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Hospice Utilization and Its Effect on Acute Care Needs at the End of Life in Medicare Beneficiaries With Hepatocellular Carcinoma

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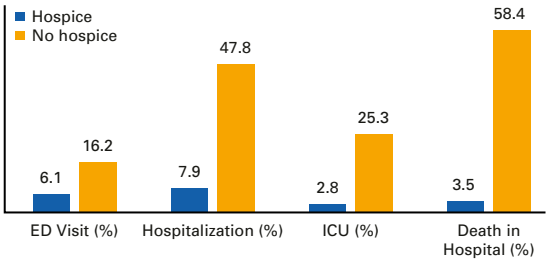
QUESTION ASKED: For patients with advanced hepatocellular carcinoma (HCC) who suffer from a high symptom burden from cancer and concomitant cirrhosis, palliative care has the potential to markedly improve the quality of end-of-life care. Do the unique processes of HCC care affect hospice use and the extent to which hospice use decreases the need for acute care services at the end of life?

SUMMARY ANSWER: Hospice use at the end of life was strongly influenced by the type of initial treatment received and specialty of consulting providers. Patients with HCC enrolled in hospice were less likely to undergo hospitalization or intensive care unit stays at the end of life and markedly less likely to die in the hospital than patients with HCC who were never enrolled in hospice.

WHAT WE DID: We compared factors associated with hospice use and the effect of hospice on acute care services between decedent patients with HCC referred to hospice before death and a matched nonhospice comparison group identified in the SEER-Medicare database.

WHAT WE FOUND: In this population-based study of Medicare beneficiaries, we found that the type of initial treatment received and consultation with an oncologist in the last months of life were strong predictors of hospice use. Although the median time from initial hospice claim to death was only 17 days, hospice use over this short period was still associated with a marked decline in emergency department visits, hospitalizations, intensive care unit stays, and in-hospital or nursing home deaths (Fig).

BIAS, CONFOUNDING FACTOR(S), REAL-LIFE IMPLICATIONS: Because of the limitations of this observational data set, we did not have data on the severity of cancer nor the severity of liver disease in the time leading up to death; therefore, we were unable to determine whether patients died of cancer or end-stage liver disease, a distinction that might affect the likelihood of hospice referral. However, given the high symptom burden from both HCC and end-stage liver disease and the marked reduction in acute care services at the end of life in these Medicare beneficiaries referred to hospice, efforts to incorporate cancer-focused palliative care into the unique multidisciplinary structure of HCC care are warranted. JOP



	ED Visit (%)	Hospitalization (%)	ICU (%)	Death in Hospital (%)
Hospice (%)	6.1	7.9	2.8	3.5
No hospice (%)	16.2	47.8	25.3	58.4
RR (95% CI)	0.38 (0.31 to 0.45)	0.16 (0.14 to 0.19)	0.11 (0.09 to 0.14)	0.06 (0.05 to 0.07)

FIG. Health care utilization at the end of life according to hospice use. Percentage and associated risk ratio (RR) of health resource use during the exposure window before death (a median of 17 days before death) is shown for the patients in the matched cohort. ED, emergency department; ICU, intensive care unit.

Hospice Utilization and Its Effect on Acute Care Needs at the End of Life in Medicare Beneficiaries With Hepatocellular Carcinoma

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Abstract

Introduction

Hepatocellular carcinoma (HCC) is a poor-prognosis cancer with a high symptom burden. Multidisciplinary HCC care is complex and unique in cancer medicine. We sought to determine whether the distinct process affects hospice use and how hospice affects end-of-life acute care utilization.

Patients and Methods

Patients dying after HCC diagnosed from 2004 to 2011 were identified within SEER-Medicare. Hospice use and associated factors were described using logistic regression. Coarse exact and propensity score matching created groups of hospice and nonhospice comparators balanced on clinical characteristics. Health care use from first hospice claim to death and the matched duration in the nonhospice group were compared.

