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Utilization of Surveillance for Hepatocellular Carcinoma Among Hepatitis C Virus–Infected Veterans in the United States

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Background: Surveillance for hepatocellular carcinoma (HCC) is recommended for patients with hepatitis C virus (HCV) infection and cirrhosis. However, whether surveillance is being done as recommended is unknown.

Objective: To examine the prevalence and determinants of HCC surveillance among HCV-infected patients with cirrhosis in Veterans Affairs (VA) health care facilities in the United States.

Design: Retrospective cohort study of HCV-infected patients using data obtained from the national VA Hepatitis C Clinical Case Registry.

Setting: 128 VA medical centers.

Patients: HCV-infected patients with cirrhosis diagnosed between fiscal years 1998 and 2005.

Measurements: Abdominal ultrasonography and measurement of α-fetoprotein for HCC surveillance were identified from administrative data by using a previously validated algorithm. Patients were categorized as having routine (tests done during at least 2 consecutive years in the 4 years after cirrhosis diagnosis), inconsistent (at least 1 test, but not routine), or no surveillance in the 4 years after cirrhosis diagnosis. Predictors of surveillance were identified by using hierarchical random-effects regression.

Results: 126 670 patients with HCV were identified; 13 002 (10.1%) had cirrhosis. Approximately 42.0% of patients with cirrhosis received 1 or more HCC surveillance tests within the first year after the cirrhosis index date; however, a decline in receipt of surveillance was observed in the following 2 to 4 years. Among patients with cirrhosis and at least 2 years of follow-up, routine surveillance occurred in 12.0%, inconsistent surveillance in 58.5%, and no surveillance in 29.5%. Lower medical and psychological comorbid conditions, presence of varices, and the absence of decompensated liver disease were associated with a higher likelihood of receiving routine surveillance.

Limitations: Hepatocellular carcinoma surveillance tests were indirectly identified from registry data. Physician recommendations could not be captured.

Conclusion: Few HCV-infected veterans with cirrhosis received routine HCC surveillance. New strategies are needed to improve the implementation of HCC surveillance in clinical practice.

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Hepatocellular carcinoma (HCC) is the fastest rising cause of cancer-related deaths in the United States (1). This increase is mostly attributable to an increase in hepatitis C virus (HCV)–related HCC (2–5). Survival with HCC is generally very poor (overall 5-year survival is <5%), except when patients receive potentially curative therapy in the form of a liver transplant, surgical resection, or tumor ablation. In these patients, a considerable improvement in survival has been observed (5-year survival ranges from 40% to 70%) (6). Although several treatment options for HCC now exist, the eligibility of patients to receive these treatments, as well as the effectiveness of these treatments, diminishes with more advanced disease. Therefore, practice guidelines recommend HCC surveillance in high-risk groups (for example, HCV-infected patients with cirrhosis) in order to detect earlier-stage HCC and ultimately increase receipt of treatment and improve survival (7, 8).

Abdominal ultrasonography and measurement of serum α-fetoprotein (AFP) are the 2 most commonly recommended tests for HCC surveillance (7–13). Although no randomized, controlled trials of HCC surveillance have been done in HCV-infected patients, 1 randomized, placebo-controlled trial in hepatitis B carriers, as well as several observational cohort and case–control studies in patients with HCV, hepatitis B, and alcoholic cirrhosis, have shown that HCC surveillance is associated with earlier HCC diagnosis, greater use of potentially curative therapy, and a significant reduction in cancer-specific mortality compared with patients with symptomatic HCC (14–21).

It is unclear how often HCC surveillance is done among at-risk patients in clinical practice. Previous studies reported very low rates of HCC surveillance before diagnosis among patients with HCC, even in the presence of a recorded cirrhosis diagnosis (22–24). No studies have examined the frequency or patterns of surveillance in HCV-infected patients with cirrhosis, a scenario that more likely reflects real-life practice settings in the United States.

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Context

Current practice guidelines recommend screening for hepatocellular carcinoma (HCC) in patients with cirrhosis.

Contribution

The evaluation of data in a Veterans Affairs database showed that routine, annual screening for HCC with either serum α-fetoprotein measurement or abdominal ultrasonography was done in only 12% of veterans with cirrhosis. Testing was done inconsistently in 58.5% and not at all in 29.5% of patients with cirrhosis.

Caution

This study could not determine whether missing screening was due to physicians' failure to recommend tests or patients' failure to adhere to testing.

Implication

Efforts are needed to improve screening for HCC in at-risk patients.

