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# Utilization of Surveillance for Hepatocellular Carcinoma among Patients with Cirrhosis in the United States

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## Abstract

**Background—**Surveillance for hepatocellular carcinoma (HCC) in patients with cirrhosis is recommended but may not be performed. The extent and determinants of HCC surveillance are unknown.

**Methods—**We conducted a population-based US cohort study of those over 65 years of age to examine utilization and determinants of pre-diagnosis surveillance in patients with HCC who were previously diagnosed with cirrhosis. Patients diagnosed with HCC during 1994-2002 were identified from the linked Surveillance, Epidemiology, and End-Results registry-Medicare databases. We identified alpha-fetoprotein and ultrasound tests performed for HCC surveillance, and examined factors associated with surveillance.

**Results—**We identified 1,873 HCC patients with a prior diagnosis of cirrhosis. In the 3 years before HCC, 17% received regular surveillance and 38% received inconsistent surveillance. In a subset of 541 patients in whom cirrhosis was recorded for 3 or more years prior to HCC, only 29% received routine surveillance and 33% inconsistent surveillance. Among all patients who received regular surveillance, approximately 52% received both alpha-fetoprotein and ultrasound, 46% received alpha-fetoprotein only, and 2% received ultrasound only. Patients receiving regular surveillance were more likely to have lived in urban areas and had higher incomes than those who did not receive surveillance. Before diagnosis, approximately 48% of patients were seen by a gastroenterologist/hepatologist or by a physician with an academic affiliation; they were approximately 4.5-fold and 2.8-fold, respectively, more likely to receive regular surveillance than those seen by a primary care physician only. Geographic variation in surveillance was observed and explained by patient and physician factors.

**Conclusions—**Less than 20% of patients with cirrhosis who developed HCC received regular surveillance. Gastroenterologists/hepatologists or physicians with an academic affiliation are more likely to perform surveillance.

### Keywords

Hepatocellular carcinoma; cirrhosis; AFP; ultrasound; surveillance

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## INTRODUCTION

The incidence of hepatocellular carcinoma (HCC) in the United States has more than doubled during the past two decades. (1) This increase is at least partially attributable to a rise in hepatitis C virus (HCV)-related HCC. (2-5) Although most patients diagnosed with HCC are diagnosed at an advanced stage of disease when survival is poor (5-year survival less than 5%), when patients receive potentially curative therapy in the form of liver transplant, surgical resection, or tumor ablation, a considerable improvement in survival has been observed (5 years, ranging between 40% and 70%). (6) However population-based studies in the United States indicate that only 11% of patients with HCC receive these potentially curative treatments. (7;8) Therefore, surveillance for HCC has been advocated to detect HCC at an early stage, when critical treatment can be applied.

A survey study that was conducted in 1998 reported that 84% of hepatologists regularly perform surveillance in patients with cirrhosis. (9) Guidelines disseminated from several consensus conferences beginning in 1991 and subsequently professional organizations recommend HCC surveillance in patients with cirrhosis who are at high risk of developing HCC. (10-16) Ultrasound and serum alpha-fetoprotein (AFP) are the most commonly used modalities for HCC surveillance. One randomized, placebo-controlled trial, as well as several observational cohort and case-control studies, have shown that patients who undergo HCC surveillance have an earlier stage of HCC at diagnosis, greater use of potentially curative therapy, and significant reduction in overall as well as cancer-specific mortality compared with patients detected with symptomatic HCC. (17-24)

The extent of utilizing HCC surveillance in clinical practice is unclear. Two small studies found very low rates of surveillance among patients diagnosed with HCC. (25;26) For example, we previously reported that less than one third of patients diagnosed with HCC at three Veterans Affairs medical centers during 1998-2003 received any HCC surveillance prior to their HCC diagnosis. (25) However, this study and others were limited by a relatively small sample size and inclusion of, predominantly, male veterans. (25;26)

To evaluate HCC surveillance in a larger and more representative sample, we have used data obtained from the linked Surveillance, Epidemiology, and End-Results (SEER) - Medicare claims to evaluate the utilization of pre-diagnosis HCC surveillance among patients with HCC who had a prior diagnosis of cirrhosis. We also examined several potential determinants of HCC surveillance, including patient, clinical, and physician factors.

## METHODS

### Data source

The SEER-Medicare dataset is SEER registry data linked with Medicare claims. Since 1988, the SEER program has collected data on incident cancer cases from 11 cancer registries in five states (Connecticut, Hawaii, Iowa, New Mexico, and Utah) and six metropolitan areas (Los Angeles, San Francisco/Oakland, San Jose, Detroit, Seattle, and Atlanta) that account for approximately 14% of the population in the United States. (27) Rural Georgia was added in 1992. In 2000, five new registry sites (Rural Georgia, Greater California, Kentucky, Louisiana, and New Jersey) were added. Consequently, the catchment area for the SEER registries currently accounts for over 25% of the population in the United States. (28) Medicare is the primary health insurer for approximately 97% of individuals age 65 years and older in the United States. Approximately 95% of Medicare beneficiaries are covered by both Part A (inpatient hospitalizations) and Part B (outpatient visits and physician office visits/services) benefits.