Results

Of 7,992 decedent patients with HCC, 63% used hospice before death, with a median duration of 18 days (interquartile range, 5-51 days). Initial treatment with surgery and ablation (odds ratio [OR], 0.63; 95% CI, 0.53 to 0.74) or chemoembolization/radioembolization (OR, 0.71; 95% CI, 0.62 to 0.80) was associated with decreased odds of subsequent hospice use compared with untreated patients. Hospice use was more likely in those consulting hematology/oncology (OR, 1.33; 95% CI, 1.13 to 1.56) but not in those consulting gastroenterology (OR, 0.79; 95% CI, 0.65 to 0.95). Hospice patients had lower rates of hospitalization (7.9% *v* 47.8%; risk ratio [RR], 0.16; 95% CI, 0.14 to 0.19), intensive care unit stay (2.8% *v* 25.3%; RR, 0.11; 95% CI, 0.09 to 0.14), and in-hospital death (3.5% *v* 58.4%; RR, 0.06; 95% CI, 0.05 to 0.07).

Conclusion

Processes of care influence which patients with HCC are referred to hospice. Hospice use has a marked effect on acute care use at the end of life in patients with HCC. Efforts to incorporate cancer-focused palliative care might improve the quality of end-of-life care in HCC.

ASSOCIATED CONTENT

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a major cause of morbidity and mortality worldwide.[1] In the United States, primary liver cancer—of which HCC is the predominant histopathology—ranks fifth in causes of cancer-related mortality.[2] HCC is a particularly difficult cancer to treat

because patients frequently present with advanced disease, and the nearly universal presence of comorbid cirrhosis among patients with HCC markedly limits treatment options.[3] As such, for most patients, the diagnosis of HCC is a terminal one.

The offer of referral to expert-level palliative care and hospice are recognized by the Institute of Medicine as key components of quality end-of-life care.[4] Hospice use in the United States has increased over the past few decades, such that approximately 60% of patients with terminal cancers enroll before death.[5] Hospice participants have lower rates of hospitalization, intensive care unit (ICU) stays, and in-hospital death.[5]

For patients with HCC who often experience a high symptom burden related to cancer (eg, pain, anorexia, fatigue) and end-stage liver disease (ESLD; eg, ascites, hepatic encephalopathy, muscle cramps), such palliative referrals are likely paramount. However, HCC care is complex in a number of ways, which may present barriers to hospice referral. First, the prognosis of patients with HCC is determined just as much by the extent of cirrhosis as by the extent of cancer.[6] Furthermore, although patients with ESLD have a high symptom burden that might benefit from hospice,[7] it is challenging to determine which patients with ESLD will die within the 6-month hospice requirement.[8,9] Second, liver transplantation overshadows the care of patients with ESLD and HCC.[9] With survival among patients with HCC who underwent transplantation as good as that among patients who underwent transplantation for other indications,[10] and as evidence emerges that patients with increasingly extensive cancers can be downstaged, undergo transplantation, and cured,[11] it may be difficult for patients and providers to balance the reality of what will likely be a terminal disease with the possibility of curative transplantation. Finally, the process of care for HCC is unique in cancer medicine in that unlike most cancers where consultation is frequently undertaken with a medical or radiation oncologist after diagnosis, HCC treatment is often overseen by a hepatologist in conjunction with transplant surgery and interventional radiology, with varying involvement of medical oncology. Therefore, although these unique multidisciplinary HCC teams are unequivocally essential for optimal outcomes in HCC,[12-14] they bring a different perspective to the care of HCC than do the multidisciplinary teams who care for patients diagnosed with other cancers.

In light of the unique process of HCC care combined with the exceptional burden of disease experienced by patients, we sought to evaluate the extent to which hospice services are used at the end of life in patients with HCC, what factors determine hospice use, and whether those enrolled in hospice were any less likely to require acute care services at the end of life.

PATIENTS AND METHODS

Patients

The cohort of patients with HCC was derived from the US National Cancer Institute's SEER-Medicare linkage. The SEER program of cancer registries collects data on incident cancer cases diagnosed within 18 population-based registries, which encompass 28% of the US population.[15,16] SEER cases have been linked to Medicare claims to facilitate research on cancer treatment.[17]

