions.

ASSOCIATED CONTENT

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INTRODUCTION

In the United States, half of all men and one third of women will develop cancer, and many are diagnosed with or eventually develop metastatic disease.[1,2] More than half a million Americans die of cancer each year,[3] most after the development of metastasis.

Chemotherapy is the primary treatment for most patients with metastatic cancer, but prognosis varies depending on cancer site, the effectiveness of therapy, comorbidity, and functional status.[4,5] Except in rare cases, however, patients with metastatic disease will not be cured. Chemotherapy

may provide symptom control, prevent complications, prolong life, or improve quality of life.

Despite scientific advances, improvements in the treatment of metastatic cancer are typically evaluated in weeks or months rather than years, and drug efficacy, measured by tumor response or disease progression, does not always correspond with improvement in survival or quality of life.[4] In many settings, especially late lines of therapy for most cancers, there may be little or no evidence of benefit from chemotherapy. Yet nearly all drugs and regimens bear some level of toxicity and detriment to quality of life.[4,6] Furthermore, although palliative chemotherapy is a reasonable treatment choice for many patients, most have inaccurate expectations of its curative potential, possibly compromising their ability to make informed treatment decisions consistent with their preferences.[7]

Recent studies have reported substantial and increasing chemotherapy use near the end of life, but less attention has been paid to the burden of treatment in terms of its adverse effects.[8-12] Studies that have taken a retrospective approach, evaluating treatment received by decedents, may yield a biased portrait of terminal care and its outcomes.[13] Our objective was to estimate the impact of systemic chemotherapy on the risk of hospitalization in patients with metastatic cancer.

METHODS

Data

We used SEER cancer registry data linked with Medicare claims.[14] SEER is a National Cancer Institute–sponsored consortium of population-based cancer registries that now cover almost 30% of Americans. For all incident cancers, the SEER registries collect information regarding site and extent of disease, sociodemographic characteristics, and first course of cancer-directed therapy, with active follow-up for date and cause of death. Medicare is the primary health insurer for 97% of the population of the United States age 65 years and older, covering inpatient hospital care, outpatient care, physician services, and, since 2006, outpatient prescription medications. This study was deemed exempt research by the Institutional Review Board at Memorial Sloan Kettering Cancer Center, and the SEER-Medicare files were used in accordance with a data use agreement from the National Cancer Institute.

Study Cohort

We identified Medicare beneficiaries age 66 years or older with a primary diagnosis of metastatic breast, colorectal, ovarian, bladder, lung, pancreas, esophageal, stomach, or prostate cancer between January 1, 2001 and December 31, 2009 who died by December 31, 2010. Identification of metastatic disease was based on disease information collected in SEER (Appendix Table A1, online only). We excluded patients enrolled in a Medicare managed care plan and those who did not have continuous Medicare coverage from 1 year before diagnosis through death, patients diagnosed only at death, and those with a history of another malignancy.

The study population was divided into two cohorts: those who received systemic chemotherapy and those who did not. Receipt of chemotherapy was identified in Medicare claims from the date of cancer diagnosis through death or the end of follow-up and included both intravenous and oral chemotherapy drugs covered under Medicare Part B (Appendix Table A2).

Chemotherapy recipients and nonrecipients were pair-matched by age at diagnosis (± 5 years), sex, race (white, black, or other), comorbidity index score, geographic region (West, Midwest, South, or Northeast), and duration of survival. Comorbidity was estimated using the Klabunde modification of the Charlson comorbidity index on the basis of inpatient, outpatient, and physician claims in the year before cancer diagnosis, and scores were categorized by standard practice as 0, 1, or 2+.[15] Patients with better-prognosis advanced cancers—breast, bladder, colorectal, ovarian, and small-cell lung cancer (SCLC)—were matched within ± 3 months survival duration. Patients with poorer-prognosis advanced cancers—pancreatic, esophageal, stomach, non–small-cell lung cancer (NSCLC), and prostate cancer—were matched within ± 1 month survival duration.[5]

