End-of-Life Care for Older Patients With Ovarian Cancer Is Intensive Despite High Rates of Hospice Use

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ABSTRACT

Purpose

To date, few studies have examined end-of-life care for patients with ovarian cancer. One study documented increased hospice use among older patients with ovarian cancer from 2000 to 2005. We sought to determine whether increased hospice use was associated with less-intensive end-of-life medical care.

Patients and Methods

We identified 6,956 individuals age ≥ 66 years living in SEER areas who were enrolled in fee-for-service Medicare, diagnosed with epithelial ovarian cancer between 1997 and 2007, and died as a result of ovarian cancer by December 2007. We examined changes in medical care during patients' last month of life over time.

Results

Between 1997 and 2007, hospice use increased significantly, and terminal hospitalizations decreased (both $P < .001$). However, during this time, we also observed statistically significant increases in intensive care unit admissions, hospitalizations, repeated emergency department visits, and health care transitions (all $P \leq .01$). In addition, the proportion of patients referred to hospice from inpatient settings rose over time ($P = .001$). Inpatients referred to hospice were more likely to enroll in hospice within 3 days of death than outpatients (adjusted odds ratio, 1.36; 95% CI, 1.12 to 1.66).

Conclusion

Older women with ovarian cancer were more likely to receive hospice services near death and less likely to die in a hospital in 2007 compared with earlier years. Despite this, use of hospital-based services increased over time, and patients underwent more transitions among health care settings near death, suggesting that the increasing use of hospice did not offset intensive end-of-life care.

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INTRODUCTION

Patients with advanced cancer are receiving increasingly aggressive medical care at the end of life,¹⁻³ despite growing evidence that high-cost, high-intensity treatments may not be associated with better patient quality of life or medical outcomes.⁴⁻⁶ To date, few studies have examined the end-of-life medical care of patients with ovarian cancer. Evidence from two recent retrospective, single-institution studies suggests that nearly 30% of patients with ovarian cancer receive aggressive care in the last month of life.^{7,8} Aggressive care comprises admissions to intensive care units (ICUs), hospitalizations, repeated emergency department visits, use of chemotherapy close to death, or late hospice referrals (ie, within 3 days of death).

A single population-based study found rising rates of hospice use among older women with ovar-

ian cancer between 2000 and 2005.⁹ Although this study did not examine other forms of end-of-life care, it suggested that the intensity of end-of-life medical care of patients with ovarian cancer may be decreasing, because hospice has been associated with reductions in hospital-based services and lower costs.¹⁰ Alternatively, if hospice is used as an add-on service to manage death after the failure of more intensive interventions, the rise in hospice care may not be accompanied by less aggressive end-of-life medical care. Recently, Teno et al³ demonstrated greater use of hospice and fewer hospital deaths through the 2000s, although increased use of ICUs, mechanical ventilation, and health care transitions near death among Medicare decedents with cancer, chronic obstructive pulmonary disease, or dementia was also seen.

In this study, we sought to confirm and extend the study by Teno et al³ by examining the intensity of

end-of-life care received by a well-characterized, population-based cohort of older women dying as a result of ovarian cancer between 1997 and 2007, a period when hospice and palliative care services were rapidly expanding.¹¹ Specifically, we aimed to determine whether increasing hospice use was accompanied by a reduction in the intensity of end-of-life medical care or, alternatively, by increased use of hospital-based services and health care transitions. In addition, we sought to explore the relationship between hospitalizations and hospice use at the end of life by comparing trends in hospice enrollment from inpatient and outpatient settings.

PATIENTS AND METHODS

Data Source

Data for this analysis came from the linkage of SEER registry data with Medicare health care claims from 1996 to 2007. The SEER program of the National Cancer Institute collects uniformly reported data from population-based cancer registries. Data from 11 registries, representing 14% of the US population, have been available since 1992. In 2000, SEER expanded to include four additional registries, now representing 28% of the population.^{12,13}

SEER data are merged with Medicare claims by a matching algorithm that links files for > 94% of SEER patients age $\geq$ 65 years. The data are linked to the National Death Index to obtain cause of death.¹⁴ Medicare claims data used for this study included the Medicare Provider Analysis and Review (MEDPAR) file for inpatient services, Hospital Outpatient Standard Analytic file for outpatient facility services, 100% Physician/Supplier file for physicians' services, Hospice file, and Durable Medical Equipment file for oral chemotherapies. The study was approved by the Harvard Medical School Committee on Human Studies.

