Practice, Knowledge and Barriers for Screening of Hepatocellular Carcinoma among High-risk Chinese Patients

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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 alpha-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 two 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 150K RMB, and longer duration of hepatitis infection. The three most frequent 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%).

CONCLUSIONS—Healthcare 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.

Keywords
hepatocellular carcinoma; high-risk Chinese patients; screening; knowledge; barriers

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 males and third among females 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, 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 5-year relative survival rate to be 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 While 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 early stage of HCC, which 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 (AASLD) 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 Alpha-fetoprotein (AFP) and abdominal ultrasound at 6-month intervals for high-risk populations.6,11 The clinical effectiveness of AFP has been demonstrated 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%. In addition, a combination of these two 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. 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.

While 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 due to a lack of knowledge and awareness among the general Chinese population and even among healthcare workers. 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 HBV vaccine. Since healthcare professionals recommend HCC screening to at-risk patients, 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 of patients with chronic HBV and/or HCV infection. Based on Chinese liver cancer screening recommendations, men aged 35 to 65 years and women aged 45 to 65 years were recruited. Patients diagnosed with the above 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. In order 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 three sections. Section One comprised of 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 three 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 interval, and patients with incomplete or no screening either never had AFP test or the combination of AFP and abdominal ultrasound. In section Two, patients were questioned if they have ever received AFP and abdominal ultrasound. If answered “yes”, patients were asked how often they received screening and the time of their most recent screening. If answered “no”, patients were asked to choose the reason (s) or barrier (s) for not having undergone screening and more than one choice were allowed.

Section Three 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 one point for each correct answer and zero points for an incorrect answer or an answer of “I do not know”.

Statistical Analysis

Data analysis was carried out with SAS 9.4 (SAS, Inc., Cary, NC), using significance level at \( P < 0.05 \). 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 Chi-square or Fisher Exact test for categorical variables and one-way ANOVA for the continuous variable. All factors were included in a multinominal logistic regression model with stepwise model selection \( (P = 0.15) \) 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, one-way ANOVA and Tukey post hoc test were utilized. In addition, multiple linear
regression analysis was conducted with stepwise model selection \((P=0.15)\) 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 demonstrated 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.

**RESULTS**

**Patient Characteristics**

A total of 352 valid questionnaires were collected with a response rate of 92%. 156 and 196 patients were recruited from Shanghai and Wuhan, respectively. The majority of patients were males (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 \((P=0.003)\), household registration \((P=0.003)\), education level \((P<0.0001)\), annual household income \((P<0.001)\), family history \((P=0.027)\), cirrhosis status \((P=0.017)\) and knowledge score \((P<0.0001)\).

**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 \((P=0.002)\) and 3.94 \((P=0.002)\) times more likely to receive routine screening, respectively, compared to patients graduated from middle school or below. Likewise, patients with a degree of high school and college or above were 2.72 \((P=0.005)\) and 2.62 \((P=0.045)\) times more likely to receive irregular screening, respectively. Patients with an immediate family member with HCC were 2.86 \((P=0.011)\) times more likely to undergo routine screening and 2.51 \((P=0.033)\) times more likely to receive irregular screening compared to patients with no family history with HCC. Additionally, cirrhotic patients were 2.39 times more likely to have routine screening compared to patients without cirrhosis \((P=0.007)\). Knowledge was also a significant predictor; a one-point increase in knowledge score significantly increased the odds of undertaking routine screening \((OR: 1.47; P<0.0001)\) or screening with irregular interval \((OR: 1.18; P=0.013)\).
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 ($P=0.003$). Patients living in urban areas ($P<0.0001$) and patients with urban household registration ($P<0.0001$) 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 ($P<0.0001$). Patients with an annual household income (RMB) of greater than 150K (approximately U.S. $22K) had better knowledge than patients who earned 40K–80K (approximately U.S. $6K–12K) and less than 40K (approximately U.S. $6K) (P<0.0001). Additionally, patients with a hepatitis infection of 0–9 years had worse knowledge than patients with hepatitis infection for 10–19 years and 20 years or more ($P<0.0001$).

