Annals of Global Health
VOL. 83, NO. 2, 2017

ISSN 2214-9996/$36.00
http://dx.doi.org/10.1016/j.aogh.2017.02.002

ORIGINAL RESEARCH

Practice, Knowledge, and Barriers for Screening of Hepatocellular Carcinoma Among High-Risk Chinese Patients

Kerui Xu, MPH, Shinobu Watanabe-Galloway, PhD, Fedja A. Rochling, MB, BCh, Jianjun Zhang, MD, Paraskevi A. Farazi, PhD, Hongyan Peng, MB, BS, Hongmei Wang, PhD, Jiangtao Luo, PhD
Omaha, Nebraska; and Wuhan, China

Abstract

BACKGROUND Hepatocellular carcinoma (HCC) is among the leading causes of cancer deaths in China. Considering its poor prognosis when diagnosed late, Chinese guidelines recommend biannual screening for HCC with abdominal ultrasound and serum α-fetoprotein (AFP) test for high-risk populations.

OBJECTIVES To investigate the practice, knowledge, and self-perceived barriers for HCC screening among high-risk hospital patients in China.

METHODS An interview-based questionnaire was conducted among Chinese patients with chronic hepatitis B and/or chronic hepatitis C infection from outpatient clinics at 2 tertiary medical institutions in Shanghai and Wuhan, China.

FINDINGS Among 352 participating patients, 50.0% had routine screening, 23.3% had irregular screening, and 26.7% had incomplete or no screening. Significant determinants for screening included higher level of education, underlying liver cirrhosis, a family history of HCC, and better knowledge concerning viral hepatitis, HCC, and HCC screening guidelines. Moreover, factors associated with better knowledge were younger age, female gender, urban residency, education level of college or above, annual household income of greater than 150,000 RMB, and longer duration of hepatitis infection. The 3 most common barriers reported for not receiving screening were not aware that screening for HCC exists (41.5%), no symptoms or discomfort (38.3%), and lack of recommendation from physicians (31.9%).

CONLUSIONS Health care professionals and community leaders should actively inform patients regarding the benefits of HCC screening through design of educational programs. Such interventions are expected to increase knowledge about HCC and HCC screening, as well as improve screening adherence and earlier diagnosis.

KEY WORDS hepatocellular carcinoma, high-risk Chinese patients, screening, knowledge, barriers

All authors have access to the data and had a role in writing the manuscript.
The study was supported by the Cancer Epidemiology Education in Special Populations (CEESP) Program of the University of Nebraska Medical Center from the National Cancer Institute (R25CA112383). The content of this project is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute.
The authors declare that they have no conflict of interests.
From the Department of Epidemiology, College of Public Health, University of Nebraska Medical Center, Omaha, NE (KX, SW-G, PAF); Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, University of Nebraska Medical Center, Omaha, NE (FAR); Department of Hepatology, Hubei Third People's Hospital, Wuhan, Hubei, China (JZ, HP); Department of Health Services Research & Administration, College of Public Health, University of Nebraska Medical Center, Omaha, NE (HW); Department of Biostatistics, College of Public Health, University of Nebraska Medical Center, Omaha, NE (JL). Address correspondence to K.X. (kerui.xu@unmc.edu).

Annals of Global Health, VOL. 83, NO. 2, 2017
March–April 2017: 281–292

INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary malignant neoplasm accounting for 85%-90% of primary liver cancer, which is the sixth most common cancer and the second-leading cause of cancer death worldwide.[1,2] Liver cancer places a huge burden on the Chinese population. China alone accounts for approximately 50% of the total number of liver cancer cases and deaths globally.[2] In addition, liver cancer is identified as the second leading cause of cancer death among men and third among women in China.[3] In an effort to control and to reduce the detrimental effects of liver cancer in China, guidelines recommend the practice of screening for early cancer detection.[4] However, unlike in other East Asian regions, such as Japan, Korea, and Taiwan, there is no government-funded nationwide HCC screening program for high-risk populations in China.[5] In China, the high-risk populations for developing HCC are patients with hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, HBV and HCV coinfection, liver cirrhosis, and diabetes mellitus and those with severe alcohol abuse or a family history of HCC.[6]

The detrimental effect of liver cancer is characterized by its poor prognosis, with a 5-year relative survival rate of 10.1% in China.[7] Currently there is no curative treatment for the intermediate or advanced stage of HCC, and most patients are diagnosed during the advanced stage, which cannot be effectively treated.[8] Although certain cancers may respond to adjuvant chemotherapy or radiation, neither chemotherapy nor radiation for late-stage HCC reduces mortality rates; nevertheless, treatments are more effective for the early stage of HCC and include surgically removing part of the liver, local ablation of small lesions, and liver transplantation.[9]

Routine screening is the best way to detect early-stage HCC and improve survival and prognosis.[9] The screening guidelines for HCC developed by the American Association for the Study of Liver Diseases recommend HCC screening every 6 months for high-risk individuals by abdominal ultrasound.[10] On the other hand, screening guidelines published by the Peking University Medical Press and expert consensus established by the Chinese Anti-Cancer Association Society of Liver Cancer, Chinese Society of Clinical Oncology, and Chinese Society of Hepatology Liver Cancer Study Group recommend biannual screening with a combination of serum α-fetoprotein (AFP) and abdominal ultrasound at 6-month intervals for high-risk populations.[6,11] The clinical effectiveness of AFP has been reported in 18,816 patients with a history of chronic hepatitis or HBV infection, and findings indicated that biannual screening with AFP and ultrasound reduced mortality by 37%.[4] In addition, a combination of these 2 screening tests has been suggested as the most effective strategy for detecting HCC at an early stage, and complementary usage improved surveillance in patients with cirrhosis.[12,13] In spite of a lack of adequate sensitivity of abdominal ultrasound and AFP, this combination is still regarded as the recommended method for HCC surveillance.[14]