Cohort

We identified all women with a first diagnosis of epithelial ovarian cancer during 1997 to 2007 who were age $\geq$ 66 years, enrolled in parts A and B of fee-for-service Medicare for $\geq$ 1 year before diagnosis, and enrolled in fee-for-service Medicare throughout the study period or until death ($N = 15,639$). We excluded patients with noninvasive disease ($n = 27$), who were diagnosed at death or autopsy ($n = 450$), without claims from 45 days before diagnosis through 180 days after ($n = 50$), with a missing date of death ($n = 5$), who died within 30 days of diagnosis ($n = 1,467$), who were alive at the end of the study period ($n = 4,043$), or who died as a result of causes other than ovarian cancer (because of concerns that they might have second cancer resulting from hereditary syndromes or that they might have died resulting from non-cancer-related causes; $n = 2,641$). The final cohort included 6,956 decedents.

Outcomes

Medical care in last month of life. We assessed use of hospice before death and terminal hospitalizations (hospital deaths). We used previously developed claims-based indicators of potentially aggressive health care within the last 30 days of life,^{1,15} including: admission to an ICU; hospitalizations; $\geq$ two emergency department visits; $\leq$ 3 days of hospice; chemotherapy; and life-extending procedures (ie, ventilation, resuscitation, or feeding tubes).²

Among patients who received hospice services, we determined the source of referral (inpatient or outpatient) using a previously developed claims-based measure.¹⁶ Specifically, hospice enrollments occurring within 2 days of hospital discharge were characterized as inpatient referrals, whereas other hospice enrollments were coded as outpatient referrals. We also examined length of stay among patients admitted to ICUs, hospitals, and hospice.

Health care transitions. We defined a health care transition as a change in the institutional health care provider identification number from claims in MEDPAR and hospice files.³ Transitions included: hospitalization, transition between facilities, discharge from facility, and enrollment in hospice (both inpatient and outpatient, because each may require change in providers). We also examined transitions previously classified as burdensome, including those occurring $\leq$ 3 days before death.¹⁷

Independent Variables

The primary independent variable of interest was year of death. Covariates obtained from medical records included age at diagnosis, race, Hispanic ethnicity, marital status, prior and subsequent cancers (except nonmelanoma skin cancers), cancer stage, grade, histology, and year of diagnosis. We assessed comorbid illness using the Klabunde modification of the Charlson score based on the 12-month period before diagnosis.^{18,19} The extent of urbanization at patients' residences was obtained from the Area Resource file. We obtained Census tract-level measures of socioeconomic status, including high school completion rate and proportion below the poverty line (zip code-level information was used for < 5% of patients with unknown Census tracts). Initial cancer-directed surgery was identified using International Classification of Diseases (ninth revision) and Current Procedural Terminology procedure codes, as previously described.^{20,21}

Analyses

We used logistic regression to assess the association of year of death with each binary dependent variable, adjusting for the patient characteristics described. Year of death entered the models via dummy variables for each year, with 1997 as the reference. We tested the null hypothesis that there was no linear trend over time by constructing a contrast test for the year dummy coefficients. Specifically, we tested that a linear combination of the year dummy coefficients was zero using equally spaced, sum-to-zero linear weights. We calculated the fitted yearly proportion of patients with each outcome, adjusted for all other covariates, based on these regression models. Specifically, we calculated average predicted probabilities for the combined samples from all years, setting the intercept to the dummy variable coefficient for each year in turn.²² Among hospice enrollees, we fit logistic regression models to examine the source of hospice referral (inpatient or outpatient), conditional on year of death and adjusted for all other covariates. Among patients who received $\leq$ 3 days of hospice, we fit logistic regression models to examine the proportion enrolled from inpatient and outpatient settings, conditional on year of death and adjusted for all other covariates.

To examine trends in the number of health care transitions over time, we fit adjusted Poisson regression models, as described. To determine the adjusted mean length of stay over time, we used a zero-truncated negative binomial model, conditional on year of death and adjusted for all other covariates.