Patients with HCC diagnosed while alive between 2004 and 2011 were identified from SEER-Medicare using SEER code C22.0 and HCC histology codes 8170-8175 and 8180, regardless of reason for Medicare eligibility (eg, $\geq$ 65 years of age, disability, renal disease). To ensure that complete claims were available for our analyses, only patients with continuous enrollment in Medicare Parts A and B, those with fee-for-service Medicare for the 6 months before and after diagnosis, and those with at least one claim in the year before diagnosis were included. Because the intent of this project was to evaluate health care utilization at the end of life, we restricted this cohort to patients who died of any cause after the incident HCC diagnosis, as has been done by others evaluating end-of-life health care use.[5,18] For the primary analysis, patients who died in the month of their diagnosis were excluded because of the possibility that these patients were incidentally found to have HCC during treatment of decompensated cirrhosis, which was the cause of their death. Such patients would be less likely to enroll in hospice and have a high rate of in-hospital death, and thus might be expected to inflate any observed hospice effect. As a sensitivity analysis, however, the entire analysis was also conducted without this restriction.

Covariables and Outcomes

Patient demographics, census tract socioeconomics, and tumor characteristics were derived from SEER. The underlying cause of liver disease and extent of liver comorbidity (defined by complications of cirrhosis: ascites, encephalopathy, varices, peritonitis, hepatorenal syndrome) were defined

by the presence of two or more claims with that diagnosis code.[19,20] Nonliver comorbidity was defined using the Klabunde modification of the Charlson Comorbidity Index,[21] excluding codes from liver disease and cancer. All claims-based covariables were defined in the 12 months before diagnosis. Treatment group was defined by the initial treatment received, which were ascertained from claims after diagnosis as previously described (codes are available from the authors on request).[20]

Health care system covariables of interest were measured in the 6 months before the start of the hospice utilization window (see Analysis section). Provider specialty was assessed for primary care physicians, gastroenterologists (there is not a specific code for hepatology), and hematology/oncology. Hospital National Cancer Institute (NCI) designation and liver transplant status was determined from the hospital file. Patients seen at more than one hospital were categorized according to the highest level of subspecialty.

Hospice use was defined by at least one claim for hospice services from the time of diagnosis to death. Acute care use was defined by emergency department (ED) visits not leading to an admission, hospitalizations, and ICU stays during the hospice utilization or matched comparison window. The place of death was derived from the discharge destination and skilled nursing facility indicator variables in the Medicare Provider Analysis and Review file.

Analysis

First, we sought to describe the use of hospice in all decedent patients after an HCC diagnosis. To do so, rates of hospice utilization, time from diagnosis to hospice referral, and time from referral to death are presented descriptively. We used multivariable logistic regression to evaluate patient factors associated with a hospice referral among the entire cohort of decedent patients with HCC.

We next sought to (1) evaluate the health care system factors in the time around hospice decision making (eg, in the months before death) associated with hospice referral and (2) the effect of hospice referral on acute care services use. We used coarsened exact matching,[5,22] to allow us to compare hospice patients with a comparison group of nonhospice patients with similar illness severity at a similar time course in their illness. To do this, we matched patients according to illness severity at diagnosis by matching on age, stage, use of prediagnosis alpha-fetoprotein screening (which we have previously found to be a strong predictor of survival in Medicare beneficiaries with HCC[20,23]), and initial treatment. Because there were residual imbalances in some covariables potentially associated with the outcome, we then applied propensity score matching using race, SEER region, and place of birth to generate the propensity score. Finally, we matched on utilization window, defined as the days from first hospice claim to death, such that for each hospice patient, the comparison group patient was alive for at least as long as the corresponding number of days before death. The start of this utilization window was also used as the anchor at which we began evaluating health care system factors predictive of hospice referral.

RESULTS

Of 11,130 patients with HCC diagnosed between 2004 and 2011 for whom complete claims were available, 9,656 (87%) died after their HCC diagnosis, 1,664 (15%) of whom died in the month of diagnosis and therefore were excluded from the primary analysis. In the 7,992 patients who survived the month of their diagnosis, the median age was 73 years (interquartile range [IQR], 66-79 years), with 1,681 patients (21%) younger than 65 years (Table 1). Only 374 patients (5%) underwent initial curative surgery (resection or transplantation) and 455 (6%) underwent ablation. Half of patients (4,048; 51%) were never treated for their HCC.

One or more claims for hospice were present in 5,056 of all patients (63%) between the time of cancer diagnosis and death. The median time from diagnosis to first hospice claim was 175 days (IQR, 59-500 days). The median time from first hospice claim to death was 18 days (IQR, 5-51 days).