—The Editors

The Veterans Affairs (VA) health care system is the largest integrated health care system in the United States and has a disproportionate number of patients with HCV. Moreover, the VA is a semiclosed system with a relatively stable patient population, which makes it a suitable setting for examining how often surveillance is done and variations in HCC surveillance practices. We therefore conducted a retrospective cohort study of all eligible HCV-infected patients with cirrhosis to identify patterns and determinants of HCC surveillance. We also examined a cohort of HCV-infected patients without cirrhosis, a group in which guidelines do not recommend surveillance.

METHODS

Study Design

We conducted a retrospective cohort study of HCV-infected patients with and without cirrhosis by using data obtained from the national VA Hepatitis C Clinical Case Registry to examine the utilization and determinants of HCC surveillance.

The institutional review board at Baylor College of Medicine and the National Institutes of Health, Office of Human Subjects Research, approved the study protocol.

Setting and Participants

The VA Hepatitis C Clinical Case Registry contains information collected from 128 VA health care facilities nationwide. Patients with HCV infection are identified on the basis of a positive antibody test for HCV or the presence of any International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), codes for HCV (codes V02.62, V070.41, V070.51, V070.44, and V070.54). Data elements include demographic characteristics, inpatient and outpatient laboratory tests, pharmacy data, and diagnosis and procedure codes. Additional details of the data source are published elsewhere (25).

For this study, we identified a cohort of HCV-infected patients on the basis of the presence of 1 positive HCV antibody test combined with at least 1 HCV ICD-9-CM code recorded from 1 October 1997 to 30 September 2005 (that is, fiscal years 1998 to 2005), with follow-up information available through 1 January 2007. The date of the first occurrence of a positive HCV antibody test or an HCV ICD-9-CM code served as the HCV index date. The subgroup of HCV-infected patients with cirrhosis was also identified by the presence of a previously validated ICD-9-CM code for cirrhosis (code 571.2, 571.5, or 571.6) (26) and assigned a cirrhosis index date based on the first appearance of a cirrhosis code. Patients included in the study cohort had to be at least 18 years of age and have at least 1 VA inpatient or outpatient visit during the 1 year before and 1 year after the cirrhosis (or HCV) index date. We excluded patients who developed HCC or died within the year after their cirrhosis (or HCV) index date.

A subgroup of HCV-infected, Medicare-enrolled veterans was also identified. Medicare-enrolled veterans can receive HCC surveillance tests outside of the VA using Medicare benefits. To capture these tests, we obtained Medicare claims data from 1 January 1999 to 31 December 2002 for all veterans in our cohort who used VA services and were eligible for Medicare (27).

Study Variables

The primary outcome of interest was the receipt of HCC surveillance. Ultrasonography and AFP done for HCC surveillance (distinct from other purposes) could not be directly ascertained from the VA Hepatitis C Clinical Case Registry; therefore, we indirectly identified these tests done for HCC surveillance by applying a previously developed and validated algorithm that used laboratory data and ICD-9-CM codes available in the registry. This algorithm was developed by using data from a cohort of 507 patients identified from the VA Hepatitis C Clinical Case Registry and was subsequently validated in 2 separate cohorts containing a combined total of 397 patients, some of whom were also in the VA Hepatitis C Clinical Case Registry. Model-based probabilities were used to predict whether AFP or ultrasonography was done for HCC surveillance (28). A dichotomization-based, single-imputation method was then applied to classify AFP and ultrasonography based on a single cut-point, which was selected to minimize the number of false-positive and -negative results. The variables retained in the final models used to identify AFP or ultrasonography for HCC surveillance were selected by using AIC (Akiake information criterion) and a variable change guided forward selection. Alcohol use, ascites, abdominal pain, diabetes, and aspartate aminotransferase laboratory values obtained within 1 year before the AFP test were included in the final AFP model. Abdominal

pain, ascites, drug dependence, HIV status, and occurrence of an AFP test within 3 months were included in the final ultrasonography model. Details of the algorithm have been published elsewhere (29).

After each AFP test and ultrasonography were classified as being done for HCC surveillance or nonsurveillance purposes by using the algorithm described previously, we determined whether each patient received a surveillance test during the 1, 2, 3, or 4 years after the cirrhosis index date for patients with complete follow-up for each period. Complete follow-up was having available follow-up (≥12 months) and at least 1 VA inpatient or outpatient encounter during each year of follow-up included in the respective analysis. The study data ended on 1 January 2007.