A sensitivity analysis was performed to consider the effect of including the 2,641 patients who died with ovarian cancer instead of as a result of ovarian cancer (ie, cause of death other than ovarian cancer) in each of the models. Among these, 52.1% died as a result of another cancer, most often breast, colon, or uterine cancer or a cancer of unknown primary site; the rest died as a result of noncancer causes. Two-sided P values < .05 were considered statistically significant. All statistical analyses were performed with SAS software (version 9.2; SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

Overall, 62.4% of the cohort was age < 80 years, and most patients were white (86.7%) and without significant medical comorbidities (67.6%; Table 1). Nearly two thirds had stage III or IV disease at diagnosis, and 71.7% had papillary serous carcinoma; 61.3% of patients underwent cytoreductive surgery.

Medical Care in Last Month of Life

Figure 1 shows the adjusted yearly proportion of patients with ovarian cancer receiving several different types of medical care in the last month of life. Over time, the proportion of patients who received hospice services increased significantly ($P < .001$), and fewer patients died in hospitals ($P < .001$). Despite increased hospice enrollment,

Table 1. Characteristics of Patients Dying As a Result of Ovarian Cancer in SEER-Medicare Cohort (N = 6,956)

Characteristic	%
Age, years	
66-70	19.8
71-74	18.4
75-79	24.2
80-84	20.7
≥ 85	16.8
Race/ethnicity	
White	86.7
Black	5.6
Hispanic	4.3
Other/unknown	3.4
Married	38.3
Charlson score*	
0	67.6
1	20.4
2	7.1
≥ 3	4.9
Cytoreductive surgery	61.3
Stage	
I/II	6.4
III	27.5
IV	36.7
Unknown	29.5
Grade	
Well differentiated	1.5
Moderately differentiated	10.1
Poorly differentiated	41.8
Unknown	46.6
Histology	
Serous	71.7
Nonserous	28.3
Prior cancer	10.1
Subsequent cancer	2.9
Survival, months	
Median	12.0
Interquartile range	3.0 to 27.0
Urban/rural location	
Major metropolitan	56.0
Metropolitan	27.8
Urban	5.7
Less urban	8.4
Rural	2.2
Registry	
Connecticut	8.4
Detroit	9.8
Hawaii	1.3
Iowa	10.1
New Mexico	2.7
Seattle	8.9
Utah	3.4
Georgia	4.3
San Jose	2.3
Los Angeles	8.6
San Francisco	4.2
Greater California	13.3
Kentucky	5.8
Louisiana	5.1
New Jersey	12.1

(continued in next column)

Table 1. Characteristics of Patients Dying As a Result of Ovarian Cancer in SEER-Medicare Cohort (N = 6,956) (continued)

Characteristic	%
High school completion, %†	
< 77	24.5
77-85.4	24.9
85.5-91.4	25.1
≥ 91.5	25.0
Unknown	0.6
Poverty, %‡	
≥ 15	21.7
8.0-14.9	23.8
4.0-7.9	26.6
≤ 4.0	21.6
Unknown	6.4

*Klabunde modification of Charlson score.

†Determined by proportion of people who have completed high school within Census tract and zip code.

‡Determined by proportion of people living below poverty line within Census tract.

however, the proportion of patients enrolling in hospice ≤ 3 days before death did not change significantly ($P = .2$; Fig 2).

Even with the decline in terminal hospitalizations, the use of many hospital-based services increased between 1997 and 2007. As shown in Figure 1, significantly more patients were admitted to ICUs ($P < .001$), hospitals ($P = .005$), and emergency departments ($P < .001$) within the last month of life over time. In contrast, few patients received potentially life-extending procedures or chemotherapy in the last month of life ($P = .01$ and $P = .07$, respectively; Fig 2).

As shown in Figure 2, the proportion of patients who enrolled in hospice from inpatient settings increased significantly over time, compared with outpatient referrals ($P = .001$). Among patients referred to hospice, inpatients were more likely than outpatients (24% v 16%) to enroll in hospice within 3 days of death (adjusted odds ratio, 1.36; 95% CI, 1.12 to 1.66; data not shown). Furthermore, among patients who received ≤ 3 days of hospice, a preceding ICU stay during the last

Fig 1. Adjusted yearly proportion of patients with ovarian cancer receiving medical care in last month of life. Logistic regression models were adjusted for age, race/ethnicity, marital status, high school completion rate and proportion below poverty line in zip code/Census tract, urban/rural location, SEER registry, medical comorbidities, stage, grade, histology, and time from diagnosis to death. P values represent linear test of trend across year coefficients in each regression model. No. of observations used in each analysis was 6,956. ED, emergency department; ICU, intensive care unit.