Although numerous studies have surveyed different populations to understand the knowledge and barriers for cervical, breast, and colorectal cancer screenings, it is difficult to find similar studies conducted for HCC screening in China. Furthermore, although no population-based data have been published about HCC screening rates in China, studies have suggested that screening rate may be low because of a lack of knowledge and awareness among the general Chinese population and even among health care workers.[15,16] In a study that included Chinese public health workers, 29% were not aware that chronic HBV infection was a major risk factor for cirrhosis and liver cancer, and 30% did not know about the importance of the HBV vaccine.[16] Because health care professionals recommend HCC screening to at-risk patients,[1,17] it is crucial to identify the barriers that hinder HCC screening so that more effective approaches can be implemented to promote screening. The main objectives of this study were to (i) investigate HCC screening practice among high-risk Chinese patients, (ii) identify the sociodemographic and clinical factors related to HCC screening practice, (iii) examine the association of sociodemographic and clinical factors with HCC screening knowledge, and (iv) identify the barriers to HCC screening.

METHODS

Study Design and Data Collection. This was a cross-sectional questionnaire study conducted from June to August 2016 at the Shanghai Public Health Clinical Center of Shanghai and Hubei Third People's Hospital of Wuhan, China. The source population were patients from outpatient clinics with a high risk of developing HCC, which comprised patients with chronic HBV and/or HCV

infection. Based on Chinese liver cancer screening recommendations, men aged 35-65 years and women aged 45-65 years were recruited.[11] Patients diagnosed with the previously stated conditions before 2015 were excluded from the study. Additionally, severely ill patients were not asked to participate.

The questionnaire was designed by the study investigators based on hepatology experts' opinions and previous studies on the screening practices of cervical cancer, breast cancer, and HBV infection.[18-20] To examine the feasibility and appropriateness of the questionnaire, a pilot test was conducted on 30 patients, with 15 from each hospital. The official interviews took place after making adjustments of the initial questionnaire. Patients from outpatient clinics who met the eligibility criteria were introduced by their hepatologists to a trained interviewer. After informed consent was obtained, an in-person interview was conducted in a private setting within the hospital. The questionnaire was anonymous and took an average of 10 minutes to complete.

Measures and Assessment. A total of 364 patients responded to the questionnaire and 12 had partial completions, which were excluded. The questionnaire consisted of 3 sections. Section 1 comprised 11 multiple-choice and fill-in-the-blank questions, and the characteristics of interest were age, gender, current region of residence, household registration, education level, annual household income, health insurance, any immediate family member with HCC, duration of known hepatitis infection, cirrhosis status, and presence of comorbidity. Household registration, which classifies individuals as rural or urban residents, is a system of controlling population migration and determining eligibility for state-provided welfare and benefits.[21] There are 3 main types of insurance programs in China: *Urban Employee's Basic Medical Insurance* (UEBMI) covers insurance for the urban working population, *Urban Resident Basic Medical Insurance* (URBMI) provides care to urban residents who are unemployed, and *New Rural Cooperative Medical System* (NCMS) provides financial subsidies for rural residents.[22]

The main outcome measure of the study was screening practice. Routine screening was defined as receiving both serum AFP and abdominal ultrasound at least every 6 months, irregular screening interval involved screening with both tests on an inconsistent basis, and patients with incomplete or no screening either never had AFP test or the combination of AFP and abdominal ultrasound. In section 2, patients were questioned if they had ever received AFP and abdominal ultrasound. If they answered yes, patients were asked how often they received screening and the time of their most recent screening. If they answered no, patients were asked to choose the reasons for not undergoing or barriers to having undergone screening, and more than 1 choice was allowed.

Section 3 consisted of 8 yes-or-no questions and 5 multiple-choice questions that examined the patients' knowledge concerning viral hepatitis, HCC, and HCC screening guidelines. Two of the multiple-choice questions had 2 correct answer choices. The knowledge score (range: 0-15) was calculated by giving 1 point for each correct answer and 0 points for an incorrect answer or an answer of "I do not know."

Statistical Analysis. Data analysis was carried out with SAS Version 9.4 (SAS Inc., Cary, NC), using significance level at $P < .05$. Descriptive statistics were performed, and frequencies and percentages were reported for categorical variables while mean and standard deviation were presented for the continuous variable. Patients' sociodemographic factors, clinical factors and knowledge were compared among the different screening practice groups using χ^2 or Fisher's exact test for categorical variables and 1-way analysis of variance for the continuous variable. All factors were included in a multinominal logistic regression model with stepwise model selection ($P = .15$) to identify the independent predictors for screening practice. Adjusted odds ratio (OR) and 95% confidence intervals were generated for variables in the final model.

To investigate the association of knowledge with sociodemographic and clinical factors, t test, 1-way analysis of variance, and Tukey post hoc test were utilized. In addition, multiple linear regression analysis was conducted with stepwise model selection ($P = .15$) to examine the independent predictors for knowledge. Model diagnostics for regression were performed and data satisfied the assumptions in a linear regression model. There was no evidence of heteroscedasticity and missing covariates, and knowledge score indicated a normal distribution pattern individually and when combined with covariates.