Data on physician characteristics (physician specialty, practice arrangement, and year of graduation) were obtained from the American Medical Association Master File (www.ama-assn.org). This database contains information on physicians who have met the educational and credentialing requirements necessary for recognition as physicians in the United States.

## Study population

All patients age 65 years and older diagnosed with HCC during 1994-2002 in one of the 16 SEER registries were eligible for inclusion in this study. *International Classification of Diseases-Oncology* histology code 8170 was used to identify patients with possible HCC. Only patients with diagnostically confirmed HCC (positive histology, cytology, laboratory test/marker, direct visualization or positive radiology tests) were eligible for inclusion. To include patients with equal exposure periods to HCC surveillance, we selected only those with continuous enrollment in Medicare Parts A and B for 3 years prior to their HCC diagnosis. We excluded patients enrolled in Medicare health maintenance organizations (HMOs) during this time period because Medicare HMO plans have not been required to submit individual claims for specific services to the Centers for Medicare and Medicaid Services. (27) HCC patients with a previously recorded diagnosis of cirrhosis were identified from Medicare claims files using previously validated ICD-9 codes (571.2, 571.5 or 571.6). (29)

## HCC surveillance tests

Current Procedural Terminology (CPT) codes were used to identify all AFP (CPT code: 82105) and ultrasound (CPT codes: 76700 and 76705) tests recorded during the 3 years prior to the HCC diagnosis date. However, AFP and ultrasound tests performed for surveillance purposes cannot be directly identified from administrative databases.

**Development and validation of HCC surveillance algorithm—**To identify tests performed for HCC surveillance (distinct from other purposes), we applied an algorithm that incorporates diagnosis and procedure codes in administrative data. We selected 788 AFP and 794 ultrasound tests performed at two large urban hospitals located in Houston, TX and Kansas City, MO. Tests were selected randomly from patients who received an AFP or ultrasound tests in these two hospitals during 2000-2003. We reviewed the medical records to determine the purpose (HCC surveillance or not) of each test, based on the information contained in the progress notes and test request forms. We considered several variables available from administrative databases that serve as potential predictors, including patient demographics, comorbidities, acute and chronic symptoms, and HCC risk factors, as well as receipt of laboratory tests, liver biopsy, and liver imaging studies within two years prior to the AFP or ultrasound test of interest.

We conducted a factor analysis to identify a reduced set of 9 components (groups of variables) using established criteria (30) (Table Supplement). Factor scores were calculated and used in logistic regression models to predict whether AFP or ultrasound tests were performed for surveillance purposes. Variables included in the final AFP model were: substance abuse, receipt of an alkaline phosphatase or bilirubin test, receipt of a serum lactic dehydrogenase (LDH) test, HCV, non-alcoholic hepatitis, diabetes, prothrombin time, ultrasound or CT scan within 90 days of AFP, diagnosis of HCC within 60 days, esophageal varices without bleeding, and HBV. Variables included in the final ultrasound model were: substance abuse, receipt of liver function tests or prothrombin time, HCV, unspecified hepatitis, liver biopsy, AFP within 90 days, diagnosis of HCC within 60 days, esophageal varices, HBV, and CT scan within 90 days of US. From the developmental model, the c-statistics for the AFP and ultrasound models were 0.83 and 0.74, respectively. To validate these models, we used a leave-out-one cross-validation method. (31) From the

crossvalidation, c-statistics for the AFP and ultrasound models were 0.81 and 0.71, respectively.

**Applying the HCC surveillance algorithm to the study cohort—**The logistic regression models described above were used to calculate the predicted probability of surveillance for each AFP and ultrasound test in the study cohort. A Monte Carlo procedure with 1,000 iterations was then used in which the surveillance status variable for each test was imputed with the binomial variables 0 or 1 according to the predicted probability of surveillance obtained from the logistic regression model. (32;33)

Patients were categorized into three mutually exclusive groups as receiving regular surveillance (had an annual AFP and/or ultrasound test during at least 2 of the 3 years prior to HCC diagnosis), inconsistent surveillance (had one or more AFP or ultrasound tests for surveillance purposes during the 3 years prior to HCC diagnosis but did not meet the criteria for regular surveillance), or no surveillance. Surveillance was examined as a trichotomous outcome variable in regression models. Models estimates and standard errors (and hence chi-square and Wald statistics) calculated. (34)

