Suboptimal Surveillance for and Knowledge of Hepatocellular Carcinoma Among Primary Care Providers

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BACKGROUND & AIMS: A large proportion of patients with cirrhosis are seen only by their primary care provider (PCP). Surveillance for hepatocellular carcinoma (HCC) therefore depends on PCPs in these cases. We aimed to assess PCP knowledge and practice of HCC surveillance.

METHODS: We contacted a random sample of 1000 North Carolina PCPs by mail. All PCPs contacted received an introductory letter followed by a 12-item questionnaire addressing HCC surveillance knowledge and practice.

RESULTS: A total of 391 PCPs (39%) completed the survey; 89% saw patients with cirrhosis in their practice, but only 45% screened for HCC. Among PCPs who screened for HCC, the most common methods were ultrasound analysis and measurement of α-fetoprotein level (66%). Reasons for surveillance included supported by evidence (72%), recommended by medical societies (42%), and malpractice liability for not performing surveillance (26%). Of PCPs who did not screen, 84% referred to gastroenterologists for surveillance decisions, 24% were unaware of recommendations, 8% were uncertain of the benefits, and 8% were concerned about cost. Hepatic resection and liver transplantation were identified as effective therapies by 67% and 56% of PCPs, respectively, but all other effective therapies were identified by less than half (transarterial chemoembolization by 42%, radiofrequency ablation by 35%, and sorafenib by 26%). The ability to identify at least 1 effective therapy was associated independently with surveillance (odds ratio, 2.1; 95% confidence interval, 1.1-4.0).

CONCLUSIONS: Most PCPs see patients with cirrhosis, but only a minority screen for HCC. PCP knowledge of effective HCC therapy options is suboptimal. Efforts to enlist PCPs in HCC surveillance may be best served by increasing their knowledge of effective therapies.

Keywords: Therapy; Screening; Hepatitis C; Hepatitis B; Cirrhosis.

See editorial on page 805; see similar article on page 791.

Hepatocellular carcinoma surveillance is recommended by all 3 major hepatology societies.1–3 Nevertheless, surveillance rates remain well below 50%, and in some populations as low as 12%.4–7 Among the many steps needed for surveillance to be accomplished, physician education and incorporation of surveillance into their practice are critical. As expected, hepatologists and gastroenterologists tend to believe in surveillance and are more likely to order it routinely for their cirrhotic patients,5–7 but only 20% to 50% of such patients are seen by such subspecialists.7,8 Primary care providers (PCPs) see most of the remainder. Therefore, if surveillance is to have any chance of reaching more than 50% of cirrhosis patients, enlistment of PCPs will be necessary. Only 3 studies have investigated the practice and knowledge of hepatocellular carcinoma (HCC) surveillance among PCPs and these 3 studies focused primarily on PCPs who see a high number of Asian patients or on surveillance for viral hepatitis rather than HCC surveillance.9–11 Therefore, we sampled PCPs from the entire North Carolina Medical Board database and limited our questionnaire to HCC surveillance only.
Methods

Institutional Review of Research

Our research project and protocol were reviewed and approved by the University of North Carolina Institutional Review Board before initiating this study.

Subjects

We used the North Carolina Medical Board database to identify practicing PCPs (physicians and doctors of osteopathy) in North Carolina. A random sample of 1000 PCPs was identified. This sample represented 14% of North Carolina PCPs.12,13

Survey

Survey methodology was based on the tailored design method.14 All subjects received an introductory letter, followed by the questionnaire in a separate mailing. The questionnaire consisted of 8 items addressing knowledge and use of HCC surveillance guidelines, as well as identification of HCC therapies. Basic demographics and practice information requested was limited to gender, years in practice, major affiliations (eg, academic facility, Veterans Affairs, private practice), and their ability to see Medicaid-covered patients. We purposely did not request more specific information that would lengthen the questionnaire, compromise anonymity, and potentially decrease the response rate. Therefore, we did not collect information on practice location, type of service area (rural vs urban), training or specific type of practice (ie, group vs solo, family practice vs internal medicine). Such limiting of variables did not allow us to construct a conceptual behavioral model for the decision to recommend surveillance. Instead, we focused on the self-reported rate of surveillance, and the modality and interval recommended. We also asked about knowledge of HCC therapies because they have changed substantially in the past decade and remain a primary justification for surveillance. No pretesting or validation of this brief survey were performed. A $10 cash incentive was included to reduce nonresponse bias and was given regardless of whether the PCP completed the questionnaire or not. A reminder/gratitude postcard was mailed to all subjects, followed by the mailing of a second questionnaire for nonresponders. An addressed return envelope with prepaid postage was included.