Hospice use was more common in older patients (adjusted odds ratio [aOR] for patients $\geq$ 75 years of age *v* those $<$ 65 years of age, 1.47; 95% CI, 1.27 to 1.69), but significantly less likely among nonwhites (aOR for blacks, 0.70; 95% CI, 0.59 to 0.83; aOR for Asians, 0.55; 95% CI, 0.48 to 0.68), as well as in men and those residing in the most rural and the poorest census tracts. A patient's initial treatment received was significantly associated with subsequent hospice referral: compared with untreated patients, hospice use was less likely in patients treated with initial curative surgery (aOR, 0.63; 95% CI, 0.53 to 0.74) and in those with initial transarterial chemoembolization or radioembolization (aOR, 0.71; 95% CI, 0.62 to 0.80).

After coarsened exact matching and propensity score matching, 2,323 pairs (4,646 individuals) of hospice patients and comparison group patients were included. These groups were balanced on key covariables; however, because we did not

Table 1. Characteristics of Decedent Patients With Hepatocellular Carcinoma and Association With Hospice Use

Characteristic	Entire Cohort (N = 7,992) No. (%)	Hospice (n = 5,056) No. (%)	No Hospice (n = 2,936) No. (%)	Likelihood of Hospice Use Adjusted OR* (95% CI)
Year of diagnosis				
2004-2007	3,724 (47)	2,407 (48)	1,317 (45)	Ref
2008-2011	4,268 (53)	2,649 (52)	1,619 (55)	1.02 (0.92 to 1.13)
Age, years				
Median (Q1, Q3)	73 (66, 79)	73 (67, 80)	71 (64.5, 78)	
≤ 64	1,681 (21)	947 (19)	734 (25)	Ref
65-74	2,891 (36)	1,775 (35)	1,116 (38)	1.17 (1.02 to 1.34)
≥ 75	3,420 (43)	2,334 (46)	1,086 (37)	1.47 (1.27 to 1.69)
Sex				
Male	5,638 (71)	3,512 (69)	2,126 (72)	Ref
Female	2,354 (29)	1,544 (31)	810 (28)	1.16 (1.03 to 1.29)
Race				
White	5,463 (68)	3,662 (72)	1,801 (61)	Ref
Black	874 (11)	511 (10)	363 (12)	0.70 (0.59 to 0.83)
Asian	808 (10)	401 (8)	407 (14)	0.55 (0.48 to 0.68)
Other	847 (11)	482 (10)	365 (12)	0.73 (0.62 to 0.87)
Tumor extent at diagnosis				
Single lesion	3,335 (42)	1,995 (39)	1,340 (46)	Ref
Multiple, no vascular invasion	2,515 (31)	1,589 (31)	926 (32)	1.18 (1.05 to 1.32)
Multiple, vascular invasion	813 (10)	580 (11)	233 (8)	1.59 (1.34 to 1.89)
Extension beyond liver	1,329 (17)	892 (18)	437 (15)	1.20 (1.04 to 1.39)
Initial treatment				
Curative surgery	374 (5)	199 (4)	175 (6)	0.63 (0.53 to 0.74)
Ablation†	455 (6)	249 (5)	206 (7)	—
TACE	1,793 (22)	999 (20)	794 (27)	0.71 (0.62 to 0.80)
TARE†	187 (2)	136 (3)	51 (2)	—
Drug or radiation therapy	1,135 (14)	725 (14)	410 (14)	0.94 (0.81 to 1.08)
Never treated	4,048 (51)	2,748 (54)	1,300 (44)	Ref
Hepatitis B‡	416 (5)	211 (4)	205 (7)	0.95 (0.76 to 1.18)
Hepatitis C	1,914 (24)	1,058 (21)	856 (29)	0.87 (0.77 to 1.00)
Alcohol	860 (11)	492 (10)	368 (13)	0.99 (0.83 to 1.18)
Other cause of liver disease	906 (11)	579 (11)	327 (11)	0.98 (0.83 to 1.16)
No. of liver comorbidities				
0	5,575 (70)	3,650 (72)	1,925 (66)	Ref
1	1,354 (17)	800 (16)	554 (19)	0.82 (0.71 to 0.93)
≥ 2	1,063 (13)	606 (12)	457 (16)	0.84 (0.71 to 1.00)
Modified Charlson score				
0	3,045 (38)	2,018 (40)	1,027 (35)	Ref
1	1,473 (18)	923 (18)	550 (19)	0.95 (0.82 to 1.09)
≥ 2	3,474 (43)	2,115 (42)	1,359 (46)	0.90 (0.80 to 1.20)