## Patient characteristics

We collected information on year of HCC diagnosis (1994-1996, 1997-1999, 2000-2002), age, gender, and race (white, black, Hispanic, other race). We obtained education and income data from US Census files that correspond to patient residence zip code level. The proportion of patients with a high school education and median income within a zip code was used as a proxy for patient education and income levels, respectively. Information on HCV, hepatitis B virus (HBV), alcoholic liver disease, hemochromatosis and duration of cirrhosis, as well as conditions used to calculate the Klabunde co-morbidity index score (35), and severity of cirrhosis (Child A or B, Child C) using a previously developed algorithm (7) were obtained. The Klaubunde co-morbidity index score is comprised of 14 conditions, where each condition is assigned a weight according to its potential for influencing mortality. The index is constructed by multiplying each condition indicator by the corresponding estimated coefficient for the condition. The sum of all weighed conditions is then totaled to yield an overall co-morbidity summary score for each patient. (35) We also examined number of physician encounters within the 3-years prior to HCC diagnosis.

## Physician characteristics

We collected information from the American Medical Association Master File on physician specialty, practice arrangement, and year of graduation. Patients were categorized as seen by an internal medicine or family practice physician only, gastroenterologist or hepatologist only, both an internal medicine or family practice physician and gastroenterologist or hepatologist, or neither. In addition, a primary physician was assigned for each patient as the provider with the highest total amount of reimbursement and number of visits. There was a high agreement (76.9% concordance) in our cohort between physician with the highest number of visits and physicians with total amount of reimbursement. The specialty of the primary physician was categorized as internal medicine or family practice, gastroenterology or hepatology, or other specialty. Practice arrangement of the primary physician was categorized as solo, group, hospital based, medical school affiliated, and other (locum tenens or HMO affiliated). Year of medical school graduation of the primary physician was also captured and examined in quartiles.

## Statistical analysis

We compared patients who received regular surveillance, inconsistent surveillance, and no surveillance, for demographic and clinical features, physician characteristics, and SEER

geographic regions. Univariate and multivariate logistic regression analyses were used for these comparisons. (36) As described above, we examined a trichotomous outcome variable (regular surveillance, inconsistent surveillance, and no surveillance) and estimated adjusted odds ratios with respect to contrasts among the levels of this variable. Each general physician characteristic (specialty of primary physician, physicians seen during the past 3 years, practice arrangement, year of graduation) was examined in a separate model, adjusting for patient factors. The association between receipt of HCC surveillance and SEER registry was examined initially in an unadjusted model and subsequently in models including patient factors and physician characteristics to explain associations observed in the unadjusted model. Wald chi-square tests were used in the model-development process and in assessing the significance of predictor variables. Odds ratios and 95% confidence intervals were calculated for each parameter estimate. All models were tested for interactions.

The study protocol was approved by the Institutional Review Board of Baylor College of Medicine and the office of Human Subjects Research of the National Institutes of Health.

## RESULTS

We identified 1,873 patients diagnosed with HCC who had a prior diagnosis of cirrhosis during 1994-2002 who fulfilled our inclusion criteria. The mean age at HCC diagnosis was 74.9 years. Most patients were men (65.7%). The largest proportion of patients was white (81.8%), followed by Hispanic (12.1%), Asian (9.4%), and black (7.9%). Approximately 25% had a previous diagnosis of alcoholic liver disease, 28% had HBV or HCV, and 16% had both alcoholic liver disease and hepatitis. Approximately 37% had a recorded diagnosis of cirrhosis for more than 2-years prior to their HCC diagnosis. The mean number of physician visits within the 3-years prior to HCC was 67.9 (s.d.=42.4)

Only 17% (n=321) of patients had received regular HCC surveillance, and an additional 38% (n=710) had received inconsistent surveillance. Among patients who had received at least one surveillance test, the median number of surveillance tests per patient was 4.0 ($1^{st}$ and $3^{rd}$ quartiles: 2.7, 5.3). Among 541 patients diagnosed with cirrhosis 3 or more years prior to HCC diagnosis, only 29% received routine surveillance, 33% inconsistent surveillance, while 38% had no surveillance.

Among all patients who had received regular surveillance, approximately 52% had received a combination of AFP and ultrasound, 46% had received AFP only, and 2% had received ultrasound only. Among those who received inconsistent surveillance, approximately 69% had received AFP only, 15% had received ultrasound only, and 15% had received both tests. Only 59 patients (3.2%) received an MRI and 1,295 patients (69.1%) a CT scan within the 3-years prior to their HCC diagnosis. If we reapply our definition of routine, inconsistent, and no surveillance to include all AFP, ultrasound, CT scans, and MRI tests irrespective of the intention of the test, we observe higher rates of routine surveillance (46.3%). If we exclude CT scans and MRI tests performed within 6 months prior to HCC diagnosis, which would have a higher likelihood of being performed for diagnostic purposes, the proportion of patients who received routine surveillance defined by any AFP, ultrasound, CT, or MRI was 43.9%.