To ensure anonymity, all questionnaires were given an alphanumeric code. The master key linking the code to the subject name was used only at the time of mailing and receipt portion of the study to determine who should receive a second-chance mailing. Data collection (receipt of questionnaires) was closed 90 days after the last mailing was completed. Thereafter, the master key was destroyed and no further questionnaires were collected or mailed out.

Analysis

Demographic, practice information, and survey responses were analyzed using basic descriptive statistics (eg, means, medians, proportions, standard deviations). We used the Pearson chi-square and t tests where appropriate to compare PCPs who screened and those who did not. Logistic regression was used to identify independent variables associated with surveillance.

Results

Subjects: Primary Care Providers

Of the 1000 PCPs to whom we mailed letters and questionnaires, 391 (39%) completed the questionnaire and mailed it back to us. Two PCPs answered questions in an incongruent or unclear manner and had to be discarded (1 PCP indicated not seeing cirrhotic patients yet performed surveillance; another did not answer whether they saw cirrhotic patients but indicated they do not screen). Characteristics of the remaining 389 PCPs are shown in Table 1. The vast majority was in private practice and saw Medicaid patients. Nearly 90% saw cirrhotic patients in their practices.

Hepatocellular Carcinoma Surveillance

Of the 345 PCPs who saw cirrhotic patients, only 45% recommended HCC surveillance. There were no significant differences between those PCPs who do recommend surveillance (n = 156) from those who do not (n = 189) in terms of gender years in practice, practice affiliation, and whether they see Medicaid patients. The most common means of surveillance used was liver ultrasound and α-fetoprotein (AFP) measurement (Figure 1). The most common interval for surveillance was 12 months (Figure 2). Nearly three quarters of those who provide surveillance do so because they believed evidence supported it (Table 2). When asked to identify barriers to

Table 1. Characteristics of Primary Care Providers (N = 389)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>234 (60.2)</td>
</tr>
<tr>
<td>Years in practice, mean (SD)</td>
<td>22 (9.9)</td>
</tr>
<tr>
<td>Primary affiliation, n (%)</td>
<td></td>
</tr>
<tr>
<td>Private practice</td>
<td>313 (80.5)</td>
</tr>
<tr>
<td>Academic setting</td>
<td>47 (12.1)</td>
</tr>
<tr>
<td>Veterans Affairs hospital or clinic</td>
<td>13 (3.3)</td>
</tr>
<tr>
<td>Health maintenance organization</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Other (not specified by respondent)</td>
<td>12 (3.1)</td>
</tr>
<tr>
<td>Encounter cirrhotic patients in practice, n (%)</td>
<td>345 (88.7)</td>
</tr>
</tbody>
</table>
surveillance, 54% identified poor patient adherence and 53% identified patient financial constraints, 49% identified lack of insurance, and 32% identified insurance constraints on coverage. Only 5% identified lack of available surveillance services (eg, radiology) as a barrier.

Among those who do not recommend surveillance, the vast majority (84%) defer to subspecialists to decide or perform surveillance (Table 3). However, 46 (24%) were unaware of any surveillance recommendations, and only 15 (8%) believed the benefit of surveillance was uncertain. Only 4% identified cost as a reason for not recommending surveillance.

### Knowledge of Hepatocellular Carcinoma Therapies and Association With Surveillance

Of the 345 PCPs who see cirrhosis patients, 230 (67%) identified resection as an effective therapy for HCC, but only 192 (56%) identified liver transplant (Table 4). Other effective treatments were identified less frequently. PCPs who were able to identify at least one modality as an effective therapy were more likely to screen, with an odds ratio of 1.9 (P = .04). On multivariate analysis (controlling for PCP gender, practice setting, years in practice, and whether they see Medicaid patients), the association between identifying at least one effective therapy and recommending surveillance remained significant (odds ratio, 2.1; 95% confidence interval, 1.1–4.0). None of the other