We ascertained age at cirrhosis (or HCV) index date, sex, and race (white, black, or other). Liver disease severity was assessed with the Model for End-Stage Liver Disease score, which was calculated by using laboratory values for serum creatinine, bilirubin, and international normalized ratio within 6 months before or after the cirrhosis (or HCV) index date (30). Higher scores indicate more severe liver disease. Laboratory data were used to determine hepatitis B virus surface antigen status. Alcohol, cocaine, and cannabis use were identified by positive laboratory test results or ICD-9-CM codes. Other substance use was determined by ICD-9-CM codes only. We also assessed the presence of ICD-9-CM codes for ascites, varices, encephalopathy, medical comorbid conditions (diabetes, coronary artery disease, chronic obstructive pulmonary disease, respiratory failure, congestive heart failure, hypertension, HIV, and end-stage renal disease), and mental health disorders (anxiety, posttraumatic stress disorder, depression, bipolar disorder, psychosis), as well as to calculate the Deyo comorbidity index score (31) (an adaptation of the Charlson Comorbidity Index) (**Appendix Table**, available at www.annals.org). The values for these variables were captured from 1 year before to 1 year after the cirrhosis (or HCV) index date.

Statistical Analysis

The prevalence of routine, inconsistent, and no HCC surveillance was evaluated among patients with and without cirrhosis who had at least 2 years of complete follow-up during the 4 years after the index dates. Routine HCC surveillance was receiving an AFP test or ultrasonography for HCC surveillance for at least 2 consecutive years during follow-up, and inconsistent surveillance was having at least 1 surveillance test but not meeting the criteria for routine surveillance. No surveillance included patients who did not receive either HCC surveillance test after cirrhosis (or HCV) diagnosis.

We also calculated the proportions of HCV-infected patients with and without cirrhosis who received a surveillance AFP test or ultrasonography during each of the 1, 2, 3, or 4 years of follow-up after the cirrhosis (or HCV) index date for those with complete follow-up during these periods. Patients with 4 years of complete follow-up were compared by using chi-square testing with patients with fewer complete years of follow-up in terms of their psychosocial factors, including alcohol, cocaine, and cannabis use.

Because HCC surveillance is primarily recommended for HCV-infected patients with cirrhosis (7, 8), the remainder of our analyses focused on this subgroup. We examined factors associated with HCC surveillance among patients with at least 2 years of data after their cirrhosis index date in a hierarchical multivariate logistic regression analysis by using a generalized logit approach in which the outcome was a trichotomous variable comparing either routine or inconsistent surveillance with no surveillance as the reference group. A primary VA physician and VA facility were assigned to each patient based on the highest number of visits with each, respectively, within the 2 years after the cirrhosis index date. Patients were clustered within primary physician by facility. Both primary physician and facility were modeled as random effects. Wald chi-square tests were used in assessing the significance of predictor variables. A stepwise regression approach was used to reduce the set of predictor variables included in the final model; only predictor variables that remained significant ($P < 0.10$) were retained. The clinical significance of each variable included in the final model was also considered. Adjusted odds ratios and 95% CIs were calculated for each predictor variable.

Sensitivity Analysis

To examine the robustness of our findings, we conducted 4 separate sensitivity analyses. First, the prevalence of HCC surveillance was calculated in all patients, regardless of the presence of complete follow-up. Second, we calculated the proportions of HCV-infected patients with and without cirrhosis who received any AFP test, abdominal ultrasonography, or computed tomography, regardless of the purpose, during the 1, 2, 3, or 4 years of follow-up after the cirrhosis (or HCV) index date. Third, the receipt of an AFP test or ultrasonography for HCC surveillance was calculated assuming that all patients with cirrhosis ($n = 11\,445$) had 4 years of complete follow-up. Finally, we conducted an analysis in a subset of Medicare-eligible patients from the VA Hepatitis C Clinical Case Registry cohort from 1999 to 2002 ($n = 39\,089$) to ascertain the effect of identifying additional AFP tests or ultrasonographies recorded in Medicare claims. We did all data manipulation and statistical analyses by using SAS, version 9.1 (SAS Institute, Cary, North Carolina).

Role of the Funding Source

The Houston Veterans Affairs Health Services Research and Development Center of Excellence and the National Cancer Institute funded the study. The funding sources had no role in the design and conduct of the study; collection, analysis, and interpretation of the data; preparation or review of the manuscript; or decision to submit the manuscript for publication.