Patients who had received regular surveillance were more likely to be younger ($p<0.001$), female ($p=0.006$), Chinese or other race ($p<0.001$), and diagnosed during more recent years ($p<0.001$) than those who had not received surveillance (Table 1). Those having a recoded diagnosis of cirrhosis for a longer duration prior to their HCC diagnosis were also more likely to receive surveillance ($p<0.001$). Only 9.8% of patients with alcoholic liver disease (in the absence of HCV or HBV) received HCC surveillance compared to 28.5% of patients

with HCV or HBV and 32.2% of patients with both alcoholic liver disease and HCV or HBV. Patients with HCC in the absence of HCV, HBV, or alcohol were least likely to receive surveillance (4.9%).

Patients living in zip codes with higher median incomes and larger proportions of residents with more than a high school education were more likely to receive regular HCC surveillance than those living in lower to median income regions or with less than a high school education ($p<0.001$ and $p=0.003$, respectively). Patients with a greater number of physician visits within the 3-years prior to their HCC diagnosis were more likely to receive HCC regular surveillance compared to patients with fewer physician visits ($p<0.001$).

The distribution of physician factors among patients in our study cohort is presented in Table 2. Approximately 48% of patients were seen by a gastroenterologist (n=722) or hepatologist (n=116), or both (n=67) at least once during the 3 years prior to their date of HCC diagnosis. Approximately 58% were seen by an internal medicine or family practice physician at least once during the 3 years prior to their HCC diagnosis, and 21% were seen by another specialist only (e.g., cardiology, endocrinology, rheumatology). Almost 32% of patients had an internal medicine or family practice physician as their primary physician prior to their HCC diagnosis, 22% had a gastroenterologist or hepatologist, and 32% had a primary physician in another specialty. Approximately 46% of primary physicians were in a group practice setting, 22% were in solo practice, and 3% were affiliated with a medical school.

Patients seen by a gastroenterologist or hepatologist alone or in combination with an internal medicine or family practice physician were approximately 5 times more likely to receive regular surveillance than those seen by an internal medicine or family practice physician only. Further, a greater proportion of patients whose primary care physician was a gastroenterologist received regular surveillance or at least one surveillance test ($p<0.001$) than patients whose primary physician was internal medicine or family practice. Patients having a physician affiliated with a medical school or who graduated from medical school during a more recent time period were also more likely to receive regular surveillance ($p=0.0004$ and 0.0074, respectively) than other patients.

These associations between receipt of surveillance and physician characteristics persisted in a multivariable logistic regression analysis adjusting for several patient and clinical factors (Table 3). Patients seen by a gastroenterologist or hepatologist only or in combination with an internal medicine or family practice physician were 2.8 and 4.5 times, respectively, more likely to receive regular surveillance than patients seen by an internal medicine or family practice physician only. Patients whose primary physician had an academic affiliation were over 3 times more likely to receive regular surveillance than patients seen by physicians in solo practice.

We found several significant differences among SEER regions in the receipt of regular surveillance in the unadjusted analysis. The Los Angeles registry had the highest percentage of patients who had undergone regular surveillance (26%). Other registries significantly lower than Los Angeles were Atlanta (OR=0.35; 95% CI: 0.15-0.81), Connecticut (OR=0.25; 95% CI: 0.12-0.51), Detroit (OR=0.50; 95% CI: 0.29-0.84), Iowa (OR=0.37; 95% CI: 0.18-0.74), Kentucky (OR=0.33; 95% CI: 0.11-0.99), and New Mexico (OR=0.13; 95% CI: 0.04-0.44). Most geographic differences were explained by patient and provider factors. In a model adjusting for demographic and clinical factors, only patients residing in the SEER regions of Connecticut and New Mexico remained significantly less likely to receive regular surveillance. After further adjusting for specialty of physicians seen during

the past 3 years, we found no significant differences in regular surveillance remaining among SEER regions (data not shown).

## DISCUSSION

Several consensus conferences as well as two professional organizations have recommended regular HCC surveillance for patients with cirrhosis who are at risk of developing HCC. (10-16) Findings from this study suggest that these recommendations have not been well adopted into clinical practice. In this population-based study, fewer than 20% of HCC patients with previously recorded cirrhosis received the recommended regular surveillance. Approximately 69% of these patients had HCV, HBV, or alcoholic liver disease recorded prior to their HCC diagnosis. Patients who were younger, Asian, diagnosed during more recent years, living in zip codes with higher income or education or in urban areas were more likely to have received regular surveillance than other groups. Women were also more likely to receive regular surveillance, which is consistent with other published findings from large database studies. (37) Patients seen by a gastroenterologist or hepatologist or by physicians affiliated with medical schools were significantly more likely to have received regular surveillance than patients seen by other types of physicians and in other practice settings. Significant geographic variations were observed in the rates of surveillance, but these were mostly explained by patient as well as physician related factors.