### Table 2. Reasons for Recommending HCC Surveillance Among PCPs Who Screen (N = 156)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence supports surveillance for HCC</td>
<td>112</td>
<td>72</td>
</tr>
<tr>
<td>Surveillance is recommended by medical societies</td>
<td>65</td>
<td>42</td>
</tr>
<tr>
<td>Not performing surveillance would pose a malpractice liability</td>
<td>41</td>
<td>26</td>
</tr>
<tr>
<td>Surveillance for HCC is cost effective</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Other*</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Did not provide a reason</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

*Other reasons given were as follows: "affects treatment options", "it is standard with our cirrhosis clinic", "it is what I would do", "patients request it", "rule out liver lesion affecting laboratory values and so forth", and "recommendation by a consultant (gastroenterologist or hepatologist)."

### Table 3. Reasons for Not Recommending HCC Surveillance Among Those PCPs Who Do Not Screen (N = 189)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer cirrhotic patients to consulting provider</td>
<td>158</td>
<td>84</td>
</tr>
<tr>
<td>Did not know it was recommended</td>
<td>46</td>
<td>24</td>
</tr>
<tr>
<td>Benefit of surveillance is uncertain</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Too costly</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Other*</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Did not provide a reason</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Other reasons given were as follows: transient population, screen the hepatitis C cirrhosis patients/not usually the alcoholic cirrhosis patients, not sure of the latest recommendations, see few cirrhotic patients and they usually are terminal or followed up by specialists, only check with hepatitis C, ultrasound often is performed as a diagnosis of cirrhosis evolving, usually do not live long enough, intend to but some slip through.
variables were associated significantly with recommend-
ing surveillance.

Discussion

Although formally recommended by hepatology soci-
eties for nearly a decade, less than half (25%–42%) of
cirrhotic patients receive HCC surveillance according to
several studies.4–7 Such low rates may occur because 20%
to 50% of cirrhosis patients are not seen by gastroen-
terologists, who tend to recommend surveillance more
than PCPs.7,8 Even after being seen by a gastroenterolo-
gist, patients may see their PCP more frequently, espe-
cially in remote regions where the distance to a
subspecialist is greater. If surveillance is to ever have a
sustainable rate greater than 50%, enlistment of PCP help
probably will be necessary. However, data regarding PCP
knowledge and beliefs about HCC surveillance are limited.

Our study indicates that only 45% of primary care
providers who see cirrhosis patients in North Carolina
recommend surveillance. Approximately 70% of PCPs
who screen do so because they believe evidence sup-
ports it. Forty-two percent understood that some medi-
cal associations recommend it. Of the majority who do
not screen, 84% deferred to subspecialists to recom-
mand or consider surveillance, and 24% were unaware
of surveillance recommendations. Only resection and
transplantation were identified correctly as effective
therapies by more than half of all respondents (67% and
35%, respectively) (Table 4). Only 35% identified radi-
ofrequency ablation, even though data suggest it rivals
resection in efficacy and is significantly less morbid.15–17
Similarly, only a minority of PCPs identified transarterial
chemoembolization and sorafenib despite randomized
terminated trials (RCT) showing survival benefit.18,19
Those PCPs able to identify at least one effective treat-
ment were twice as likely to recommend surveillance.

Of those who perform surveillance, ultrasound (US)
and AFP, in combination, was used most commonly, and
12 months was the most common interval (Figures 1
and 2). These data may reflect older American Associa-
tion for the Study of Liver Diseases recommendations
from 2005 in which AFP was mentioned as an alternative
option, if US was suboptimal or unavailable, and the

| Table 4. Effective HCC Therapies Identified by PCPs Who See Cirrhosis Patients (N = 345) |
|---------------------------------|-----|-----|
| Hepatic resection               | 230 | 67  |
| Liver transplantation           | 192 | 56  |
| Transarterial chemoembolization | 146 | 42  |
| Radiofrequency ablation         | 121 | 35  |
| Sorafenib                       | 91  | 26  |
| Did not identify any choices as effective therapies | 50  | 15  |

NOTE. Respondents were asked to choose all that apply.

suggested interval was up to 12 months. In 2010, the
AFP measurement was eliminated completely and the
interval was limited to 6 months.