Ethical Consideration. This study was approved by the Institutional Review Board at the University of Nebraska Medical Center and the Ethics Committees of Shanghai Public Health Clinical Center and Hubei Third People's Hospital.

Annals of Global Health, VOL. 83, NO. 2, 2017
March–April 2017: 281–292

Table 1. A Comparison of Screening Practice by Sociodemographic Characteristics, Clinical Characteristics, and Knowledge Score (N = 352)

	Routine Screening (N = 176) N (%)	Irregular Screening Interval (N = 82) N (%)	Incomplete/No Screening (N = 94) N (%)	*P*
Age group (y)				.57
35-44	33 (18.8)	22 (26.8)	18 (19.2)	
45-54	65 (36.9)	24 (29.3)	33 (35.1)	
55-65	78 (44.3)	36 (43.9)	43 (45.7)	
Gender				.12
Male	117 (66.5)	70 (74.5)	64 (78.1)	
Female	59 (33.5)	24 (25.5)	18 (22.0)	
Residence				.003*
Urban	160 (90.9)	71 (86.6)	71 (75.5)	
Rural	16 (9.1)	11 (13.4)	23 (24.5)	
Household registration				.003*
Urban	145 (82.4)	67 (81.7)	61 (64.9)	
Rural	31 (17.6)	15 (18.3)	33 (35.1)	
Education level				<.0001*
Middle school or below	45 (25.6)	25 (30.5)	55 (58.5)	
High school	71 (40.3)	39 (47.6)	28 (29.8)	
College or above	60 (34.1)	18 (22.0)	11 (11.7)	
Household income (RMB)				<.001*
<40K	37 (21.0)	22 (26.8)	43 (45.7)	
40K-80K	66 (37.5)	33 (40.2)	33 (35.1)	
80K-150K	41 (23.3)	18 (22.0)	13 (13.8)	
>150K	32 (18.2)	8 (11.0)	5 (5.3)	
Insurance type				.17
UEBMI	129 (73.3)	56 (68.3)	54 (57.5)	
URBMI	16 (9.1)	10 (12.2)	13 (13.8)	
NCMS	12 (6.8)	7 (8.5)	16 (17.0)	
Out-of-pocket	12 (6.8)	6 (7.3)	5 (5.3)	
Other	7 (4.0)	3 (3.7)	6 (6.4)	
Family history				.027*
Yes	45 (25.6)	19 (23.2)	11 (11.7)	
No	131 (74.4)	63 (76.8)	83 (88.3)	
Hepatitis duration (y)				.050
0-9	47 (26.7)	24 (29.3)	40 (42.6)	
10-19	45 (25.6)	26 (31.7)	23 (24.5)	
≥20	84 (47.7)	32 (39.0)	31 (33.0)	
Cirrhosis status				.017*
Yes	78 (44.3)	27 (32.9)	26 (27.7)	
No	98 (55.7)	55 (67.1)	68 (72.3)	
Comorbidity				.78
0	88 (50.0)	37 (45.1)	52 (55.3)	
1	53 (30.1)	29 (35.4)	23 (24.5)	
2	23 (13.1)	10 (12.2)	14 (14.9)	
≥3	12 (6.8)	6 (7.3)	5 (5.3)	
Knowledge score, mean (SD)	10.1 (2.5)	8.6 (2.6)	7.4 (2.5)	<.0001*

NCMS, New Rural Cooperative Medical System; UEBMI, Urban Employee's Basic Medical Insurance; URBMI, Urban Resident Basic Medical Insurance.
* Statistical significance at $P < .05$.

RESULTS

Patient Characteristics. A total of 352 valid questionnaires were collected with a response rate of 92%. Totals of 156 and 196 patients were recruited from Shanghai and Wuhan, respectively. The majority of patients were men (71.3%), currently resided in urban regions (85.8%), had urban

household registration (77.6%) and UEBMI health insurance (67.9%), had no immediate relative diagnosed with HCC (78.7%), and were cirrhotic (62.8%). The mean knowledge score was 9.0 (SD: 2.8). A total of 176 patients (50.0%) had routine screening, 82 (23.3%) had irregular screening, and 94 (26.7%) had incomplete or no screening. Out of the 94 patients with incomplete or no screening, 83 had received ultrasound only and 11 never had either AFP or ultrasound. As shown in Table 1, screening practice was significantly associated with residence ($P = .003$), household registration ($P = .003$), education level ($P < .0001$), annual household income ($P < .001$), family history ($P = .027$), cirrhosis status ($P = .017$), and knowledge score ($P < .0001$).

Predictors of HCC Screening Practice. Table 2 shows the results of multinominal logistic regression on factors associated with screening practice. Education level, family history, cirrhosis status, and knowledge were significantly associated with screening practice. Patients with an education level of high school and college or above were 2.80 ($P = .002$) and 3.94 ($P = .002$) times more likely to receive routine screening, respectively, compared with patients who were middle school graduates or below. Likewise, patients with a degree of high school and college or above were 2.72 ($P = .005$) and 2.62 ($P = .045$) times more likely to receive irregular screening, respectively. Patients with an immediate family member with HCC were 2.86 times more likely to undergo routine screening ($P = .011$) and 2.51 times more likely to receive irregular screening ($P = .033$) compared with patients with no family history with HCC. Additionally, cirrhotic patients were 2.39 times more likely to have routine screening compared with patients without cirrhosis ($P = .007$). Knowledge was also a significant predictor; a 1-point increase in knowledge score significantly increased the odds of undertaking routine screening (OR: 1.47; $P < .0001$) or screening with irregular interval (OR: 1.18; $P = .013$).