Table 1. **Distribution of Patient Characteristics and Clinical Factors Among HCV-Infected Patients With and Without Cirrhosis**

Variable	HCV-Infected Patients With Cirrhosis (n = 13 002)	HCV-Infected Patients Without Cirrhosis (n = 113 668)
HCV index year, *n (%)*		
1998	2490 (19.1)	10 353 (9.1)
1999	2519 (19.3)	13 578 (12.0)
2000	2254 (17.3)	15 334 (13.5)
2001	2107 (16.2)	18 797 (16.5)
2002	1508 (11.6)	17 781 (15.6)
2003	1051 (8.1)	15 618 (13.7)
2004	759 (5.8)	13 402 (11.8)
2005	320 (2.3)	8805 (7.8)
Cirrhosis index year, *n (%)*		
<1998	433 (3.3)	–
1998	795 (6.1)	–
1999	1148 (8.8)	–
2000	1324 (10.2)	–
2001	1613 (12.4)	–
2002	1771 (13.6)	–
2003	1832 (14.1)	–
2004	2049 (15.8)	–
2005	2037 (15.7)	–
Age, *n (%)*		
<40 y	242 (1.9)	5757 (5.1)
40–50 y	5560 (42.8)	57 115 (50.2)
51–64 y	6184 (47.6)	42 098 (37.0)
>65 y	1016 (7.8)	8698 (7.7)
Women, *n (%)*	231 (1.8)	3606 (3.2)
Men, *n (%)*	12 771 (98.2)	110 062 (96.8)
Race, *n (%)*		
White	8382 (64.5)	61 244 (53.9)
Black	2538 (19.5)	36 073 (31.7)
Other	1189 (9.1)	6800 (6.0)
Missing	893 (6.9)	9551 (8.4)
Median inpatient and outpatient encounters in the 1 y after HCV index date (IQR)	17.0 (9–31)	14.0 (7–28)

HCV = hepatitis C virus; IQR = interquartile range.

RESULTS

We identified 126 670 patients with an HCV index date from 1 October 1997 to 30 September 2005 (fiscal years 1998 to 2005) who fulfilled the inclusion and exclusion criteria. Of these patients, 13 002 (10.2%) had received a diagnosis of cirrhosis (**Table 1**). Patients were included in the prevalence of surveillance estimates presented in **Table 2** only if they had complete follow-up in the indicated periods, as defined in the Methods section. We excluded 2076 patients with cirrhosis who had less than 2 years of complete follow-up during the 4 years after the index date for the routine, inconsistent, and no surveillance estimates. We found that only 12.0% of patients with cirrhosis received routine surveillance, 58.5% received inconsistent surveillance in at least 2 consecutive years in the 4 years after the cirrhosis index date, and 29.5% did not receive any surveillance. To calculate the 1-, 2-, 3-, and 4-year prevalence of surveillance estimates in **Table 2**, we excluded 1557, 2076, 1843, and 2249 patients with cirrhosis, respectively, because of incomplete follow-up during the indicated periods. Approximately 42.0% (n = 4809) of patients with cirrhosis received at least 1 AFP test or ultrasonography for HCC surveillance during the 1 year after the index date; of these, 34.4% received an AFP test, 20.7% received ultrasonography, and 44.9% received both tests. The proportions of patients with cirrhosis who received at least 1 AFP test or ultrasonography for surveillance remained steady (about 36%) during years 2, 3, and 4 after the cirrhosis index date.

In a sensitivity analysis of all patients with cirrhosis, regardless of whether complete follow-up information was available, receipt of an AFP test or ultrasonography for HCC surveillance in year 2 decreased to 33.2% (3797 of 11 445), 31.3% (3581 of 11 445) in year 3, and 28.1% (3219 of 11 445) in year 4. These estimates included HCC surveillance tests for patients who were previously excluded because of incomplete follow-up. Patients with 4 years of complete follow-up (n = 5277) were significantly less likely to drink alcohol than patients with shorter follow-up periods (n = 6168), respectively (42.8% vs. 48.7%; $P <$ 0.001). No significant differences in follow-up were observed regarding the use of cocaine or cannabis.

Patients with cirrhosis who received routine surveillance had a lower Model for End-Stage Liver Disease score and were less likely to have several specific comorbid conditions (ascites, coronary artery disease, chronic obstructive pulmonary disease, diabetes, psychosis, alcohol use, and other substance use) than were those who had not received surveillance and were more likely to receive a diagnosis of cirrhosis during more recent years (**Table 3**). These factors remained statistically significant in a multilevel model in which patients were grouped hierarchically within VA providers and VA facilities (**Table 4**).

In addition to the temporal trends of HCC surveillance based on the cirrhosis index date, we examined annual changes in receipt of HCC surveillance in patients with cirrhosis, regardless of time of diagnosis. A trend toward increasing receipt of routine surveillance was observed from 6.9% in 1998 to 19.9% in 2005.

Among 113 668 patients without cirrhosis, approximately 29.7% received at least 1 AFP test or ultrasonography for HCC surveillance during the year after the HCV index date, and only 3.3% of patients received routine surveillance (**Table 2**). Among these patients, 32.8% received an AFP test, 29.9% received ultrasonography, and 37.3% received both tests.