(continued on following page)

Table 1. Characteristics of Decedent Patients With Hepatocellular Carcinoma and Association With Hospice Use (continued)

Characteristic	Entire Cohort (N = 7,992) No. (%)	Hospice (n = 5,056) No. (%)	No Hospice (n = 2,936) No. (%)	Likelihood of Hospice Use Adjusted OR* (95% CI)
Prediagnosis AFP screening				
0	5,311 (66)	3,479 (69)	1,832 (62)	Ref
1	1,340 (17)	819 (16)	521 (18)	1.04 (0.91 to 1.20)
≥ 2	1,341 (17)	758 (15)	583 (20)	1.08 (0.93 to 1.27)
Census tract				
Metropolitan	7,031 (88)	4,425 (88)	2,606 (89)	Ref
Urban	389 (5)	269 (5)	120 (4)	1.03 (0.81 to 1.30)
Rural	572 (7)	362 (7)	210 (7)	0.66 (0.53 to 0.81)
Census tract % < poverty				
1st quartile (lowest)	2,009 (25)	1,339 (27)	670 (23)	Ref
2nd quartile	1,968 (25)	1,273 (26)	695 (24)	0.95 (0.83 to 1.09)
3rd quartile	1,966 (25)	1,228 (25)	738 (25)	0.89 (0.77 to 1.03)
4th quartile (highest)	1,952 (25)	1,143 (23)	809 (28)	0.83 (0.71 to 0.97)

Abbreviations: AFP, alpha-fetoprotein; OR, odds ratio; Ref, reference; TACE, transarterial chemoembolization; TARE, transarterial radioembolization.
*The logistic regression model also included SEER region with significant geographic variation, country of birth, and marital status, which were not independently associated with hospice use.
†Cell combined with cell above for the multivariable model.
‡Causes of liver disease are not mutually exclusive and do not sum to 100%; the reported OR is compared with the no category for each cause independently.

directly match on survival time, the median survival from diagnosis was longer in hospice patients (9 months; IQR, 3-22 months), than comparison group patients (8 months; IQR, 3-21 months). This difference in survival reflects a difference in the time from diagnosis to the start of the hospice (and matched utilization window), which was a median of 229 days for the hospice group and 212 days for the comparison group (Appendix Table A1, online only). In the 6 months leading up to the start of the utilization window, patients referred to hospice were significantly more likely to be seen at an NCI-designated comprehensive cancer center (16% *v* 13%; aOR, 1.19; 95% CI, 1.00 to 1.43), but not more likely to be seen at a liver transplant center (42% *v* 40%; aOR, 0.98; 95% CI, 0.85 to 1.15; Table 2). Twenty-eight percent of hospice patients and 35% of comparison group patients did not see a gastroenterologist or hematologist/oncologist in the 6 months before the utilization window. Compared with these patients, consultation with an oncologist alone (aOR, 1.33; 95% CI, 1.13 to 1.56) or in addition to a gastroenterologist (aOR, 1.31; 95% CI, 1.10 to 1.55) was associated with increased odds of hospice referral. Consultation with a gastroenterologist without an oncologist, however, was associated with decreased odds of hospice use (aOR, 0.79; 95% CI, 0.65 to 0.95). Patients requiring multiple hospital admissions (excluding admissions for cancer-directed therapies) before the utilization window were significantly more likely to be referred to hospice.