Outcomes

The primary end point was hospital admission, identified in inpatient claims between cancer diagnosis and the first of hospice admission or death. We also identified the subset of admissions associated with a primary or secondary diagnosis code suggestive of an adverse effect of chemotherapy. These included hematologic complications, gastrointestinal complications, dehydration, deep venous thrombosis or pulmonary embolus, infection or fever, malnutrition or failure to thrive, cardiac complications, and constitutional symptoms (delirium, drug psychoses, and malaise or fatigue).[16-18]

Covariates

In addition to the characteristics used in matching, we examined marital status, urban or rural residence, and year of

diagnosis. Median income in the census tract of residence was used as a marker of socioeconomic status.

Analysis

Unadjusted associations between receipt of chemotherapy and unmatched characteristics were assessed using χ^2 statistics. Differences between matched cohorts in the frequency of hospital admission were evaluated for all hospitalizations and for the subset of likely toxicity-related events. We estimated unadjusted relative risks by cancer site and compared hospitalization rates using McNemar's test for matched pairs.

The association between chemotherapy and hospitalization was estimated in separate multivariable Cox proportional hazards regression models for each cancer site. The time origin was month of diagnosis, and chemotherapy was treated as a time-dependent exposure from the time of first claim for chemotherapy. Analyses accounted for the matched-pairs design and included unmatched demographic and disease characteristics as covariates. Observations were censored at the time of hospice admission or death. All analyses were performed in SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Cohort Characteristics

We identified 36,676 patients who received chemotherapy for a metastatic cancer diagnosis, of whom 50% were matched to a patient with the same diagnosis who did not receive chemotherapy. The rate of successful matching varied from 31% of patients with esophageal cancer to 60% of patients with NSCLC. Distributions of sex, marital status, and comorbidity and region were similar between chemotherapy recipients who were successfully matched and those who were not. More of the matched chemotherapy recipients were from the South (26% *v* 17%), more were white (87% *v* 83%), and the matched patients were slightly older than the unmatched patients (mean age, 76 *v* 74 years). Median overall survival was substantially shorter in chemotherapy recipients who were successfully matched compared with those who were unmatched. The difference in median survival between matched and unmatched chemotherapy recipients varied from 6 months in patients with pancreatic cancer (3 months *v* 9 months) to 20 months in patients with breast cancer (9 months *v* 30 months).

Lung cancer accounted for the greatest proportion of cases included in the analysis (41%, NSCLC and SCLC combined), followed by colorectal cancer (20%) and pancreatic cancer (15%; Table 1). Just over half of the patients were men, 87% were white, and 58% had a Charlson comorbidity score of zero. Thirty-five percent of chemotherapy recipients also received radiation therapy, compared with 24% of those who did not receive chemotherapy. The chemotherapy cohort included a greater proportion of patients who were married, resided in urban areas, and lived in higher-income census tracts. Although chemotherapy recipients and nonrecipients were matched on survival duration (± 3 months or ± 1 month), in the better-prognosis cancers, survival was approximately 1 month greater on average in patients who received chemotherapy compared with those who did not. In the poorer-prognosis cancers, the difference in mean survival was less than 0.5 months. Fifty-six percent of chemotherapy recipients and 62% of nonrecipients entered hospice at any time before death.

Hospitalizations

Ninety-two percent of chemotherapy recipients had at least one hospital admission for any cause, compared with 83% of matched nonrecipients (Fig 1). Just over half of the chemotherapy cohort had a likely toxicity-related hospitalization, compared with 34% of their matched peers. The mean number of hospitalizations was also greater among those who received chemotherapy than those who did not (2.62 *v* 1.96). Of the substantial proportion of patients in both groups who ever entered hospice, less than 2% had a first hospitalization after hospice admission—events that were excluded from the primary end point.