Factors Associated With HCC Screening Knowledge. The association between sociodemographic and clinical characteristics with knowledge was generated from univariate analysis (Table 3). Patients from age group 35-44 had better knowledge than patients aged 55-65 years ($P = .003$). Patients living in urban areas ($P < .0001$) and patients with urban household registration ($P < .0001$) also exhibited better knowledge. Moreover, patients with a college education or above had better knowledge than patients with degrees of high school and middle school or below ($P < .0001$). Patients with an annual household income (RMB) of >150,000 (approximately US$22,000) had better knowledge than patients who earned 40,000-80,000 (approximately US$6,000-12,000) and <40,000 (approximately US$6,000) ($P < .0001$). Additionally, patients with

Table 2. Multinomial Logistic Regression of the Effect of Sociodemographic Characteristics, Clinical Characteristics, and Knowledge Score on Screening Practice (N = 352)

	Routine Screening vs Incomplete/No Screening		Irregular Screening Interval vs Incomplete/No Screening	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Gender				
Male	Reference		Reference	
Female	1.56 (0.81, 3.00)	.18	0.85 (0.41, 1.78)	.66
Education level				
Middle school or below	Reference		Reference	
High school	2.80 (1.45, 5.41)	.002*	2.72 (1.36, 5.46)	.005*
College or above	3.94 (1.67, 9.27)	.002*	2.62 (1.02, 6.73)	.045*
Family history				
No	Reference		Reference	
Yes	2.86 (1.28, 6.40)	.011*	2.51 (1.08, 5.82)	.033*
Cirrhosis status				
No	Reference		Reference	
Yes	2.39 (1.28, 4.46)	.007*	1.40 (0.71, 2.76)	.33
Knowledge score	1.47 (1.30, 1.67)	<.0001*	1.18 (1.04, 1.35)	.013*

CI, confidence interval; OR, odds ratio.
* Statistical significance at $P < .05$.

Annals of Global Health, VOL. 83, NO. 2, 2017
March–April 2017: 281–292

Table 3. A Comparison of Knowledge Score by Sociodemographic and Clinical Characteristics (N = 352)

	Knowledge Score		
	Mean	SD	*P*
Age group (y)			.003*
35-44	9.9	3.0	
45-54	9.0	2.8	
55-65	8.6	2.7	
Gender			.73
Male	9.0	2.9	
Female	9.1	2.6	
Residence			<.0001*
Urban	9.4	2.7	
Rural	7.1	2.6	
Household registration			<.0001*
Urban	9.4	2.7	
Rural	7.7	2.6	
Education level			<.0001*
Middle school or below	8.0	2.6	
High school	8.9	2.6	
College or above	10.7	2.5	
Household income (RMB)			<.0001*
<40K	7.8	2.5	
40K-80K	9.0	2.7	
80K-150K	9.7	2.8	
>150K	10.7	2.6	
Insurance type			<.0001*
UEBMI	9.4	2.7	
URBMI	8.8	2.4	
NCMS	6.8	2.5	
Out-of-pocket	9.6	3.0	
Other	8.8	3.1	
Family history			.48
Yes	9.2	3.0	
No	9.0	2.7	
Hepatitis duration (y)			<.0001*
0-9	8.1	2.6	
10-19	9.2	2.6	
≥20	9.6	2.9	
Cirrhosis status			.58
Yes	9.1	3.0	
No	9.0	2.7	
Comorbidity			.68
0	9.1	2.9	
1	9.2	2.8	
2	8.6	2.6	
≥3	9.0	2.8	

NCMS, New Rural Cooperative Medical System; SD, standard definition; UEBMI, Urban Employee's Basic Medical Insurance; URBMI, Urban Resident Basic Medical Insurance.
* Statistical significance at $P < .05$.

a hepatitis infection of 0-9 years' duration had worse knowledge than patients with hepatitis infection for 10-19 years and ≥20 years ($P < .0001$).

Predictors of HCC Screening Knowledge. Table 4 illustrates the results of multiple linear regression on the significant predictors for knowledge. Patients aged 55-65 years and 45-54 years had knowledge score of 1.49 point ($P < .001$) and 0.98 point ($P = .010$) lower than patients from age group of 35-44. Female patients scored 0.72 point higher in knowledge score compared with male patients ($P = .020$), and patients living in rural areas had knowledge score of 1.25 points lower than patients living in urban areas ($P = .002$). In addition, patients with a college degree or above had 1.67 points higher in knowledge score than patients with a middle school degree or below ($P < .0001$). Patients with annual household income (RMB) of greater than 150,000 and 40,000-80,000 scored 1.48 points ($P = .004$) and 0.70 point ($P = .041$) higher in knowledge score than patients who earned less than 40,000. Furthermore, patients with a hepatitis infection for ≥20 years and 10-19 years had 1.59 points ($P < .0001$) and 0.92 point ($P = .007$) higher in knowledge score than patients with hepatitis infection for 0-9 years.

Specific Knowledge of Viral Hepatitis, HCC, and HCC Screening Guidelines. Questions addressing knowledge are presented in Supplemental Table 1. The question with the highest percentage of overall correct response (88.1%) was "Is excessive alcohol consumption considered a risk factor for HCC?" The 3 questions with the lowest percentage of overall correct responses were "Does hepatitis have to cause cirrhosis before developing HCC?" (31.3%), "Prior to participation, did you know the purpose of the liver AFP test?" (39.8%), and "When should patients with chronic hepatitis start to undergo HCC screening?" (41.2%). As illustrated, patients with routine screening were most likely to answer each knowledge question correctly.