Although the median duration of the exposure window was only 17 days before death, patients with a hospice claim were markedly less likely to use hospital-based acute care. At the end of life, hospice patients had fewer ED visits not resulting in admission (6.1% *v* 16.2%; risk ratio [RR], 0.38; 95% CI, 0.31 to 0.45), hospitalizations (7.9% *v* 47.8%; RR, 0.16; 95% CI, 0.14 to 0.19), and ICU stays (2.8% *v* 25.3%; RR, 0.11; 95% CI, 0.09 to 0.14; Fig 1). Of all hospital admissions, ascites (32% hospice, 44% comparison) and acute kidney failure (21% hospice, 28% comparison) were the most common admitting diagnoses. The following diagnoses were significantly less likely in hospice patient admissions: acute kidney failure (RR, 0.75; 95% CI, 0.61 to 2.17); acute respiratory failure (RR, 0.47; 95% CI, 0.32 to 0.68); sepsis (RR, 0.58; 95% CI, 0.45 to 0.76); and pneumonia (RR, 0.70; 95% CI, 0.50 to 0.98). A similar percentage of admissions had a comorbid severity modifier code for liver cancer, suggesting an equal distribution of active HCC during these admissions. Patients referred to hospice were markedly less likely to die in the hospital or a nursing facility,

Table 2. Association of Health Care System Engagement and Hospice Use

Characteristic	Hospice (n = 2,323) No. (%)	No Hospice (n = 2,323) No. (%)	Likelihood of Hospice Use Adjusted* OR (95% CI)
Hospital NCI Designation			
None	1,904 (82)	1,968 (85)	Ref
Clinical	47 (2)	55 (2)	0.87 (0.58 to 1.31)
Comprehensive	372 (16)	300 (13)	1.19 (1.00 to 1.43)
Hospital liver transplant status			
Not liver txp center	1,358 (58)	1,403 (60)	Ref
Liver txp center	965 (42)	920 (40)	0.98 (0.85 to 1.15)
Specialist consultation			
Neither gastroenterology nor oncology	655 (28)	805 (35)	Ref
Gastroenterology only	351 (15)	463 (20)	0.79 (0.65 to 0.95)
Oncology only	590 (25)	489 (21)	1.33 (1.13 to 1.56)
Gastroenterology and oncology	727 (31)	566 (24)	1.31 (1.10 to 1.55)
No. hospital admissions			
0	871 (37)	1,092 (47)	Ref
1	620 (27)	510 (22)	1.46 (1.25 to 1.71)
2	405 (17)	342 (15)	1.42(1.19 to 1.71)
3	186 (8)	157 (7)	1.41 (1.11 to 1.80)
4	96 (4)	102 (4)	1.12 (0.83 to 1.52)
5	62 (3)	46 (2)	1.62 (1.08 to 2.41)
≥ 6	83 (4)	74 (3)	1.33 (0.95 to 1.86)

NOTE. After multilevel matching, the use of various specialty services in the 6 months before the hospice utilization window (a median of 17 days before death) and the adjusted odds ratio for hospice use is shown for each factor. Primary hospital is defined as the highest level of care during that time (eg, patients seen at an NCI comprehensive center one or more times are categorized as comprehensive).

Abbreviations: NCI, National Cancer Institute; Ref, reference; txp, transplant.

*Model was adjusted for all variables listed. Additional patient characteristics were not included as this was performed in the matched cohort.

at 3.5%, than were patients who did not use hospice services, at 58.4% (RR, 0.06; 95% CI, 0.05 to 0.07).

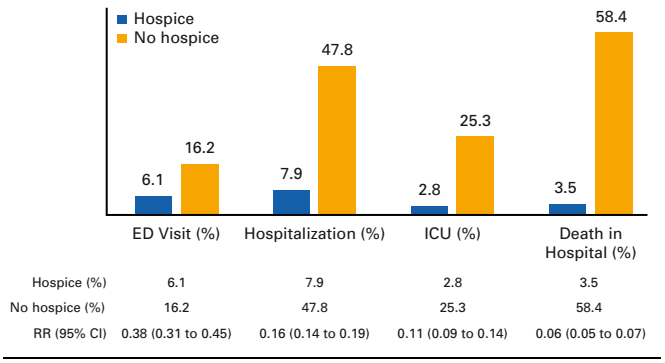

FIG 1. Health care utilization at the end of life according to hospice use. Percentage and associated risk ratio (RR) of health resource use during the exposure window before death (a median of 17 days before death) is shown for the patients in the matched cohort. ED, emergency department; ICU, intensive care unit.