Results from our sensitivity analyses confirmed the generally low utilization of HCC surveillance. First, when all AFP and ultrasound tests were counted as surveillance irrespective of intent, the rates of regular and inconsistent surveillance improved to 35% and 50%, respectively. While these figures overestimate the true prevalence of HCC surveillance, they remain relatively low. Second, we estimated HCC surveillance in a subset of patients with diagnosed cirrhosis for 3 or more years prior to HCC diagnosis. The rate of routine surveillance remained low (29%) among these patients.

The findings from this study pertained to practices during 1994 to 2002. Most of the consensus conference statements recommending HCC surveillance were published between 1991 and 2001. (10;12;13;16) Approximately 53.7% of the study sample was diagnosed in 2000-2002 (after the consensus conferences) and in these patients regular and inconsistent surveillance was recorded in 20.6% and 37.7%, respectively. A survey in 1998 indicated that most hepatologists claimed that they preformed regular surveillance for HCC. (9) It is difficult to reconcile these self reported practices with real life practices; the survey could have suffered from selection bias, and the otherwise known self reported exaggeration of compliance with recommended practices. Further, a poor dissemination of the knowledge on how to best utilize surveillance is further evidenced by the high prevalence of Child C class patients who received regular surveillance. A recent study found that HCC surveillance becomes futile in patients with advanced cirrhosis not listed for transplantation. (38) Given that the two “corner stone” international guidelines for HCC management were released in 2001 (EASL) and in 2005 (AASLD), it is possible that HCC routine HCC surveillance study has progressively improved during more recent years. Indeed this study found that an increasing proportion of patients who received “regular” surveillance over time (from 9% in 1994-1996 to 21% in 2000-2002) while the proportion of patients who received inconsistent surveillance did not change over time.

Regular surveillance was less frequently observed in rural areas. Much of the geographic variation observed was explained by patient demographic and clinical factors. New Mexico, Utah, and rural Georgia had the lowest regular surveillance rates, with fewer than 5% of HCC patients with cirrhosis residing in these regions receiving regular surveillance. The absence of overt signs and symptoms of liver disease, failure to identify and record them,

and/or failure to attach the proper relevance in terms of HCC risk are all possible explanations. In addition, reduced access to care in rural areas likely contributed to the lower rates of surveillance observed in some areas.

Although generally low, regular HCC surveillance was significantly more common in academic or medical school settings than in community based practices. Patients who were seen by a gastroenterologist or hepatologist were significantly more likely to receive regular surveillance than patients seen by internal medicine or family practice physicians. Reasons for these findings are unknown but could include limited or outdated knowledge, lack of financial incentive, limited infrastructure for providing follow-up reminders, lack or limited access to appropriate testing for positive or equivocal surveillance results (e.g., magnetic resonance imaging), and limited access to referral for potentially curative therapy (e.g., liver transplantation, radiofrequency ablation). This finding suggests that patients with known liver disease should be referred to appropriate specialties.

The study findings should be interpreted within its possible limitations. First, HCC surveillance tests cannot be directly identified from administrative data. We developed and validated an algorithm with good predictive value to identify both AFP and ultrasound tests performed for surveillance purposes. Nevertheless, misclassification is still possible although, given the very low prevalence of surveillance, the effect of misclassification on the overall findings is likely to be minimal. Second, we were unable to capture physician intention or recommendation to perform a surveillance test and the patients' responses or adherence to these recommendations. Only tests that were actually performed could be identified using our data source, but not tests that were requested but not performed. These issues need to be examined in future studies. Third, the study cohort included only Medicare-enrolled patients who were 65 years and older; and, therefore, findings may not be generalizable to younger patients. A similar study in younger patients could provide fairly different results, as we found that relatively younger individuals in our cohort were more significantly likely to receive regular surveillance as compared to older age groups. However, these limitations are outweighed by the large numbers of patients identified with HCC from the 16 community-based regions across the country, as well as the highly valid and complete cancer and testing data in SEER-Medicare. In addition, results from SEER public access data indicated that 60% of all HCC patients are age 65 and older; thus, our study cohort is representative of a large and relevant segment of patients with HCC.