Barriers to Participate in HCC Screening. The frequencies of self-perceived barriers were analyzed and are described (Supplemental Table 2). The top 5 reasons for not receiving HCC screening were "Not aware that screening for HCC exists" (41.5%), "No symptoms or discomfort" (38.3%), "Lack of recommendation from physicians" (31.9%), "Do not know the benefits of screening" (22.3%), and "Since HCC is difficult to treat, why bother to undergo screening" (18.1%).

DISCUSSION

To our knowledge, this is the first study to evaluate the practice, knowledge, and barriers for HCC

screening among high-risk hospital patients in China. The results showed that only 50.0% of patients underwent standard routine screening. A meta-analysis involving 19 published studies on HCC surveillance adherence rate among 16,446 high-risk patients found that the overall adherence was 61.0%.[23] This meta-analysis mainly comprised of studies from Europe and North America, and surveillance was defined as a combination of imaging plus AFP.[23] Moreover, retrospective studies on HCC surveillance conducted in East Asian regions, including Japan, Taiwan, and Hong Kong, indicated that adherence rates varied from 15.2%-79.0% among high-risk hospital patients.[24]

Similar to our findings, a study found that patients with degrees of high school or college or above had greater odds of undergoing routine screening. Moreover, a study that investigated the use of HCC surveillance among US cirrhotic patients reported that patients with more than a high school education were more likely to receive regular HCC screening than patients with less than a high school education.[25] A study consisting of patients with chronic HBV, conducted in the San Francisco Bay Area and composed of 92% Asian populations, found that patients with cirrhosis were more likely to have optimal HCC screening than patients without cirrhosis.[26] Furthermore, Zhao et al[23] found that cirrhotic patients had significantly higher surveillance adherence rates than patients with chronic HBV. These results support our finding that cirrhosis was a significant determinant for receiving routine screening. Furthermore, patients with better knowledge concerning viral hepatitis, HCC, and screening guidelines were more likely to be screened. Likewise, a survey that investigated HCC screening practice among San Francisco health care providers with large Asian American populations found that better knowledge concerning HCC and surveillance was associated with performing HCC screening.[27]

Our finding indicated that younger patients had better knowledge, and this is supported by a study conducted in chronic hepatitis patients in Taiwan, which reported that patients' age was negatively associated with hepatitis knowledge and health

Table 4. Multiple Linear Regression of the Effect of Sociodemographic and Clinical Characteristics on Knowledge Score (N = 352)

	Knowledge Score			
	β-Coefficient	SE	95% CI	*P*
Age group (y)				
35-44	Reference			
45-54	-0.98	0.38	(-1.73, -0.24)	.010*
55-65	-1.49	0.38	(-2.24, -0.75)	<.001*
Gender				
Male	Reference			
Female	0.72	0.30	(0.11, 1.31)	.020*
Residence				
Urban	Reference			
Rural	-1.25	0.41	(-2.06, -0.45)	.002*
Education level				
Middle school or below	Reference			
High school	0.46	0.33	(-0.18, 1.10)	.16
College or above	1.67	0.41	(0.87, 2.47)	<.0001*
Household income (RMB)				
<40K	Reference			
40K-80K	0.70	0.34	(0.03, 1.37)	.041*
80K-150K	0.65	0.44	(-0.22, 1.51)	.14
>150K	1.48	0.51	(0.48, 2.47)	.004*
Hepatitis duration (y)				
0-9	Reference			
10-19	0.92	0.34	(0.25, 1.59)	.007*
≥20	1.59	0.31	(0.98, 2.21)	<.0001*

CI, confidence interval; SE, standard error.
* Statistical significance at $P < .05$.

Annals of Global Health, VOL. 83, NO. 2, 2017
March–April 2017: 281–292

perceptions.[28] Moreover, our results indicated that residents residing in rural regions had worse knowledge, and this was even found among Chinese health care and public health professionals, in which individuals from rural provinces had worse knowledge about HBV and liver cancer than those from urban provinces.[16] Studies conducted among hepatitis patients in Taiwan, general hospital patients in China, and cirrhotic patients at the University of Michigan have found that education level was a major factor for indicating better knowledge in hepatitis and HCC[15,28,29]; these results are in accordance with our findings. Additionally, higher annual household income was an important factor on knowledge; Chen et al[28] discovered that household income was not only an important determinant on knowledge, but it was also positively corrected with perceived susceptibility, benefits, barriers, and cues to action.

The knowledge question that was mostly missed was "Does hepatitis have to cause cirrhosis before developing HCC?" because only 31.3% of the overall population and 25.5% of patients with incomplete or no screening answered it correctly. Although the majority of patients with HBV or HCV who develop HCC have cirrhosis, HBV and HCV are able to cause HCC in the absence of cirrhosis.[30,31] This misconception may have affected screening practice because patients without cirrhosis may feel safe at the moment and believe they have another stage to go through before developing HCC. In addition, 44.9% of patients with routine screening and 63.4% with irregular screening did not know the purpose of the liver AFP test before participation in this study. Many patients underwent AFP simply because they were asked to do so by their hepatologists, but there was a lack of explanation and education about receiving HCC screening.