The proportion of patients with toxicity-related hospitalization and the unadjusted relative risk associated with chemotherapy varied by cancer site (Table 2). The largest difference in risk of likely toxicity-related hospitalization, comparing patients who did and did not receive chemotherapy, was seen in SCLC (56% *v* 30%; relative risk, 1.87) and the smallest difference was in prostate cancer (56% *v* 48%; relative risk, 1.17). The unadjusted probability of a toxicity-related hospitalization was significantly greater in the group that received chemotherapy ($P < .05$).

Among specific causes of toxicity-related hospitalizations, some diagnoses were more common among chemotherapy recipients than their matched peers (Appendix Fig A1). Compared with those who do not receive chemotherapy, chemotherapy recipients had substantially higher rates of hospitalization for infection or fever (21% *v* 15%), hematologic complications (11% *v* 3%), dehydration (13% *v* 6%), and

Table 1. Characteristics of Cohort by Receipt of Chemotherapy

Characteristic	Chemotherapy No.	Chemotherapy Col %	No Chemotherapy No.	No Chemotherapy Col %	*P*
All cancers	18,486	—	18,486	—	
Site					
Bladder	206	1	206	1	
Breast	1,127	6	1,127	6	
Colorectal	3,625	20	3,625	20	
Esophageal	278	2	278	2	
Non–small-cell lung	4,705	25	4,705	25	
Ovary	630	3	630	3	
Pancreas	2,813	15	2,813	15	
Prostate	1,321	7	1,321	7	
Small-cell lung	2,996	16	2,996	16	
Stomach	785	4	785	4	
Age at diagnosis, years					
66-69	3,590	19	3,071	17	< .001
70-74	4,934	27	4,418	24	
75-79	5,076	27	4,777	26	
80-84	3,384	18	4,029	22	
≥ 85	1,502	8	2,191	12	
Sex					
Male	9,641	52	9,641	52	
Female	8,845	48	8,845	48	
Race					
White	16,105	87	16,105	87	
Black	1,427	8	1,427	8	
Other	954	5	954	5	
Census tract median income, quartile					
1st	4,094	22	4,899	27	< .001
2nd	4,558	25	4,799	26	
3rd	4,742	26	4,537	25	
4th	5,059	27	4,198	23	
Unknown	33	< 1	53	< 1	
Urban-rural residence					
Metropolitan	15,464	84	15,057	81	< .001
Nonmetropolitan	3,022	16	3,429	19	
Region					
Northeast	4,095	22	4,095	22	
South	4,880	26	4,880	26	
Midwest	2,210	12	2,210	12	
West	7,301	39	7,301	39	
Married					
Yes	10,310	56	8,341	45	< .001
No	7,659	41	9,518	51	
Unknown	517	3	627	3	

(continued on following column)

Table 1. Characteristics of Cohort by Receipt of Chemotherapy (continued)

Characteristic	Chemotherapy No.	Chemotherapy Col %	No Chemotherapy No.	No Chemotherapy Col %	*P*
Charlson comorbidity score					
0	10,745	58	10,745	58	
1	4,537	25	4,537	25	
2+	3,204	17	3,204	17	
Radiation therapy					
Yes	6,562	35	4,369	24	< .001
No	11,924	65	14,117	76	

NOTE. Column percentages show distribution of characteristics within each group (chemotherapy recipients and nonrecipients). Chemotherapy recipients and nonrecipients were pair-matched by age, sex, race, SEER region, comorbidity score, and survival duration.

pulmonary embolus or deep venous thrombosis (9% *v* 4%). The proportions of patients hospitalized for gastrointestinal complications, malnutrition, cardiac complications, or constitutional symptoms were somewhat greater in chemotherapy recipients, although the differences were modest.