Two studies reported higher rates of surveillance
among PCPs (79%–89%), but the PCPs in these studies
were highly biased toward increased HCC awareness.
Both studies targeted PCPs from communities with high
proportions of Asians, who have significantly higher
prevalences of hepatitis B infection and consequent
cirrhosis. In addition, PCPs in these studies may recom-
mand surveillance more often because supporting evi-
dence is stronger (Level I, RCT data) for surveillance in
hepatitis B–related liver disease20 than cirrhosis from
other etiologies (Level II, observational, cohort data).21
One study surveyed 11 San Francisco clinics with a pa-
tient population that is 25% Asian.10 Moreover, 1 in 4 of
the PCPs themselves were Asian and half had patient
panels that were more than 25% Asian. The other study
surveyed 3 Northern California counties, but again 1 in 4
of the PCPs were Asians, 43% spoke an Asian language,
and 30% of their catchment was Asian. Such PCP groups
will have an increased interest in HCC surveillance
compared with PCPs from other areas of the United
States. The nation as a whole is only 5% Asian.22 The
only other study examining PCPs focused primarily on
surveillance for hepatitis C and B infections.12,13 HCC sur-
veillance questions were limited and did not specify the
presence or absence of cirrhosis. None of the 3 studies
asked about HCC therapies or whether respondents
actually see cirrhosis patients in their practices.

We focused on HCC surveillance and therapy. We
surveyed a random sample of PCPs from across the state
of North Carolina. Therefore, our data are more repre-
sentative of communities with an Asian prevalence closer
to the national average. Only 2.5% of North Carolina
residents are of Asian descent.13 Unlike prior surveys, we
also asked whether PCPs actually saw cirrhosis patients
in their practice. Such determination is critical because
PCPs may render an opinion on HCC surveillance but
never actually see a cirrhotic patient. Some may divert
cirrhosis patients away from their clinic, or work in
clinics in which cirrhosis patients are rare (eg, student
health clinics).

We also wanted to understand PCP knowledge of HCC
therapies because effective therapies are arguably the
most compelling justification for surveillance.12,23 HCC
therapies have evolved greatly in the past 12 years. Our
survey suggests that PCP knowledge of more recently
established treatments is relatively poor compared with
established surgical interventions. Filling this knowledge
gap regarding RCT data for transarterial chemo-
embolization, radiofrequency ablation, and sorafenib
could increase surveillance rates by PCPs because the
ability to identify at least one effective therapy inde-
pendently doubled the odds of surveillance. Also, more
than 80% of PCPs who do not screen deferred the
decision to subspecialists, and despite some con-
troversy in the literature regarding HCC surveillance
recommendations, only 8% did not screen because they felt the benefit was uncertain. Therefore, a large number of PCPs may recommend surveillance, if guidance and education are provided.

Our study was limited by a response rate (39%) that was lower than prior HCC surveillance surveys of PCPs (62%–71%). As mentioned, these prior studies targeted Asian community PCPs who very likely have a deeper knowledge and interest in HCC. Our response rate is more in line with less targeted provider surveys. An analysis of 130 surveys of US health care professionals, conducted from 1996 to 2005, yielded a median response rate of 51%, with an interquartile range of 38% to 65%. Moreover, the response rate for health care professionals decreased significantly with the percentage of surveys having more than 60% response decreasing from 63% before 2000 to 35% in 2005 to 2008. PCPs who see having more than 60% response decreasing from 63% before 2000 to 35% in 2005 to 2008.27 PCPs who see

Our survey also was limited in scope. The questionnaire was purposely kept brief to limit the nonresponse rate. Many other variables needed for a full behavior model such as PCP access to subspecialists and volume of cirrhotic patients seen were not included. Thus, therapy knowledge that was associated with surveillance may be merely a surrogate for other more pertinent variables not captured in our survey.

Our study provides data on HCC surveillance and knowledge of HCC therapy in an unselected population of PCPs who see cirrhotic patients in practices not enriched with Asians. The data suggest that HCC surveillance rates and knowledge of therapies are low. It also suggests an opportunity to increase community surveillance rates by closing the gap in knowledge, particularly regarding effective therapy options. Moreover, the majority of PCPs who do not screen may be amenable to surveillance if educated and guided by subspecialists. Enlisting PCP help in initiating surveillance may eliminate unnecessary referrals for opinion and certainly will help with sustaining surveillance once started. It is probably the only practical way to increase and sustain surveillance rates on a broader scale.

References


Reprint requests
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The authors disclose no conflicts.

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