Fig 2. Adjusted yearly proportion of end-of-life medical care and health care transitions of patients with ovarian cancer. Logistic regression models were adjusted for age, race/ethnicity, marital status, high school completion rate and proportion below poverty line in zip code/Census tract, urban/rural location, SEER registry, medical comorbidities, stage, grade, histology, and time from diagnosis to death. *P* values represent linear test of trend across year coefficients in each regression model. No. of observations used in each analysis was 6,956, except for models estimating source of hospice referral and hospice enrollment ≤ 3 days of death ($n = 2,853$), which were analyzed among hospice enrollees only.

month of life was more likely in 2007 compared with 1997 (31.3% *v* 5.0%; $P < .001$).

Health Care Transitions and Length of Stay

The adjusted proportion of patients who underwent health care transitions in the last month of life increased somewhat over time ($P = .008$; Fig 2). Similarly, the mean number of transitions increased slightly, driven mostly by a greater number of patients who experienced $\geq$ three transitions (eg, adjusted mean number in 1997 *v* 2007: 1.3 *v* 1.6; $P = .003$). In contrast, the time between the last transition and death remained stable over time ($P = .8$; data not shown).

In adjusted analyses, nearly 20% of decedents underwent a health care transition in the last 3 days of life, a proportion that did not change significantly over time ($P = .4$), despite the increasing use of hospice services. Among these patients, 34.2% were admitted to hospice, 32.9% were admitted to a hospital from home, 29.7% were transferred between acute care settings (eg, hospital to nursing home), and 3.0% were discharged from a hospital to home without hospice services.

As shown in Figure 3, the average adjusted total number of days spent in ICUs, hospitals, or hospice during the last month of life did not change significantly over time. Although increasing numbers of hospitalized patients were referred to hospice, the average hospital length of stay did not decrease over time ($P = .5$). Similarly, although more patients were referred to hospice over time, the average hospice length of stay remained stable ($P = .1$).

In sensitivity analyses including patients who died as a result of any cause, patients who died as a result of causes other than ovarian cancer had higher rates of intensive end-of-life care ($P < .001$) and lower rates of hospice use ($P < .001$) compared with patients who died as a result of ovarian cancer. Otherwise, the trends were similar, except for the use of life-extending procedures, which did not change over time among patients who died as a result of other causes ($P = .2$).

Fig 3. Adjusted yearly mean lengths of stay for patients with ovarian cancer during last month of life. Zero-truncated binomial models were adjusted for age, race/ethnicity, marital status, high school completion rate and proportion below poverty line in zip code/Census tract, urban/rural location, SEER registry, medical comorbidities, stage, grade, histology, and time from diagnosis to death. *P* values represent linear test of trend across year coefficients in each regression model. No. of observations used in each model was as follows: intensive care unit (ICU), $n = 734$; hospital, $n = 2,851$; and hospice, $n = 2,853$.

DISCUSSION

In this large population-based cohort of older women dying as a result of ovarian cancer, we found that despite increasing use of hospice over time, women with ovarian cancer remained at high risk for receiving intensive hospital-based medical care near death. We observed increasing use of ICUs, hospitals, and emergency departments in the last month of life between 1997 and 2007, at a time when palliative care and hospice services were rapidly expanding,¹¹ and no reduction in lengths of stay in hospitals and ICUs or late hospice referrals. These results heighten concerns that hospice may be used as an add-on service to manage death after the failure of more intensive interventions.³

We also observed a change in hospice enrollment patterns that has not been previously reported, to our knowledge. Between 1997 and 2007, the number of patients enrolling in hospice in the last month of life increased, with the greatest growth among patients who enrolled immediately after a hospitalization. In addition, we found increasing rates of hospice enrollment after an ICU stay among those who received ≤ 3 days of services. Rising rates of inpatient hospice referrals likely explains why terminal hospitalizations decreased over time, despite an increased number of hospitalizations near death.

Most patients in this study experienced at least one health care transition at the end of life, and nearly 20% experienced a transition within 3 days of death. Among those who underwent late transitions, nearly two thirds were transferred from one acute care setting to another or were hospitalized near death. End-of-life hospitalizations may occur in the setting of uncontrolled symptoms, which require inpatient care. However, a recent study found that oncologists estimated that 20% of hospitalizations among patients with GI cancers were potentially avoidable, suggesting that there is room for improvement.²³

Similarly, although qualitative studies of bereaved caregivers have found that timely hospice referrals may not be possible in one third of patients,²⁴ we previously found that late hospice referrals and

terminal hospitalizations were associated with worse patient quality of life near death and increased psychiatric morbidity in surviving caregivers.^{4,25} In contrast, few studies have examined how late transitions between acute care settings (eg, hospital to nursing home) influence patients' end-of-life experiences and caregivers' bereavement adjustment. Although our data did not allow ascertainment of why these late transitions occurred, it is possible that patients or caregivers requested them. Future research should prospectively examine whether transitions close to death reflect patients' or caregivers' informed preferences and whether they are associated with patient quality of death and caregiver outcomes.