In a sensitivity analysis examining the frequency of all AFP test, ultrasonographies, and computed tomographies, regardless of the purpose, the proportion of patients who received at least one of these tests remained higher among patients with cirrhosis (72.3% in the first year, decreasing to 57.0% in the fourth year after the cirrhosis index date) (**Table 2**).

Among the 39 089 Medicare-eligible patients in the study cohort, less than 1.0% of patients had an AFP test

Table 2. **Prevalence of HCC Surveillance in HCV-Infected Patients With and Without Cirrhosis**

Variable	HCV-Infected Patients With Cirrhosis	HCV-Infected Patients Without Cirrhosis	*P* Value
HCC surveillance*			
Routine, *n/n (%)*	1123/9369 (12.0)	3303/99 862 (3.3)	<0.001†
Inconsistent, *n (%)*	5482 (58.5)	46 498 (46.6)	<0.001†
None, *n (%)*	2764 (29.5)	50 061 (50.1)	Reference
AFP test or ultrasonography for HCC surveillance after index date, *n/n (%)*			
1 y	4809/11 445 (42.0)	33 726/113 668 (29.7)	<0.001‡
2 y	3341/9369 (35.7)	18 232/99 862 (18.3)	<0.001‡
3 y	2756/7526 (36.6)	14 788/82 858 (17.8)	<0.001‡
4 y	1971/5277 (37.4)	11 868/66 051 (18.0)	<0.001‡
Any AFP test, abdominal ultrasonography, or CT regardless of purpose after index date, *n/n (%)*			
1 y	8278/11 445 (72.3)	47 784/113 668 (42.0)	<0.001‡
2 y	5696/9369 (60.8)	26 082/99 862 (26.1)	<0.001‡
3 y	4473/7526 (59.4)	20 953/82 858 (25.3)	<0.001‡
4 y	3010/5277 (57.0)	16 756/66 051 (25.4)	<0.001‡

AFP = α-fetoprotein; CT = computed tomography; HCC = hepatocellular carcinoma; HCV = hepatitis C virus.
* Among patients with at least 2-y follow-up.
† *P* values derived from Wald chi-square tests were calculated by using hierarchical univariate logistic regression. Patients were grouped within Veterans Affairs providers and facilities.
‡ *P* values derived from Pearson chi-square tests based on contingency tables comparing persons with cirrhosis with those without cirrhosis within each year.

(115 at year 1, 106 at year 2, and 66 at year 3) or ultrasonography (234 at year 1, 232 at year 2, and 137 at year 3) identified in Medicare claims only in the first 3 years after the HCV index date.

DISCUSSION

In this study of care within the VA health care system, most (88%) HCV-infected patients with cirrhosis did not receive routine HCC surveillance, as recommended by guidelines. Approximately 42% of patients with cirrhosis received at least 1 surveillance test within the first year after the cirrhosis index date; however, receipt of HCC surveillance considerably decreased in the following 2 to 3 years. Most HCV-infected patients with cirrhosis received sporadic or no HCC surveillance.

Our primary analyses focused on routine surveillance using AFP tests or ultrasonography, as identified indirectly using a validated algorithm for HCC surveillance (27). However, it is possible that ultrasonography or computed tomography may be done to diagnose other conditions, such as gallbladder or pancreas disorders. Although these tests do not count as surveillance tests, they can affect future decisions about performing additional HCC surveillance tests. We found that at least one of these tests was done in 72.3% of patients with cirrhosis (of which computed tomography accounted for only 1.2%) in the first year after the cirrhosis index date and in each subsequent year, slightly more than half of patients received any of these tests. These utilization rates probably overestimate the true prevalence of HCC surveillance. Furthermore, performing a single or an irregular surveillance test is not likely to be very useful. Therefore, we believe that our primary analyses of routine receipt of HCC surveillance tests in patients with cirrhosis present the most relevant findings of the study.

Implementation of HCC surveillance guidelines is low in clinical practice. Several factors may contribute to this observation, including the need for repeated surveillance during relatively short periods, potential difficulty in following up with patients after a positive or an equivocal surveillance test, the somewhat complicated diagnostic evaluation for HCC, and the limited availability of liver transplantation centers to refer patients who receive a diagnosis of HCC. Future studies are needed to examine the effect of these factors on the utilization of HCC surveillance in clinical practice. The low estimates of HCC surveillance that we report sharply contrast the findings of a 1998 survey, in which 84% of hepatologists claimed that they did routine surveillance for HCC (32). It is possible that the survey estimates may be inflated because of recall bias or that they reflect only a small segment of specialized providers that do not represent most physicians involved in the care of patients with cirrhosis.