"Not aware that screening for HCC exists" was the most common reason for not having undergone screening, which illustrates a serious deficiency in HCC screening knowledge. Such lack of knowledge among high-risk patients indicates that insufficient knowledge and awareness also likely exists in the general Chinese population, which results in inadequate preventive measures and enables HCC to be prevalent. Another important barrier was "No symptoms or discomfort," which was cited as the second most common reason for refusing cervical cancer screening among women from a region in China with high cervical cancer incidence.[19] In traditional Chinese culture, visiting physicians is usually for the purpose of treating and managing illnesses rather than prevention, putting an emphasis on dealing with health crises over health promotion.[32] Studies that examined cervical, breast, and colon cancer screening practices among Chinese American women and Chinese immigrants discovered that physician recommendation was a major factor for screening adherence.[33-35] Likewise in our study, "Lack of recommendation from physicians" was cited as one of the key reasons for not participating in screening. Because physicians are often regarded as authoritative figures in Chinese culture,[36] it is crucial for Chinese physicians and health care providers to take the lead and educate patients about the importance of HCC screening. Whereas US studies on HCC surveillance reported financial reasons to be a substantial barrier for screening,[26,27] only 16.0% of patients with incomplete or no screening listed financial difficulty as a barrier in our study. This finding is also consistent with our result that neither annual household income nor insurance status had a significant impact on screening practice. The reason could be due to the cost of HCC screening, in which a combination of AFP and ultrasound is listed to be 90 RMB (approximately US$13) at Shanghai Public Health Clinical Center and 200 RMB (approximately US$29) at Hubei Third People's Hospital. These prices are reasonable considering household income, and screening cost becomes even lower with insurance coverage. Other barriers observed included "Do not know the benefits of screening," "Since HCC is difficult to treat, why bother undergo screening," "Afraid of detecting HCC," "Lack of time," "Difficult to access medical facilities," "Do not believe that HCC screening is an effective prevention," and "Not afraid of developing HCC." As reported, the majority of the barriers are associated with a lack of understanding, knowledge, and awareness about HCC screening; therefore, there is a need to bring out public attention and correct these misconceptions. Improving an individual's knowledge regarding HCC will likely lead to a change in behavior. Health care professionals and community leaders should provide extensive education to inform high-risk populations about the importance of HCC screening and that screening is beneficial because treatments for HCC can be offered with early detection. Moreover, it is crucial to educate high-risk patients about adopting healthy lifestyles and continuously reinforce the importance of HCC screening.

In China, many HBV carriers are living under a great amount of stress and often face discrimination in life and work because of social stigma.

Discrimination against HBV carriers is a major issue in China, and many health care services even report a positive test result to the patient's school or employer.[16] In addition, it is still a common belief that HBV is transmittable through eating together and contacts, which underlies the prejudice against infected individuals.[37] Because social pressure generated from the society may have deterred high-risk patients from undertaking screening, there is a need to identity individuals with psychological issues and offer the appropriate counseling, which could involve providing education regarding HCC, alleviating emotional stress, managing crisis, recommending lifestyle modifications, and giving encouragements.

The main strengths of this study are that the response rate was high and the sample size was large enough to generate statistically meaningful findings; however, this study is subject to some limitations. Because electronic medical record systems were not available at the studied institutions, formal verification for data accuracy was not performed. Although we relied on self-report, quality controls and best efforts were delivered to assure data collected were reliable. Because our collaborating institutions are major tertiary hospitals in large urban cities, and because major gaps in economic development and health disparities exist between urban and rural regions in China,[38] future studies can be carried out in rural and less economically developed regions. It would be reasonable to assume that screening adherence rate in many economically impoverished regions in China is lower than the rate observed in our study. Moreover, because patients who visit health care facilities tend to have better health awareness, it would be of interest to investigate HCC screening practice among high-risk patients from a community-based setting in China.

CONCLUSIONS AND FUTURE DIRECTIONS

Because China alone accounts for half of the liver cancer cases and deaths globally,[2] understanding the reasons for the lack of HCC screening in high-risk populations could assist health care professionals to develop more effective intervention methods for early detection. Because screening helps to detect HCC at an early stage, effective treatments may be offered to achieve better chances of survival. Unlike the screening approaches formulated for certain other cancers, which target the general population, strategies for improving HCC screening should be different. Our findings suggest that appropriate and effective educational programs should be established. Chinese health care practitioners and community health promotion leaders should pursue an active role to implement and use educational programs as an intervention to improve high-risk patients' awareness, knowledge, and perceptions about HCC screening. These educational programs should target patients with low socioeconomic status, patients who reside in rural areas, and middle-aged and older patients. At the same time, professional counseling could be provided to assist patients with social or psychological issues regarding hepatitis or HCC. In addition, the approach of entering high-risk patients into disease management programs and providing automatic reminders could potentially improve screening adherence[39,40]; this calls for the wide implementation and adaptation of electronic health record systems in China. Further studies conducted in multiple diverse areas in China are warranted.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to Dr. Hongzhou Lu from Shanghai Public Health Clinical Center and Dr. Liming Liu from Hubei Third People's Hospital. The authors also thank Cancer Epidemiology Education in Special Populations Program, University of Nebraska Medical Center College of Public Health, Shanghai Public Health Clinical Center and Hubei Third People's Hospital.

REFERENCES

1. El-Serag HB, Davila JA. Surveillance for hepatocellular carcinoma: in whom and how? Therap Adv Gastroenterol 2011;4:5–10.
2. Torre LA, Bray F, Siegel R, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.
3. Chen WQ, Zheng RS, Zhang SW. Liver cancer incidence and mortality in China, 2009. Chin J Cancer 2013;32:162–9.

4. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. J Cancer Res Clin Oncol 2004;130:417–22.
5. Kudo M, Han KH, Kokudo N, et al. Liver cancer working group report. Jpn J Clin Oncol 2010;40(suppl 1): i19–27.
6. Song P, Gao J, Inagaki Y, et al. Biomarkers: evaluation of screening for and early diagnosis of hepatocellular carcinoma in Japan and China. Liver Cancer 2013;2:31–9.
7. Zeng H, Zheng R, Guo Y, et al. Cancer survival in China, 2003-2005: a population-based study. Int J Cancer 2015;136:1921–30.
8. Singal AG, Pillai A, Tiro J. Early detection, curative treatment, and survival rates for hepatocellular carcinoma surveillance in patients with cirrhosis: a meta-analysis. PLoS Med 2014;11: e1001624.
9. Sherman M, Bruix J, Porayko M, Tran T; AASLD Practice Guidelines Committee. Screening for hepatocellular carcinoma: the rationale for the American Association for the study of liver diseases recommendations. Hepatology 2012;56:793–6.
10. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology 2011;53:1020–2.
11. Dong ZW. The Guidelines for the Screening and Early Diagnosis and Treatment of Cancer in China. Peking, China: Peking University Medical Press; 2005.
12. Singal AG, Conjeevaram HS, Voilk ML, et al. Effective of hepatocellular carcinoma surveillance in patients with cirrhosis. Cancer Epidemiol Biomarkers Prev 2012;21:793–9.
13. Chang TS, Wu YC, Tung SY, et al. Alpha-fetoprotein measurement benefits hepatocellular carcinoma surveillance in patients in cirrhosis. Am J Gastroenterol 2015;110:836–44.
14. Attwa MH, El-Etreby SA. Guide for diagnosis and treatment of hepatocellular carcinoma. World J Hepatol 2015;7:1632–51.
15. He WJ, Xu MY, Xu RR, et al. Inpatients' knowledge about primary liver cancer and hepatitis. Asian Pac J Cancer Prev 2013;14:4913–8.
16. Chao J, Chang ET, So SK. Hepatitis B and liver cancer knowledge and practices among health care and public health professionals in China: a cross-sectional study. BMC Public Health 2010;10:98.
17. Qin S. Guidelines on the diagnosis and treatment of primary liver cancer (2011 edition). Chin Chin Oncol 2012;1:10.
18. Park MJ, Park E, Choi KS, Jun JK, Lee HY. Sociodemographic gradients in breast and cervical cancer screening in Korea: the Korean National Cancer Screening Survey (KNCSS) 2005-2009. BMC Cancer 2011;11:257.
19. Jia Y, Li S, Yang R, et al. Knowledge about cervical cancer and barriers of screening program among women in Wufeng County, a high-incidence region of cervical cancer in China. PLoS One 2013;8:e67005.
20. Strong C, Hur K, Kim F, Pan J, Tran S, Juon H. Sociodemographic characteristic, knowledge and prevalence of viral hepatitis infection among Vietnamese Americans at community screenings. J Immigr Minor Health 2014;17:298–301.
21. Chan KW. The household registration system and migrant labor in China: notes on a debate. Pop Develop Rev 2010;36:357–64.
22. Wang S, Liu L, Li L, Liu J. Comparison of Chinese inpatients with different types of insurance before and after the 2009 health care reform. BMC Health Serv Res 2014;14:443.
23. Zhao C, Jin M, Le RH, et al. M01505 Meta-analysis: hepatocellular carcinoma (HCC) surveillance adherence rate (SAR) in high risk patients. Gastroenterology 2016;150:S1134.
24. Zhao C, Nguyen MH. Hepatocellular carcinoma screening and surveillance: practice guidelines and real-life practice. J Clin Gastroenterol 2016;50:120–33.
25. Davila JA, Morgan RO, Richardson OA, Du XL, McGlynn KA, El-Serag HB. Use of surveillance for hepatocellular carcinoma among patients with cirrhosis in the United States. Hepatology 2010;52:132–41.
26. Wang C, Chen V, Vu V, et al. Poor adherence and low persistency rates for hepatocellular carcinoma surveillance in patients with chronic hepatitis B. Medicine 2016;95:e4744.
27. Khalili M, Guy J, Yu A, et al. Hepatitis B and hepatocellular carcinoma screening among Asian Americans: survey of safety net health care provider. Dig Dis Sci 2011;56:1516–23.
28. Chen YW, Liu CC, Perng DS. Perceptions about preventing hepatocellular carcinoma among patients with chronic hepatitis in Taiwan. World J Gastroenterol 2013;19:3459–65.
29. Singal AG, Volk ML, Rakoski MO, et al. Patient involvement in health care is associated with higher rates of surveillance for hepatocellular carcinoma. J Clin Gastroenterol 2011;45: 727–32.
30. Yang JD, Kim WR, Coelho R, et al. Cirrhosis is present in most patients with hepatitis B and hepatocellular carcinoma. Clin Gastroenterol Hepatol 2011;9:64–70.
31. Madhoun MF, Fazili J, Bright BC, Bader T, Roberts DN, Bronze MS. Hepatitis C prevalence in patients in hepatocellular carcinoma without cirrhosis. Am J Med Sci 2010;339: 169–73.
32. Dayer-Berenson L. Cultural Competencies for Nurses: Impact on Health and Illness. Burlington, MA: Jones & Bartlett Learning; 2013.
33. Taylor VM, Jackson JC, Tu SP, et al. Cervical cancer screening among Chinese Americans. Cancer Detect Prev 2002;26:139–45.
34. Wang JH, Mandelblatt JS, Liang W, Yi B, Ma IJ, Schwartz MD. Knowledge, cultural, and attitudinal barriers to mammography screening among nonadherent immigrant Chinese women: ever versus never screened status. Cancer 2009;115:4828–38.
35. Wang JH, Liang W, Chen MY, et al. The influence of culture and cancer worry on colon cancer screening among older Chinese-American women. Ethn Dis 2006;16:404–11.
36. Ferketich A, Wewers ME, Kwong K, et al. Smoking cessation interventions among Chinese Americans: the role of families, physicians, and the media. Nicot Toba Res 2004;6:241–8.
37. Kan Q, Wen J, Xue R. Discrimination against people with hepatitis B in China. Lancet 2015;386:245–6.
38. Meng Q, Zhang J, Yan F, Hoekstra EJ, Zhou J. One country, two worlds—the health disparity in China. Glob Public Health 2012;7: 124–36.
39. Aberra FB, Essenmacher M, Fisher N, Volk ML. Quality improvement measures lead to higher surveillance rates for hepatocellular carcinoma in patients in cirrhosis. Dig Dis Sci 2013;58:1157–60.
40. Beste LA, Ioannou GN, Yang Y, Chang MF, Ross D, Dominitz JA. Improved surveillance for hepatocellular carcinoma with a primary care-oriented clinical reminder. Clin Gastroenterol Hepatol 2015;13:172–9.