In nearly all cancers, chemotherapy recipients had a greater risk of hospitalization—for likely treatment toxicities and for any cause—than those who did not, accounting for the matched-pairs design and controlling for additional demographic characteristics (Table 2). The adjusted impact of chemotherapy was greatest among patients with esophageal cancer, on both the risk of likely toxicity-related hospitalization (adjusted hazard ratio, 2.00; 95% CI, 1.11 to 3.60; $P < .02$) and the risk of hospitalization for any cause (adjusted hazard ratio,

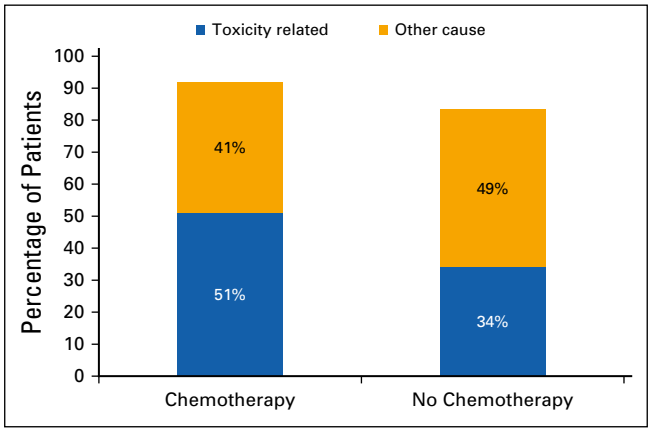

FIG 1. Hospitalization by cause and receipt of chemotherapy.

Table 2. Impact of Chemotherapy on Risk of Hospitalization by Cancer Site

Cancer Site	Chemotherapy (%)	No Chemotherapy (%)	Unadjusted RR	Adjusted HR (95% CI)	*P*
Toxicity-related					
Bladder	57	43	1.33	0.99 (0.56 to 1.76)	NS
Breast	54	45	1.20	1.43 (1.15 to 1.79)	.0016
Colorectal	51	34	1.50	1.49 (1.29 to 1.72)	< .001
Esophageal	44	30	1.47	2.00 (1.11 to 3.60)	.0208
Non–small-cell lung	52	36	1.44	1.54 (1.37 to 1.72)	< .001
Ovary	55	35	1.57	1.38 (0.96 to 1.98)	NS
Pancreas	41	27	1.52	1.59 (1.34 to 1.87)	< .001
Prostate	56	48	1.17	1.22 (1.01 to 1.47)	.0443
Small-cell lung	56	30	1.87	1.87 (1.58 to 2.20)	< .001
Stomach	48	30	1.60	1.78 (1.34 to 2.35)	< .001
Any cause					
Bladder	95	83	1.14	1.35 (0.64 to 2.86)	NS
Breast	91	88	1.03	1.47 (1.13 to 1.90)	.0036
Colorectal	95	89	1.07	1.44 (1.16 to 1.78)	.001
Esophageal	90	74	1.22	2.55 (1.55 to 4.20)	< .001
Non–small-cell lung	90	81	1.11	1.59 (1.40 to 1.81)	< .001
Ovary	97	88	1.10	2.31 (1.64 to 3.26)	< .001
Pancreas	88	81	1.09	1.28 (1.09 to 1.51)	.0029
Prostate	89	80	1.11	1.30 (1.04 to 1.62)	.0230
Small-cell lung	94	81	1.16	2.31 (2.02 to 2.63)	< .001
Stomach	92	84	1.10	1.72 (1.28 to 2.32)	< .001

NOTE. Chemotherapy recipients and nonrecipients were pair-matched by age, sex, race, SEER region, comorbidity score, and survival duration. Unadjusted relative risk compares the proportion of patients with a hospitalization in the chemotherapy group to the proportion in the no chemotherapy group. The unadjusted probability of toxicity-related rate was significantly greater in the group that received chemotherapy ($P < .05$) by McNemar's test for matched pairs. Adjusted hazard ratios from multivariable regression model, where chemotherapy was modeled as a time-dependent exposure. Hazard ratios for the impact of chemotherapy on risk of each outcome were adjusted for additional characteristics, including urban-rural residence, marital status, income quartile, and receipt of radiation therapy.