Greater diffusion of practice guidelines probably accounts for some of the increase in routine surveillance in patients with more recent diagnoses of cirrhosis observed in this study. Similar findings were observed in our previous study among Medicare patients conducted by using the Surveillance, Epidemiology, and End Results and Medicare databases (merged to become 1 database for research purposes) (23). Although HCC surveillance recommendations were available before the beginning of our study in 1998, the main international guideline recommending HCC surveillance was released by the European

Table 3. **Comparison of Demographic Characteristics, Clinical Factors, and Comorbid Conditions Among 9369 HCV-Infected Patients With Cirrhosis and at Least 2 Years of Follow-up Who Received Routine, Inconsistent, or No Surveillance**

Variable	Routine Surveillance (*n* = 1123)	Inconsistent Surveillance (*n* = 5482)	No Surveillance (*n* = 2764)	*P* Value for Routine vs. No Surveillance*	*P* Value for Inconsistent vs. No Surveillance*
Cirrhosis index year, *n* (%)				<0.001	<0.001
<1998	16 (4.7)	185 (53.8)	143 (41.6)		
1998	48 (6.9)	381 (54.5)	270 (38.6)		
1999	95 (9.4)	600 (59.5)	314 (31.1)		
2000	112 (9.9)	695 (61.8)	318 (28.3)		
2001	164 (12.2)	804 (59.9)	374 (27.9)		
2002	185 (13.0)	866 (60.9)	370 (26.0)		
2003	160 (11.1)	893 (62.1)	383 (26.7)		
2004	269 (16.6)	873 (53.8)	480 (29.6)		
2005†	74 (19.9)	185 (49.9)	112 (30.2)		
Age, *n* (%)				<0.001	0.003
<50 y	394 (35.1)	2192 (40.0)	1213 (43.9)		
51–64 y	640 (57.0)	2907 (53.0)	1378 (49.9)		
>65 y	89 (7.9)	383 (7.0)	173 (6.2)		
Women, *n* (%)	22 (2.0)	108 (2.0)	51 (1.9)	–	–
Men, *n* (%)	1101 (98.0)	5374 (98.0)	2713 (98.2)	–	–
Race, *n* (%)				0.001	0.117
White	765 (68.1)	3618 (66.0)	1788 (64.7)		
Black	179 (15.9)	1042 (19.0)	579 (20.9)		
Other	98 (8.7)	544 (9.9)	249 (9.0)		
Missing	81 (7.2)	278 (5.1)	148 (5.4)		
Median inpatient and outpatient encounters in the 1 y after cirrhosis index date (IQR)	20 (12–31)	18 (10–31)	16 (8–32)	<0.001	<0.001
Model for End-Stage Liver Disease score, *n* (%)				<0.001	<0.001
<15	27 (2.4)	165 (3.0)	82 (3.0)		
15–20	780 (69.5)	3035 (55.4)	1256 (45.4)		
>20	11 (1.0)	42 (0.8)	25 (0.9)		
Missing	305 (27.2)	2240 (40.9)	1401 (50.7)		
Deyo comorbidity index score, *n* (%)				<0.001	<0.001
0	801 (71.3)	3723 (67.9)	1755 (63.5)		
1–2	274 (24.4)	1506 (27.5)	850 (30.8)		
≥3	48 (4.3)	253 (4.6)	159 (5.8)		
Comorbid conditions, *n* (%)					
Medical					
Ascites	52 (4.6)	625 (11.4)	437 (15.8)	<0.001	<0.001
Varices	203 (18.1)	398 (14.4)	811 (14.8)	0.004	0.63
Coronary artery disease	87 (7.8)	296 (10.7)	541 (9.9)	0.005	0.23
Chronic heart failure	37 (3.3)	149 (5.4)	190 (3.5)	0.006	<0.001
Chronic obstructive pulmonary disease or respiratory failure	85 (7.6)	631 (11.5)	475 (17.2)	<0.001	<0.001
Diabetes	255 (22.7)	721 (26.1)	1386 (25.3)	0.028	0.43
Encephalopathy	40 (3.6)	155 (5.6)	280 (5.1)	0.008	0.34
Hepatitis B virus	17 (1.5)	102 (1.9)	35 (1.3)	0.54	0.046
HIV	20 (1.8)	97 (1.8)	77 (2.8)	0.069	0.002
Hypertension	464 (41.3)	2476 (45.2)	1246 (45.1)	0.032	0.941
Mental health					
Anxiety or posttraumatic stress disorder	239 (21.3)	1442 (26.3)	808 (29.2)	<0.001	0.005
Bipolar disorder or depression	217 (19.3)	763 (27.6)	1386 (25.3)	<0.001	0.023
Psychosis	60 (5.3)	473 (8.6)	330 (11.9)	<0.001	<0.001
Substance use, *n* (%)					
Alcohol	340 (30.3)	2270 (41.4)	1546 (55.9)	<0.001	<0.001
Cannabis	65 (5.8)	145 (5.3)	235 (4.3)	0.50	0.050
Cocaine	24 (2.1)	153 (2.8)	128 (4.6)	<0.001	<0.001
Other	140 (12.5)	1180 (21.5)	780 (28.2)	<0.001	<0.001

HCV = hepatitis C virus; IQR = interquartile range.
* *P* values derived from Pearson chi-square tests based on contingency tables.
† 2 y of data were not available for all patients with a cirrhosis index date in 2005.