In conclusion, the use of recommended HCC surveillance is generally low. In addition to patient demographic and clinical characteristics, physician specialty and practice arrangement were highly associated with regular HCC surveillance. Future studies are needed to evaluate the knowledge, attitudes and barriers for HCC surveillance and to develop appropriate, targeted interventions to increase the dissemination of this practice.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

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| **AFP** | Alpha-fetoprotein |
| **CT** | computed tomography |
| **HCC** | hepatocellular carcinoma |
| **VA** | Veterans Administration |

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**Table 1**

A comparison of patient demographic and clinical factors among three groups of HCC patients with a prior diagnosis of cirrhosis who received regular HCC surveillance, at least one HCC surveillance test but no regular surveillance, or no HCC surveillance in the 3 years prior to their HCC diagnosis. (N=1,873)

| | Overall (%) | Regular surveillance* (%) | Inconsistent surveillance** (%) | No surveillance (%) | P Value for regular surveillance vs. no surveillance*** |
|---|---|---|---|---|---|
| **Total** | 1873 (100.0) | 321 (17.1) | 710 (38.0) | 842 (44.9) | |
| Mean age at HCC diagnosis (s.d.) | 74.9 (5.5) | 73.7 (4.8) | 74.5 (5.2) | 75.6 (5.9) | 0.0024 |
| Gender | | | | | 0.006 |
| Male | 1231 (65.7) | 183 (14.9) | 490 (39.8) | 557 (45.3) | |
| Female | 642 (34.3) | 138 (21.5) | 220 (34.2) | 285 (44.3) | |
| Race | | | | | <0.001 |
| White | 1158 (61.8) | 172 (14.9) | 445 (38.4) | 541 (46.7) | |
| Black | 147 (7.9) | 18 (12.2) | 42 (28.6) | 87 (59.2) | |
| Hispanic | 227 (12.1) | 38 (16.8) | 77 (33.9) | 112 (49.3) | |
| Chinese | 85 (4.5) | 27 (31.8) | 34 (40.0) | 24 (28.2) | |
| Japanese | 61 (3.3) | 14 (22.9) | 29 (47.5) | 18 (29.6) | |
| Other race | 195 (10.4) | 52 (26.7) | 83 (42.6) | 60 (30.7) | |
| Year of HCC diagnosis (%) | | | | | <0.001 |
| 1994-1996 | 411 (21.9) | 36 (8.8) | 157 (38.2) | 218 (53.0) | |
| 1997-1999 | 457 (24.4) | 77 (16.8) | 174 (38.1) | 206 (45.1) | |
| 2000-2002 | 1005 (53.7) | 208 (20.7) | 379 (37.7) | 418 (41.6) | |
| Duration of cirrhosis prior to HCC | | | | | <0.001 |
| <2 | 1188 (63.4) | 113 (9.5) | 477 (40.2) | 598 (50.3) | |
| >2 | 685 (36.6) | 208 (30.4) | 233 (34.0) | 244 (35.6) | |
| Mean number of physician visits within 3-years prior to HCC | 67.9 (42.4) | 83.8 (45.4) | 67.8 (38.9) | 62.1 (42.4) | <0.001 |
| SEER registry | | | | | <0.001 |
| Detroit | 223 (11.9) | 32 (14.3) | 86 (38.6) | 105 (47.1) | |
| San Francisco | 135 (7.2) | 29 (21.6) | 53 (39.2) | 53 (39.2) | |
| Connecticut | 149 (8.0) | 13 (8.7) | 51 (34.2) | 85 (57.1) | |

| | Overall (%) | Regular surveillance* (%) | Inconsistent surveillance** (%) | No surveillance (%) | P Value for regular surveillance vs. no surveillance*** |
|---|---|---|---|---|---|
| Hawaii | 64 (3.4) | 15 (23.4) | 30 (46.9) | 19 (29.7) | |
| Iowa | 107 (5.7) | 13 (12.1) | 36 (33.7) | 58 (54.2) | |
| New Mexico | ***** | ***** | ***** | ***** | |
| Seattle | 123 (6.6) | 18 (14.6) | 57 (46.4) | 48 (39.0) | |
| Utah | ***** | ***** | ***** | ***** | |
| Atlanta | 75 (4.0) | 9 (12.0) | 26 (34.7) | 40 (53.3) | |
| San Jose | 62 (3.3) | 20 (32.3) | 19 (30.6) | 23 (37.1) | |
| Los Angeles | 373 (19.9) | 85 (22.8) | 148 (39.7) | 140 (37.5) | |
| Rural Georgia | ***** | ***** | ***** | ***** | |
| Greater California | 201 (10.8) | 38 (18.9) | 76 (37.8) | 87 (43.3) | |
| Kentucky | 50 (2.7) | 5 (10.0) | 19 (38.0) | 26 (52.0) | |
| Louisiana | 49 (2.6) | 13 (26.5) | 16 (32.7) | 20 (40.8) | |
| New Jersey | 169 (9.0) | 27 (16.0) | 67 (39.6) | 75 (44.4) | |
| Income | | | | | <0.0001 |
| <$32,500 | 434 (23.2) | 57 (13.2) | 143 (32.9) | 234 (53.9) | |
| $32,501-$41,820 | 432 (23.1) | 69 (16.0) | 165 (38.2) | 198 (45.8) | |
| $41,821-54,590 | 444 (23.7) | 87 (19.6) | 178 (40.1) | 179 (40.3) | |
| >$54,590 | 492 (26.3) | 96 (19.5) | 196 (39.8) | 200 (40.7) | |
| Missing | 71 (3.7) | 12 (16.9) | 28 (39.4) | 31 (43.7) | |
| High school degree by zip code (%) | | | | | |
| 0 - 25 | 494 (26.4) | 104 (21.0) | 192 (38.9) | 198 (40.1) | 0.003 |
| 26 - 50 | 481 (25.7) | 98 (20.4) | 186 (38.7) | 197 (40.9) | |
| 51 - 75 | 456 (24.4) | 58 (12.7) | 174 (38.2) | 224 (49.1) | |
| >76 | 442 (23.6) | 61 (13.8) | 158 (35.7) | 223 (50.5) | |
| HCC etiology | | | | | |
| Alcoholic liver disease only | 466 (24.9) | 46 (9.8) | 175 (37.6) | 245 (52.6) | <0.0001 |
| HBV or HCV only | 526 (28.1) | 150 (28.5) | 222 (42.3) | 153 (29.2) | |
| Both alcoholic liver disease and hepatitis | 301 (16.1) | 97 (32.2) | 121 (40.2) | 83 (27.6) | |