Supplemental Table 1. Frequency of Correct Answer on Specific Knowledge Questions; Answers That Counted as a Full Point Are Indicated in Brackets After Questions (N = 352)

Question	Correct Answer Among Patients With Routine Screening	Correct Answer Among Patients With Irregular Screening Interval	Correct Answer Among Patients With Incomplete/ No Screening	Correct Answer Among Overall Population
Q1. Prior to participation, did you know the purpose of the liver AFP test? (*Yes*)	97 (55.1%)	30 (36.6%)	13 (13.8%)	140 (39.8%)
Q2. Is HBV or HCV commonly transmitted through consuming contaminated food? (*No*)	122 (69.3%)	46 (56.1%)	40 (42.6%)	208 (59.1%)
Q3. Can HBV or HCV be transmitted through sexual intercourse? (*Yes*)	132 (75.0%)	54 (65.9%)	66 (70.2%)	252 (71.5%)
Q4. Is excessive alcohol consumption considered a risk factor for HCC? (*Yes*)	158 (89.8%)	73 (89.0%)	79 (84.0%)	310 (88.1%)
Q5. Have you heard of aflatoxin and its carcinogenic role in HCC? (*Yes*)	113 (64.2%)	45 (54.9%)	45 (47.9%)	203 (57.7%)
Q6. Does hepatitis have to cause cirrhosis before developing HCC? (*No*)	60 (34.1%)	26 (31.7%)	24 (25.5%)	110 (31.3%)
Q7. Can HCC metastasize to other organs in the body? (*Yes*)	142 (80.7%)	58 (70.7%)	65 (69.1%)	265 (75.3%)
Q8. Do symptoms usually show up in the early stage of HCC? (*No*)	97 (55.1%)	39 (47.6%)	47 (50.0%)	183 (52.0%)
Q9. Which of the choices are common symptoms of HCC? (*Yellow of the skin*)	129 (73.3%)	56 (68.3%)	60 (63.8%)	245 (69.6%)
Q10. Which of the choices are common symptoms of HCC? (*Unexplained weight loss*)	121 (68.9%)	39 (47.6%)	44 (46.8%)	204 (58.0%)
Q11. Which of the following lifestyles are important to prevent HCC? (*All the above: smoking cessation, alcohol drinking cessation, limit the intake of salty foods, consumption of high fruit and vegetables*)	128 (72.7%)	50 (61.0%)	45 (47.9%)	223 (63.4%)
Q12. Which of the two choices are the most common tests used for HCC screening? (*Ultrasound*)	144 (81.8%)	61 (74.4%)	59 (62.8%)	264 (75.0%)
Q13. Which of the two choices are the most common tests used for HCC screening? (*AFP*)	112 (63.6%)	37 (45.1%)	26 (27.7%)	175 (49.7%)
Q14. How often should patients with chronic hepatitis undergo HCC screening? (*At least every half year*)	150 (85.2%)	55 (67.1%)	49 (52.1%)	254 (72.2%)
Q15. When should patients with chronic hepatitis start to undergo HCC screening? (*Men at age 35 and women at age 45*)	81 (46.0%)	33 (40.2%)	31 (33.0%)	145 (41.2%)

HCC, hepatocellular carcinoma.

Annals of Global Health, VOL. 83, NO. 2, 2017
March–April 2017: 281–292

Supplemental Table 2. Barriers to Participation in HCC Screening Among Patients Who Had Incomplete or No Screening (N = 94)

Barriers	Frequency
1. Not aware that screening for HCC exists	39 (41.5%)
2. No symptoms or discomfort	36 (38.3%)
3. Lack of recommendation from physicians	30 (31.9%)
4. Do not know the benefits of screening	21 (22.3%)
5. Because HCC is difficult to treat, why bother undergo screening	17 (18.1%)
6. Financially difficult to afford screening	15 (16.0%)
7. Afraid of detecting HCC	13 (13.8%)
8. Lack of time	12 (12.8%)
9. Difficult to access medical facilities	7 (7.4%)
10. Do not believe that HCC screening is an effective prevention	5 (5.3%)
11. Not afraid of developing HCC	3 (3.2%)

HCC, hepatocellular carcinoma.