Association for the Study of the Liver in 2001 (7). Nevertheless, the rate of increase is slow, and the overall implementation seems to be very inadequate. We recommend planning active interventions to improve HCC surveillance.

Current practice guidelines do not recommend HCC surveillance in HCV-infected patients without cirrhosis. However, approximately 29.7% of HCV-infected patients without cirrhosis had at least 1 surveillance test in the first year after diagnosis, and 3.3% had routine surveillance. It is possible that some of these patients had cirrhosis that was missed by our study definition. Although surveillance in these patients may not be inappropriate or wasteful, this provides evidence of confusion and poor implementation of guidelines, especially in the context of low utilization of HCC surveillance in the group at highest risk (that is, patients with cirrhosis).

We found that several patient-related factors, including presence of comorbid conditions, advanced liver disease, and alcohol use, were associated with a lower likelihood of receiving routine HCC surveillance. The presence of severe comorbid conditions may reduce the likelihood of receiving potentially curative therapy if HCC should develop, thereby diminishing physician enthusiasm for surveillance. We could not accurately ascertain the severity or reversibility of comorbid conditions in our study. However, with the emergence of efficacious palliative treatments, such as ablation, transarterial chemoembolization, and sorafenib, excluding patients with moderate or controlled comorbid conditions from HCC surveillance may not be justified (8, 33, 34). Patients who received routine surveillance were slightly more likely to have mild to moderate liver disease; this is to be expected because HCC surveillance may be futile in patients with advanced cirrhosis not listed for transplantation (35). Finally, patients who drank alcohol were less likely to receive routine HCC surveillance and also were less likely to have 4 years of complete follow-up after the cirrhosis index date, thus suggesting that these patients were less likely to be engaged in regular health care activities, including receipt of HCC surveillance.

Patients who use the VA health care system may receive care outside the VA using supplemental insurance or, most likely in our sample, Medicare benefits. However, less than 1% of all Medicare-eligible patients in our study had an AFP test or ultrasonography identified in Medicare claims files only. Given the large number of patients in our study cohort, the few tests identified in Medicare claims would not have substantially changed our results.

Our findings should be interpreted within our study's limitations. Hepatocellular carcinoma surveillance tests could not be directly identified from administrative data (29). Therefore, we developed and validated an algorithm with good predictive values to identify both AFP tests and ultrasonography done for surveillance purposes. Although the algorithm for ultrasonography less accurately identifies HCC on a surveillance test (27), the total number of ultrasonographies was minimal compared with the total number of AFP tests. Therefore, misclassification of ultrasonography would have only a small effect on the overall estimates of HCC surveillance. Finally, we were unable to

Table 4. **Results From a Model Examining the Effect of Patient Characteristics, Clinical Factors, and Comorbid Conditions on Receipt of Routine Surveillance Versus No Surveillance Among HCV-Infected Patients With Cirrhosis and at Least 2 Years of Follow-up***

Variable	Routine vs. No Surveillance	
	Adjusted Odds Ratio (95% CI)	*P* Value
Cirrhosis index year		
<1998	0.49 (0.21–1.17)	0.112
1998	Reference	
1999	3.37 (1.96–5.80)	<0.001
2000	4.48 (2.60–7.73)	<0.001
2001	4.75 (2.79–8.08)	<0.001
2002	7.45 (4.40–12.59)	<0.001
2003	4.41 (2.57–7.55)	<0.001
2004	6.22 (3.73–10.37)	<0.001
2005	9.06 (4.80–17.08)	<0.001
Age		
<50 y	0.79 (0.64–0.99)	0.040
50–64 y	Reference	
>65 y	1.05 (0.67–1.63)	0.834
Race		
White	Reference	
Black	0.60 (0.45–0.81)	0.001
Other	0.73 (0.49–1.08)	0.112
Missing	1.39 (0.90–2.14)	0.135
Total inpatient and outpatient encounters in the 1 y after cirrhosis index date (per 10 visits)	1.01 (1.00–1.01)	0.001
Model for End-Stage Liver Disease score		
<15	Reference	
15–20	0.38 (0.19–0.77)	0.007
>20	0.79 (0.26–2.42)	0.685
Missing	0.13 (0.11–0.17)	<0.001
Comorbid conditions		
Medical		
Ascites	0.07 (0.04–0.01)	<0.001
Varices	2.56 (1.90–3.45)	<0.001
Coronary artery disease	0.46 (0.31–0.69)	<0.001
Chronic obstructive pulmonary disease or respiratory failure	0.49 (0.35–0.71)	<0.001
Diabetes	0.65 (0.51–0.84)	0.001
Mental health		
Psychosis	0.43 (0.29–0.66)	0.001
Substance use		
Alcohol	0.34 (0.27–0.43)	<0.001
Cannabis	3.52 (2.19–5.66)	<0.001
Other	0.28 (0.20–0.38)	<0.001