| | Overall (%) | Regular surveillance* (%) | Inconsistent surveillance** (%) | No surveillance (%) | P Value for regular surveillance vs. no surveillance*** |
|---|---|---|---|---|---|
| Idiopathic | 580 (30.9) | 28 (4.9) | 192 (32.9) | 360 (62.2) | |
| Hemochromatosis**** | 51 (2.7) | 7 (13.7) | 19 (37.3) | 25 (49.0) | 0.9 |
| Liver disease severity | | | | | 0.02 |
| Child score A or B | 1363 (72.8) | 210 (15.4) | 505 (37.1) | 648 (47.5) | |
| Child score C | 510 (27.2) | 111 (21.8) | 205 (40.1) | 194 (38.1) | |
| Co-morbidity score | | | | | 0.5 |
| 0-7 | 496 (26.5) | 86 (17.3) | 172 (34.7) | 238 (48.0) | |
| 8-10 | 441 (23.6) | 82 (18.6) | 167 (38.0) | 192 (43.4) | |
| 11-13 | 447 (23.8) | 75 (16.8) | 164 (36.8) | 208 (46.4) | |
| >14 | 489 (26.1) | 78 (16.0) | 206 (42.1) | 205 (41.9) | |

*Received at least one surveillance test in 2 of the 3 years prior to HCC diagnosis

**Received at least one surveillance test but did not receive regular surveillance

***p Value from the Wald chi-square test

****In the absence of HCV, HBV, or alcoholic liver disease

*****Not able to be reported

HCC = hepatocellular carcinoma
sd = standard deviation
SEER = Surveillance, Epidemiology and End Results Registry
HCV = hepatitis C virus
HBV = hepatitis B virus

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**Table 2**

A comparison of physician characteristics among HCC patients with a prior diagnosis of cirrhosis who received regular HCC surveillance, inconsistent surveillance, or no HCC surveillance in the 3 years prior to their HCC diagnosis. (N=1,873)

| | Overall (%) | Regular surveillance* (%) | Inconsistent surveillance** (%) | No surveillance (%) | P Value for regular surveillance vs. no surveillance*** |
|---|---|---|---|---|---|
| **Total** | 1873 (100.0) | 321 (17.1) | 710 (38.0) | 842 (44.9) | |
| Specialty of primary physician | | | | | <0.001 |
| Internal medicine/family practice | 591 (31.6) | 114 (19.3) | 236 (39.9) | 241 (40.8) | |
| Gastroenterologist/hepatologist | 409 (21.7) | 108 (26.4) | 169 (41.3) | 132 (32.3) | |
| Other | 591 (31.6) | 70 (11.8) | 202 (34.2) | 319 (54.0) | |
| Unknown | 282 (15.1) | 29 (10.3) | 103 (36.5) | 150 (53.2) | |
| Physicians seen during past 3 years | | | | | <0.001 |
| Internal Medicine/family practice only | 534 (28.5) | 57 (10.7) | 207 (38.8) | 270 (50.5) | |
| Gastroenterologist/hepatologist only | 358 (19.1) | 76 (21.2) | 153 (42.7) | 129 (36.1) | |
| Internal medicine/family practice and gastroenterologist/ hepatologist | 548 (29.3) | 171 (31.2) | 218 (39.8) | 159 (29.0) | |
| None of the above | 388 (20.8) | 16 (4.1) | 129 (33.3) | 243 (62.6) | |
| Unknown | 45 (2.3) | 1 (2.2) | 3 (6.7) | 41 (91.1) | |
| Practice arrangement | | | | | 0.0004 |
| Solo practice | 405 (21.6) | 82 (20.2) | 164 (40.5) | 159 (39.3) | |
| Group practice | 866 (46.2) | 147 (17.0) | 325 (37.5) | 394 (45.5) | |
| Hospital | 135 (7.2) | 23 (17.0) | 49 (36.3) | 63 (46.7) | |
| Medical school | 59 (3.2) | 18 (30.5) | 27 (45.8) | 14 (23.7) | |
| Other | 14 (0.8) | 3 (21.4) | 3 (21.4) | 8 (57.2) | |
| Unknown | 394 (21.0) | 48 (12.2) | 142 (36.0) | 204 (51.8) | |
| Year of graduation | | | | | 0.0074 |
| Before or during 1968 | 321 (17.1) | 58 (18.1) | 122 (38.0) | 141 (43.9) | |
| 1969-1975 | 365 (19.5) | 63 (17.3) | 147 (40.3) | 155 (42.4) | |
| 1976-1982 | 482 (25.7) | 82 (17.0) | 186 (38.6) | 214 (44.4) | |
| 1983 and after | 423 (22.6) | 89 (21.0) | 152 (35.9) | 182 (43.1) | |