Nearly half of patients were hospitalized in the last month of life, where they spent an average of 1 week as inpatients. Despite high rates of hospitalization among patients with advanced cancer near death,² the reasons for late hospitalizations are relatively understudied. One single-institution, retrospective study found that two thirds of hospitalized patients with metastatic cancers were admitted for uncontrolled symptoms, such as pain or dyspnea, which might be managed in outpatient settings (eg, with narcotics or palliative thoracenteses).²⁶ Another large prospective, population-based study found that more than half of end-of-life discussions occurred in an inpatient setting within weeks of death.²⁷ Together these findings suggest that some end-of-life hospitalizations often catalyze a rapid transition in goals of care, which might be averted with earlier integration of outpatient palliative care or end-of-life discussions, both of which are associated with better quality of life and less physical distress near death.^{4,28} Future studies should prospectively examine whether late hospitalizations are avoidable in a heterogeneous sample of patients with metastatic cancers, particularly because terminal hospitalizations are a significant driver of variations in end-of-life spending.⁶

Our study has several limitations. First, we studied older women insured by Medicare who resided in SEER areas and died as a result of ovarian cancer during 1997 to 2007. Practice patterns may differ in younger and commercially insured patients, although the median age at ovarian cancer diagnosis is 63 years. Our findings also may not be generalizable to other cancers or patients diagnosed more recently. Second, we studied end-of-life care among decedents, which has certain limitations, because physicians must make decisions prospectively.²⁹ Although prospective cohort studies of terminally ill patients with cancer offer many advantages—including the ability to assess patients' quality of life, functional status, and preferences over time as well as potential survival benefits associated with more-intensive treatment^{30,31}—they have other limitations, including selection bias.³² In addition, we were unable to discern whether the increasing use of intensive inpatient services reflected overall trends in increasing health care intensity among all patients, as previously suggested.^{6,33} Future studies should prospectively examine whether cancer care is becoming more intensive over time among both survivors and decedents. Finally, we relied on death certificate data to

ascertain causes of death, which may be inaccurate. However, the vast majority of patients had advanced disease at diagnosis, increasing the likelihood that the determination of ovarian cancer death was accurate, and results of sensitivity analyses including patients who died as a result of cancer and those who died as a result of other causes were similar.

Despite these limitations, our study has many strengths. To date, few researchers have examined end-of-life medical care of patients with ovarian cancer. Although one study documented rising use of hospice among older patients with ovarian cancer,⁹ our study is the first, to our knowledge, to examine the intensity of medical care near death of patients with ovarian cancer over time in a population-based cohort. In addition, we examined a well-characterized cohort of older women with ovarian cancer from the time of diagnosis until death resulting from ovarian cancer, instead of patients with terminal cancers identified from administrative data based on diagnosis codes for poor-prognosis cancers who had previously been hospitalized^{3,34} and might therefore have higher odds of receiving intensive medical care near death than a general population of patients with cancer. Second, we examined trends in end-of-life care over time, while accounting for factors already known to influence the intensity of end-of-life medical care of patients with cancer (eg, comorbid medical illness and time from diagnosis to death),^{1,15,35} which may increase the reliability of our results.

In conclusion, our findings suggest that the expansion of hospice services over recent decades has not been accompanied by a reduction in the intensity of end-of-life medical care received by older patients with ovarian cancer. Although terminal hospitalizations have decreased, the use of hospital-based services near death has increased significantly. These trends suggest that patients are receiving more, but not necessarily better, care. Earlier and more regular discussions about patients' and families' preferences for end-of-life care—and the potential benefits and harms of intensive care near death—may help decrease the use of hospital-based care near death, although determining effective strategies for doing this requires further study, because patients' choices may be influenced by the ways in which options are presented.³⁶

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Alexi A. Wright, Nancy L. Keating

Financial support: Alexi A. Wright

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Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

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