For a sensitivity analysis, we retained patients dying in the month of their diagnosis in the analysis, which resulted in a sample of 9,656 patients and 2,511 pairs after multilevel matching. Doing so, NCI comprehensive status (OR, 1.11; 95% CI, 0.92 to 1.32) and gastroenterology consultation (OR, 1.03; 95% CI, 0.86 to 1.23) were no longer associated with hospice use. The reduction of acute health care utilization by hospice was not changed: hospice patients were significantly less likely to be hospitalized (7.3% *v* 44%; RR, 0.16; 95% CI, 0.14 to 0.16); have an ICU stay (2.8% *v* 22.0%; RR, 0.13; 95% CI, 0.10 to 0.16); and die in the hospital (3.7% *v* 59.7%; RR, 0.06; 95% CI, 0.05 to 0.08).

DISCUSSION

In this population-based study of Medicare beneficiaries, we found that 63% of patients with HCC used hospice services before death. Although the median time from initial hospice claim to death was only 17 days, hospice use over this short

period was still associated with a marked decline in ED visits, hospitalizations, ICU stays, and in-hospital or nursing home deaths. In addition to confirming previously identified differences in use of hospice by sex, race, and rural residence,[24] we found that the type of initial treatment received and consultation with an oncologist in the last months of life were strong predictors of hospice use.

Our findings in HCC should be taken in the context of two recently published articles, which thoroughly evaluated health care use (including hospice) and place of death among cancer patients with Medicare dying in the modern era.[5,18] The 60% rate of hospice referral, short duration of hospice enrollment, and reduction in acute care services among patients with HCC with Medicare are in line with what was reported in a large cohort of Medicare patients who died in 2011 with poor-prognosis cancers.[5] A notable difference in HCC, however, was the marked reduction for in-hospital death between hospice users and the comparison group, with a nearly 60% rate of in-hospital or nursing facility death for those patients not referred to hospice compared with only 3% of hospice users. For comparison, a recent international evaluation of the place of death found that only 26% of deaths among elderly US patients with cancer occur in the hospital or a skilled nursing facility.[18]

Because of the limitations of this observational data set, we do not have data on the severity of cancer nor the severity of liver disease in the time leading up to death; therefore, we are unable to determine whether patients died of cancer or ESLD. This is an important limitation because determining which patients with ESLD should be considered for hospice referral in the absence of HCC is difficult,[8] and we would expect lower rates of hospice use and greater rates of hospitalization among patients dying predominantly from ESLD. An imbalance in ESLD deaths could partially account for the difference in hospitalizations and in-hospital deaths between the hospice and comparison groups, however, after multilevel matching, the hospice and nonhospice comparison groups were balanced on tumor extent at diagnosis and treatment also had similarly short median survivals, which suggests any such imbalance is likely to be small.

We must also consider that many patients with cirrhosis do not receive ongoing care for their liver disease or screening for HCC,[25] and these patients may discover their cancer diagnosis at the time of decompensation from ESLD before death. This reality is likely reflected in the large proportion of patients in our cohort before restriction who were diagnosed in the month of their death (13% hospice, 24% nonhospice comparison group). Because such patients are often acutely ill with a high rate of in-hospital mortality,[26] we excluded patients dying in the month of their diagnosis from our primary analysis of hospice use. By doing so, we narrowed the scope of our research question to a slightly better prognosis group of patients with HCC. However, in sensitivity analyses in which we retained these patients, the findings were remarkably similar. Thus, the in-hospital death imbalance is not solely attributable to a larger number of critically ill patients with decompensated ESLD too unstable for transfer to home hospice. Rather, we hypothesize that the marked difference in in-hospital deaths between groups might reflect that the considerable symptom burden of patients with advanced liver cancer is too complex for caregivers to manage at home without additional support such as that offered by hospice. Further work to elucidate the needs of patients with ESLD and HCC at the end-of-life—and the needs of their caregivers—is clearly warranted.

We hypothesized that because of the unique characteristics of the treating disciplines and the pivotal role of liver transplantation in HCC, health system characteristics would be associated with hospice use at the end of life. Despite the fact that all patients in this cohort died, patients initially treated with liver-directed therapy (regardless of subsequent treatment) were significantly less likely to be referred to hospice. Given that few of these patients had liver transplantation or resection, and the same was true of both resected patients and patients with transarterial chemoembolization/radioembolization, our finding is unlikely to represent unrelated death in patients cured of their HCC. Rather, we believe this finding supports our hypothesis that the unique process of care in HCC—in which providers whose specialty is not cancer specific take a leading role—does influence hospice referral at the end of life. Furthermore, receipt of care at an NCI-designated cancer center (regardless of provider seen) and consultation with a medical oncologist were strongly associated with hospice referral, whereas patients seen at liver transplant centers were not more likely to be referred to hospice. Further evaluation of how to increase cancer-focused palliative care in the unique multidisciplinary structure of HCC care is warranted.