| | Overall (%) | Regular surveillance* (%) | Inconsistent surveillance** (%) | No surveillance (%) | P Value for regular surveillance vs. no surveillance*** |
|---|---|---|---|---|---|
| Unknown | 282 (15.1) | 29 (10.3) | 103 (36.5) | 150 (53.2) | |

* Received at least one surveillance test in 2 of the 3 years prior to HCC diagnosis

** Received at least one surveillance test but did not receive regular surveillance

*** P value from the Wald chi-square test

**Table 3**

Results from four independent trichotomous logistic regression models examining the effect of each physician factor on receipt of regular or inconsistent surveillance among HCC patients with a prior diagnosis of cirrhosis. Each model is adjusted for patient age, race, gender, income, geographic location, year of HCC diagnosis, number of physician encounters in the 3-years prior to HCC diagnosis and duration of cirrhosis prior to HCC. (n=1,873)

| | **Regular surveillance vs. no surveillance** | | **Inconsistent surveillance vs. no surveillance** | |
|---|---|---|---|---|
| | **Adjusted Odds Ratio (95% CI)** | **p-value** | **Adjusted Odds Ratio (95% CI)** | **p-value** |
| Model 1: Specialties of all physicians seen during the past 3-years | | | | |
| Internal medicine/family practice only | 1.00 | - | 1.00 | - |
| Gastroenterologist/hepatologist only | 2.80 (1.73-4.53) | <0.001 | 1.79 (1.28-2.50) | 0.001 |
| Internal medicine/family practice and gastroenterologist/hepatologist | 4.50 (2.91-6.96) | <0.001 | 1.62 (1.14-2.31) | 0.007 |
| None of the above | 0.39 (0.19-0.78) | 0.0076 | 0.76 (0.54-1.06) | 0.108 |
| Unknown | <0.01 (0.00->10.00) | 0.9836 | 0.30 (0.07-1.28) | 0.104 |
| Model 2: Specialty of primary physician | | | | |
| Internal medicine/family practice | 1.00 | - | 1.00 | - |
| Gastroenterologist/hepatologist | 1.96 (1.30-2.97) | 0.001 | 1.96 (1.30-22.97) | 0.001 |
| Other | 0.56 (0.37-0.86) | 0.007 | 0.56 (0.37-0.86) | 0.007 |
| Unknown | 0.52 (0.29-0.91) | 0.023 | 0.89 (0.61-1.31) | 0.560 |
| Model 3: Practice arrangement of primary physician | | | | |
| Solo practice | 1.00 | - | 1.00 | - |
| Group practice | 0.98 (0.65-1.47) | 0.911 | 0.91 (0.65-1.25) | 0.548 |
| Hospital | 0.85 (0.44-1.66) | 0.636 | 0.84 (0.50-1.42) | 0.516 |
| Medical school | 3.73 (1.51-9.21) | 0.004 | 2.28 (1.00-5.20) | 0.049 |
| Other | 0.94 (0.16-5.51) | 0.941 | 0.40 (0.08-2.15) | 0.288 |
| Unknown | 0.54 (0.33-0.90) | 0.019 | 0.77 (0.53-1.12) | 0.166 |
| Model 4: Year of graduation of primary physician | | | | |
| Before or during 1968 | 1.00 | - | 1.00 | - |
| 1969-1975 | 0.94 (0.56-1.57) | 0.803 | 1.08 (0.73-1.61) | 0.708 |
| 1976-1982 | 0.99 (0.62-1.62) | 0.981 | 1.02 (0.70-1.49) | 0.920 |
| 1983 and after | 1.08 (0.66-1.76) | 0.774 | 0.98 (0.66-1.45) | 0.904 |