
Referral Patterns and Treatment Choices for Patients with Hepatocellular Carcinoma: A United States Population-Based Study

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- BACKGROUND:** Patterns of care of physician specialists may differ for patients with hepatocellular carcinoma (HCC). Reasons underlying variations are poorly understood. One source of variation may be disparate referral rates to specialists, leading to differences in cancer-directed treatments.
- STUDY DESIGN:** Surveillance, Epidemiology, and End Results (SEER)-linked Medicare database was queried for patients with HCC, diagnosed between 1998 and 2007, who consulted 1 or more physicians after diagnosis. Visit and procedure records were abstracted from Medicare billing records. Factors associated with specialist consult and subsequent treatment were examined.
- RESULTS:** There were 6,752 patients with HCC identified; 1,379 (20%) patients had early-stage disease. Median age was 73 years; the majority were male (66%), white (60%), and from the West region (56%). After diagnosis, referral to a specialist varied considerably (hepatology/gastroenterology, 60%; medical oncology, 62%; surgery, 56%; interventional radiology [IR], 33%; radiation oncology, 9%). Twenty-two percent of patients saw 1 specialist; 39% saw 3 or more specialists. Time between diagnosis and visitation with a specialist varied (surgery, 37 days vs IR, 55 days; $p = 0.04$). Factors associated with referral to a specialist included younger age (odds ratio [OR] 2.16), Asian race (OR 1.49), geographic region (Northeast OR 2.10), and presence of early-stage disease (OR 2.21) (all $p < 0.05$). Among patients with early-stage disease, 77% saw a surgeon, while 50% had a consultation with medical oncologist. Receipt of therapy among patients with early-stage disease varied (no therapy, 30%; surgery, 39%; IR, 9%; chemotherapy, 23%). Factors associated with receipt of therapy included younger age (OR 2.48) and early-stage disease (OR 2.20).
- CONCLUSIONS:** After HCC diagnosis, referral to a specialist varied considerably. Both clinical and nonclinical factors were associated with consultation. Disparities in referral to a specialist and subsequent therapy need to be better understood to ensure all HCC patients receive appropriate care. (J Am Coll Surg 2013;217:896–906. © 2013 by the American College of Surgeons)
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Hepatocellular carcinoma (HCC) is the most common primary liver cancer and is the third leading cause of cancer mortality.^{1,2} In the United States, the incidence is 4.9 per 100,000 and has been steadily rising at a rate

of 4.5% per year for the last 3 decades.² In men, HCC is the fastest growing cause of cancer-related death. Most patients with HCC are over age 65, and the highest age-specific rates occur among persons aged 75 and older.³ Surgery is the only curative treatment for HCC. However, most patients are not surgical candidates due to advanced disease at presentation or prohibitive comorbidities. Therefore, treatment often presents a challenge and entails a multidisciplinary approach. Nonsurgical therapeutic options for patients include chemotherapy, ablation, and interventional radiologic (IR) procedures such as transarterial chemoembolization (TACE) or bland embolization (TAE). Although the treatment options for patients with advanced HCC have increased over the last couple of decades, the overall survival of patients with

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Abbreviations and Acronyms

HCC	=	hepatocellular carcinoma
HR	=	hazard ratio
IR	=	interventional radiology
OR	=	odds ratio
SES	=	socioeconomic status
TACE	=	transarterial chemoembolization
TAE	=	bland embolization

HCC remains dismal, with a cause-specific survival of less than 50% at 1 year.²

The use of cancer-directed treatments is multifactorial and is related to both clinical and nonclinical factors. Variation in treatment recommendations have been associated with race, age, socioeconomic status (SES), health insurance status, type of institution, and geographic region, which, in turn, may account for differences in survival.⁴⁻¹⁰ Disparities in access to treatment for HCC have been noted in the literature, but involved relatively small sample sizes, single institutions,^{11,12} regional experiences,¹³ and primarily focused on 1 treatment modality (ie, transplantation or hepatectomy). Recently, our group reported survey-based data that demonstrated how both clinical and nonclinical factors affect physician decision-making in the treatment of patients with HCC.¹⁴⁻¹⁶ These data suggested that a subset of patients with early-stage HCC may not be offered curative intent treatment.¹⁴⁻¹⁶ Earle and colleagues⁴ proposed studying disparities in the receipt of treatment as a 2-step process that involves studying patterns of referral to a specialist and subsequent treatment of referred patients. This model has been used in lung, esophageal, and ovarian cancers.^{4,17,18} Due to the paucity of comprehensive information on factors affecting referral and receipt of treatment for HCC, we used the 2-step process proposed by Earle and associates⁴ to explore disparities in referral patterns, treatment choices, and outcomes in a population-based sample of patients with HCC, using the SEER-linked Medicare database.

METHODS

Patients

We queried the SEER-linked Medicare database for patients with a diagnosis of pathologically confirmed HCC between January 1, 1998 and December 31, 2007. Details of the SEER-Medicare database and linkage techniques have been described.¹⁹⁻²¹ Exclusion criteria included patients with less than 1 year of Medicare coverage in parts A and B, enrollment in an HMO plan in the 12 months preceding the diagnosis, diagnosis of a primary cancer other than HCC within 5 years of HCC diagnosis, enrollment in Medicare due to disability

or end-stage renal disease, and patients who survived less than 30 days after HCC diagnosis. The final cohort consisted of 6,752 patients.

Physician consultation information in the 180 days around the time of diagnosis was obtained from Medicare provider files. Physicians were categorized as primary care physicians (general practitioner, family practice, internal medicine, geriatric medicine), gastroenterologists, surgeons (general surgeon, surgical oncologist, transplant surgeon), medical oncologists (hematologist, medical oncologist), radiation oncologists, and interventional radiologists.²² In order to reduce variability of specialty designation in the billing records, we attributed 1 specialty designation to each physician identifier (UPIN). Gastroenterologists and medical oncologists billing elsewhere under a primary care specialty designation were given their specialty designation for all bills. Patients who received surgery, TACE/TAE, or chemotherapy were, by definition, seen by a surgeon, interventional radiologist, or medical oncologist, respectively.¹⁷ We reviewed the billing records of patients not undergoing surgery to determine if they had ever been seen by a physician who had billed for a liver resection or transplantation, to ensure that surgeons with and without specialty designation in Medicare would be captured.^{4,17}

Treatment-related information was obtained from inpatient, outpatient, and provider files. Patients undergoing transplantation or resection on the liver were considered to have had curative intent surgery for HCC. Information on surgery not recorded in the Medicare database was abstracted from the SEER "surgery of primary site" variable. Information on IR procedures (TACE/TAE) and chemotherapy was extracted only from the Medicare database in the 6 months after diagnosis of HCC.

The Elixhauser comorbidity score was used to quantify comorbidity burden.²³ Comorbidities were extracted using standard procedures from the inpatient and outpatient claims for each patient. A numerical comorbidity score was calculated²⁴ and categorized as "high" if the score was ≥ 7 (corresponds to the 75th percentile cutoff in this cohort). Information on liver-related conditions relevant to the etiology, treatment, and prognosis of HCC including hepatitis C virus status, hepatitis B status, nonalcoholic cirrhosis, portal hypertension, and alcoholic liver disease was abstracted from the Medicare files based on ICD-9 codes.¹⁵

Demographic characteristics include age at diagnosis, sex, race (non-Hispanic white, black, Asian, Hispanic white, other), census region (Northeast, West, Midwest, South), and SES. We classified SES into quintiles of income using established techniques,²⁰ and further classified into top 3 or bottom 2 quintiles.

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