Abbreviations: HR, hazard ratio; NS, not statistically significant; RR, relative risk.

2.55; 95% CI, 1.55 to 4.20; $P < .001$). In patients with bladder cancer, chemotherapy did not have a significant impact on the risk of toxicity-related or any-cause hospitalization.

DISCUSSION

Cancer remains the second leading cause of mortality in the United States.[3] Despite advances in tumor profiling and drug development, improvements in health outcomes have been limited, and many new drugs are associated with both adverse effects and high costs.[19-21] Thus, for patients with metastatic cancer, the expected benefits of chemotherapy must be weighed against the possibility of treatment-related toxicities.[6,22] In our analysis of a population-based cohort of older adults with advanced cancer, chemotherapy was associated with increased risk of hospitalization, and a considerable proportion of admissions were attributable to likely chemotherapy-related toxicities.

Although some amount of chemotherapy-related inpatient care may be unavoidable, hospitalizations may be occurring more frequently than they should.[23,24] One study found that approximately one third of hospital admissions in patients receiving chemotherapy were treatment related, and almost half of those patients were receiving treatment with palliative, as opposed to curative, intent.[25] Some hospitalizations may reflect a failure to adequately manage common problems with prophylactic interventions and efficient outpatient care.[4,26-29] In our analysis, infection and fever, dehydration, and hematologic complications were the most common treatment-related diagnoses associated with hospitalization. Neutropenic fever is potentially preventable with evidence-based use of growth factors for patients receiving myelosuppressive chemotherapy regimens.[30] Some patients with infection and neutropenia can be, and prefer to be, managed with close observation and oral antibiotics in the outpatient setting, incurring substantially lower costs and reducing their risk of hospital-acquired infection.[26,27,30-32]

In many advanced cancers the efficacy of chemotherapy, especially in early lines of treatment, has been well established by numerous clinical trials. In these instances, the expected benefits of chemotherapy—in terms of symptom control and extension of progression-free survival—are nontrivial and may clearly exceed the burden of adverse effects. More rarely, chemotherapy in the metastatic setting has been shown to extend overall survival.[33,34] We would not dissuade patients from treatment when evidence supports a likely and meaningful improvement in quality or length of life. However, the less sensitive a cancer is to chemotherapy, the greater the consideration needed when making treatment decisions.[8] Compared with the other tumor types we evaluated, advanced NSCLC and metastatic cancers of the stomach, esophagus, pancreas, and prostate are generally less sensitive to chemotherapy.[5,8] However, we found that chemotherapy almost doubled the risk of likely toxicity-related hospitalization for patients with metastatic cancer of the stomach or esophagus and increased the risk by more than 50% in metastatic pancreatic cancer and NSCLC. Given the limited expected benefit of chemotherapy in these cancers, it is not clear how many patients would choose chemotherapy if they understood the likely toxicities and resulting detriment to the quality of their already reduced life expectancy.

The point at which the risks of chemotherapy exceed the benefits is highly subjective and often unknown. As disease progresses despite palliative chemotherapy, the risk increases that survival improvements and symptom relief may be marginal and that the harmful effects of treatment may dominate.[35] For physicians, expert recommendations provide little clear or evidence-based guidance about when to stop offering or administering chemotherapy. For example, the National Comprehensive Cancer Network guidelines recommend multiple lines of cancer-directed therapy for patients with tumors of limited survival times, despite a paucity of high-quality evidence supporting a meaningful benefit in terms of survival or quality of life.[36] In contrast, 40% of patients with breast cancer will have some disease control from fourth-line chemotherapy for up to 4 months, even if survival is not extended.[37] Regardless of cancer type, changing the focus of decision making from which drug to try next to how best to preserve function and quality of life can be especially challenging for clinicians.[38]