HCV = hepatitis C virus.
* Patients are clustered within physicians by facility. Those without a provider (n = 66) were excluded from the analysis.

capture physician recommendations to perform surveillance or patient adherence to these recommendations.

To our knowledge, our study is the largest to date on HCC surveillance in HCV-infected patients with cirrhosis. Our study includes other strengths: several years of complete follow-up, inclusion of data from recent years reflecting contemporary practice, accurate definitions of cirrhosis validated by previous chart reviews using our study database, and examination of a range of variables that may affect the utilization of HCC surveillance.

In conclusion, routine HCC surveillance with either an AFP test or ultrasonography is low among HCV-infected patients with cirrhosis, despite recommendations for HCC surveillance in these high-risk patients. 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.

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Appendix Table. **ICD-9-CM Diagnostic Codes to Ascertain the Presence of Comorbid Conditions Potentially Associated With Receiving Hepatocellular Carcinoma Surveillance**

Condition	ICD-9-CM Code
Anxiety	300.00–300.02, 300.09–300.16, 300.19–300.23, 300.29, 300.3, 300.5–300.7, 300.81–300.82, 307.40–307.45, 307.47–307.49, 307.80–307.81, 307.89, 307.9–308.4, 308.9, 309.81, 312.30, 312.31, 312.33–312.35, 312.39, 327.02, 327.15, 327.30–327.37, 327.39
Posttraumatic stress disorder	309.81
Bipolar disorder	296.40–296.46, 296.50–296.56, 296.60–296.66, 296.7, 296.80–296.82, 296.89
Depression	296.20, 296.21, 296.23–296.26, 296.30–296.36, 300.4
Coronary artery disease	411.0–411.1, 411.8, 411.81, 411.89, 412, 413.0, 413.9, 414.0, 414.00–414.01, 414.03, 414.06, 414.8–414.9, V458.1–V458.2, or procedure codes: 361.0–361.7, 361.9, 362, 363, 363.1, 363.2, 363.9, 360.1–360.2, 360.8, 00.66
Chronic obstructive pulmonary disease	490, 491.0, 491.1, 491.2, 491.20, 491.21, 491.22, 491.8, 491.9, 492.0, 492.8, 494, 494.0, 494.41, 496 in the absence of respiratory failure
Congestive heart failure	398.91, 428.0. 428.1, 428.20, 428.22–428.23, 428.30–428.33, 428.40–428.43, and 428.9
Respiratory failure	517.3, 518.5, 518.81, 518.82, 518.83, 518.84, 799.1, V461.1,V461.2, V461.3, V461.4, V462
Diabetes	250.0–250.9, 357.2, 362.0, 366.41
End-stage renal disease	585.5, 585.6, 909.35, 909.37, G0314, G0315, G0316, G0317, G0318, G0319
Hypertension	401.0–401.1. 401.9, 402.00–402.01, 402.10–402.11, 402.90–402.91, 403.0–403.1, 403.90–403.91, 404.0–404.1, 404.9, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99, 437.2
HIV	V08, 042, 079.53, 279.10, 279.19
Psychosis	296.90, 296.99, 298.0, 295.00–295.05, 295.10–295.15, 295.20–295.25, 295.30–295.35, 295.40–295.45, 295.50–295.55, 295.60–295.65, 295.70–295.75, 295.80–295.85, 295.90–295.95, 299.00–299.01, 299.10–299.11, 299.80–299.81, 299.90–299.91, 297.0–297.3, 297.8–297.9, 298.1–298.4, 298.8–298.9
Alcohol use	303.9, V11.3, 291, 303, 305.0, 291.81
Cannabis use	305.2
Cocaine use	305.6
Other substance use	305.3, 305.4, 305.5, 305.7, 292, 304

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Correction: Surveillance for Hepatocellular Carcinoma in the United States

In the recent article by Davila and colleagues (1), in Table 1 the row labels "Men" and "Women" were switched. This has been corrected in the online version.

Reference

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