In summary, we found that patients with HCC enrolled in hospice were less likely to undergo hospitalization or ICU stays at the end of life and markedly less likely to die in the hospital

than patients with HCC who were never enrolled in hospice. Given the high cost of in-hospital care, efforts to expand hospice use to a greater proportion of patients with HCC are likely to be cost neutral or even cost saving. JOP

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Hospice Utilization and Its Effect on Acute Care Needs at the End of Life in Medicare Beneficiaries With Hepatocellular Carcinoma

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Appendix

Table A1. Characteristics of Patients With Hepatocellular Carcinoma After Multilevel Matching

Characteristic*	Hospice (n = 2,323) No. (%)	No Hospice (n = 2,323) No. (%)
Age, years		
Median (Q1, Q3)	72 (66, 78)	71 (66, 78)
< 64	506 (22)	527 (23)
65-74	937 (40)	931 (40)
≥ 75	880 (38)	865 (37)
Sex		
Male	1,645 (71)	1,700 (73)
Female	678 (29)	623 (27)
Race		
White	1,616 (70)	1,603 (69)
Black	252 (11)	252 (11)
Asian	218 (9)	222 (10)
Other	237 (10)	246 (11)
Tumor extent at diagnosis		
Single lesion	1,047 (45)	1,037 (45)
Multiple, no vascular invasion	749 (32)	752 (32)
Multiple with vascular invasion	180 (8)	187 (8)
Extension beyond liver	347 (15)	347 (15)
Survival (months)		
Median (Q1, Q3)	9 (3, 22)	8 (3, 21)
Diagnosis to Hospice (days)		
Median (Q1, Q3)	229 (80, 610)	212 (69, 575)
Hospice to death (days)		
Median (Q1, Q3)	17 (5, 46)	17 (5, 46)
Initial treatment		
Curative surgery	115 (5)	131 (6)
Ablation	161 (7)	130 (6)
TACE	589 (25)	612 (26)
TARE	67 (3)	45 (2)
Sorafenib	193 (8)	170 (7)
Radiation	68 (3)	51 (2)
Other drug therapy	82 (4)	86 (4)
Never treated	1,048 (45)	1,098 (47)
Hepatitis B†	120 (5)	130 (6)
Hepatitis C	581 (25)	634 (27)
Alcohol	260 (11)	295 (13)
Other cause of liver disease	264 (11)	276 (12)

(continued in next column)

Table A1. Characteristics of Patients With Hepatocellular Carcinoma After Multilevel Matching (continued)

Characteristic*	Hospice (n = 2,323) No. (%)	No Hospice (n = 2,323) No. (%)
No. of liver comorbidities		
0	1,645 (71)	1,544 (66)
1	362 (16)	427 (18)
≥ 2	316 (14)	352 (15)
Modified Charlson score		
0	875 (38)	842 (36)
1	445 (19)	432 (19)
2+	1,003 (43)	1,049 (45)
Prior AFP screening		
0	1,470 (63)	1,508 (65)
1	408 (18)	395 (17)
2+	445 (19)	420 (18)
Census tract		
Metro	2,068 (89)	2,028 (87)
Urban	118 (5)	110 (5)
Rural	137 (6)	185 (8)
Census tract % < poverty		
1st quartile (lowest)	594 (26)	542 (24)
2nd quartile	587 (26)	560 (24)
3rd quartile	561 (24)	575 (25)
4th quartile (highest)	554 (24)	627 (27)

Abbreviations: AFP, alpha-fetoprotein; TACE, transarterial chemoembolization; TARE, transarterial radioembolization.

*Groups were also balanced on era of diagnosis (pre/post 2007), SEER region, marital status. Data not shown here for brevity.

†Causes of liver disease are not mutually exclusive and do not sum to 100%.