Given the shifting and subjective nature of the tradeoff between benefits and harms of chemotherapy in advanced cancer, individualization of treatment and early palliative care may be the optimal approach.[39,40] The survival benefit found in a recent randomized trial of this strategy among patients with lung cancer was unexpected, but plausible.[39] Early palliative care may enhance the management of adverse effects, allowing patients to receive more regimens of chemotherapy. The integrated model of care may also facilitate cessation of anticancer therapy at the end of life when the harmful adverse effects of aggressive treatment exceed the possible benefits.[40]

There are several limitations to our analysis. We compared cohorts of patients with metastatic cancer who did and did not receive chemotherapy, matched by key demographic and health characteristics and controlling for important unmatched characteristics, to estimate the difference in risk of hospitalization likely attributable to chemotherapy. This approach, consistent with previous studies of treatment complications[41-43] and with the epidemiologic concept of attributable or excess risk,[44] does not require direct attribution of each hospitalization to a specific cause, a task that is challenging even with detailed clinical information.[45] However, there may have been residual confounding by unmeasured factors, such as pretreatment symptom burden, performance status, and functional status, other risk factors for treatment-related adverse effects, patient preferences, or physician recommendations. Omission of these unobserved factors that may be associated with receipt of chemotherapy and with the risk of hospitalization could have biased our estimates.[46] Similarly, our definition of likely toxicity-related hospitalizations does not definitively distinguish hospitalizations directly attributable to chemotherapy toxicity from those attributable to cancer symptoms. Indeed, many patients who did not receive chemotherapy had a hospitalization associated with a likely toxicity-related diagnosis. However, by identifying hospitalizations for diagnoses that reflect common chemotherapy toxicities, we could analyze the subset of hospitalizations most likely to be associated with adverse effects of chemotherapy.

Although Medicare claims can be used to identify receipt of chemotherapy, we could not reliably distinguish agents, regimens, or dosages that were appropriate and potentially beneficial from those that were not. We could not reliably identify distinct, successive lines of therapy, nor could we identify patients who received integrated early palliative care. We identified only treatment-related complications severe enough to warrant a hospital admission, and thus we may have underestimated the incidence of some toxicities.[47] And although the complications we identified are likely associated with changes in physical function, social function, and quality

of life, we were not able to assess these end points directly. Finally, our results may not be generalizable to all older adults with metastatic solid tumors. Although the SEER-Medicare population is fairly representative of the nationwide Medicare population,[14] our analysis was limited to the subset of patients who received chemotherapy and could be matched to nonrecipients. Matched and unmatched chemotherapy recipients were similar with respect to important demographic and health characteristics, including age and comorbidity. However, even though all patients had a diagnosis of metastatic cancer, unmatched chemotherapy recipients had substantially longer survival after diagnosis, suggesting that they were healthier or had more favorable disease characteristics than the matched patients included in the study. Thus, our findings might be limited to older patients with advanced cancer who have a generally poor prognosis or limited expected survival.

Older patients receiving chemotherapy for incurable advanced malignancies are at high risk of hospitalization, of which a nonnegligible proportion is likely attributable to adverse effects of treatment. Infection, fever, dehydration, and hematologic complications constitute a large proportion of these events, some of which may be preventable through evidence-based patient management, prophylactic interventions, and effective outpatient care. Understanding the common reasons for hospital admissions and developing toxicity management programs and educational resources for patients and their families may help minimize adverse effects and reduce hospitalizations in this population with limited life expectancy. Furthermore, the integration of early palliative care into the treatment pathway of patients with advanced cancer may improve health outcomes and preserve quality of life and of death.

Our study provides information about the risks of hospitalization in older adults with advanced cancer and the substantial increase in these risks associated with chemotherapy. This information is applicable to the many patients diagnosed with metastatic cancer annually who face difficult decisions about the risks they are willing to accept for therapies with varying benefits in terms of cancer control, quality of life, and survival. Our findings are especially important now, given the high cost of new chemotherapy drugs, many of which offer only modest benefits. Our results also inform the movement toward patient-centered care at the end of life. JOP

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Authors' Disclosures of Potential Conflicts of Interest

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Hospitalizations in Older Adults With Advanced Cancer: The Role of Chemotherapy

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Appendix

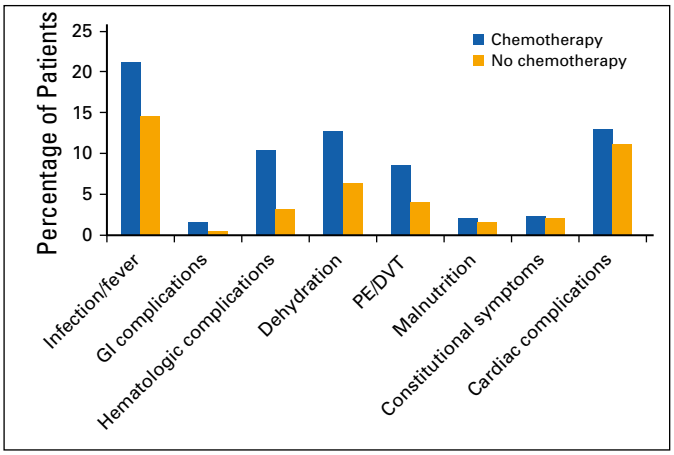

FIG A1. Specific causes of toxicity-related hospitalizations. DVT, deep venous thrombosis; PE, pulmonary embolus.

Table A1. Site and Extent-of-Disease Codes Used to Identify Cancers Metastatic at Diagnosis

Tumor Type	SEER Site Recode (CODKM)	ICD-O-3 Topography Code	EOD-10 Extent Code	Collaborative Staging Metastasis Code
Breast	46	C50.0-C50.6, C50.8-C50.9	85	10, 40, 42, 44, 50
Bladder	58	C67.0-C67.9	85	10, 11, 40, 50
Colorectal	15-23, 25-26	C18.0-C18.9, C19.9, C20.9	85	08, 10, 40, 50 (colon) 10, 11, 12, 40, 50 (rectum)
Ovarian	50	C56.9	85	10, 40, 50
Stomach	12		85	10, 40, 50
Pancreas	33	C25.0-C25.9	85	10, 40, 50
Esophagus	11	C15.0-C15.5, C15.8, C15.9	85	10, 11, 12, 40, 50
Lung	39	C34.0-C34.3, C34.8, C34.9	85	10, 35, 37, 39, 40, 50
Prostate	54	C61.9	85	11, 12, 30, 35, 40, 45, 50, 55

Abbreviations: EOD, extent of disease; ICD-O-3, International Classification of Diseases for Oncology, 3rd edition.

Table A2. Billing Codes Used to Identify Chemotherapy in Medicare Claims

Modality	ICD-9 Procedure Codes	Health Care Common Procedure Coding System Codes*
Systemic chemotherapy†	99.25, V58.1, V66.2, V67.2, E93.07, E93.31	J9000-J9999, J8520-J8999, G0355-G0362, G9021-G9032, C9414-C9419, C9420-9438, S9325-S9379, S9494-S9497, 96400-96599, 36260, 36640, 95990, 95991, A4301, C1166, C1167, C1168, C9110, C9205, C9207, C9213, C9214, C9215, C9216, C9411, E0782, E0783, E0785, E0786, J0640, J2405, K0415, KO416, Q0083, Q0084, Q0085, Q0179, S0177, S0181

Abbreviation: ICD-9, International Classification of Diseases, 9th edition.

*Codes for hormonal therapy (J9003, J9165, J9175, J9202, J9209, J9212, J9213, J9214, J9215, J9216, J9217, J9218, J9219, J9225, J9226, J9240, J9395) were excluded.

†Includes intravenous, intramuscular, and orally administered agents, as indicated by specific codes.