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 ($P<0.001$) and 0.98 point ($P=0.010$) lower than patients from age group of 35–44. Female patients scored 0.72 point higher in knowledge score compared to male patients ($P=0.020$), and patients living in rural areas had knowledge score of 1.25 points lower than patients living in urban areas ($P=0.002$). 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 ($P<0.0001$). Patients with annual household income (RMB) of greater than 150K and 40K–80K scored 1.48 points ($P=0.004$) and 0.70 point ($P=0.041$) higher in knowledge score than patients who earned less than 40K. Furthermore, patients with a hepatitis infection of 20 years or more and 10–19 years had 1.59 points ($P<0.0001$) and 0.92 point ($P=0.007$) higher in knowledge score than patients with hepatitis infection for 0–9 years.

Specific Knowledge on Viral Hepatitis, HCC, and HCC Screening Guidelines

Questions addressing knowledge are presented in Supplemental Table 5. The question with the highest percentage of overall correct response was “Is excessive alcohol consumption considered a risk factor for HCC?” (88.1%). The three 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 6). The top five 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%. This meta-analysis mainly comprised of studies from Europe and North America, and surveillance was defined as a combination of imaging plus AFP. Moreover, retrospective studies on HCC surveillance conducted in East Asian regions, including Japan, Taiwan and Hong Kong, demonstrated that adherence rates varied from 15.2% to 79.0% among high-risk hospital patients.

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 utilization of HCC surveillance among U.S. 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. A study consisting of patients with chronic HBV, conducted in the San Francisco Bay Area and comprised of 92% Asian populations, found that patients with cirrhosis were more likely to have optimal HCC screening than patients without cirrhosis. Furthermore, Zhao et al. 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 healthcare providers with large Asian American populations demonstrated that better knowledge concerning HCC and surveillance was associated with performing HCC screening.

Our finding indicated that younger patients had better knowledge, and this is supported by a study conducted in chronic hepatitis patients in Taiwan, which found that patients’ age was negatively associated with hepatitis knowledge and health perceptions. Moreover, our results demonstrated that residents residing in rural regions had worse knowledge, and this was even shown among Chinese healthcare and public health professionals, in which individuals from rural provinces had worse knowledge about HBV and liver cancer than those from urban provinces. Studies conducted among hepatitis patients in Taiwan, general hospital patients in China, and cirrhotic patients at the University of Michigan have shown that education level was a major factor for demonstrating better knowledge in hepatitis and HCC; these results are in accordance with our finding. Additionally, higher annual household income was an important factor on knowledge; Chen et al. discovered that household income was not only an important determinant on knowledge, but it was also positively correlated 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?”, as 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{33–35} Likewise in our study, “Lack of recommendation from physicians” was cited as one of the key reasons for not participating in screening. Since physicians are often regarded as authoritative figures in Chinese culture,\textsuperscript{35} it is crucial for Chinese physicians and healthcare providers to take the lead and educate patients about the importance of HCC screening. Whereas U.S. studies on HCC surveillance observed financial reasons to be a substantial barrier for screening,\textsuperscript{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 U.S. $13) at Shanghai Public Health Clinical Center and 200 RMB (approximately U.S. $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 shown, 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. Healthcare 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 are frequently facing discrimination in life and work due to social stigma. Discrimination against HBV carriers is a major issue in China, and many healthcare services even report a positive test result to the patient’s school or employer. In addition, it is still a common belief that HBV is transmittable through eating together and contacts, which underlies the prejudice against infected individuals. Since 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. Since 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. Since 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, 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, since patients who visit healthcare 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**

Since China alone accounts for half of the liver cancer cases and deaths globally, understanding the reasons for the lack of HCC screening in high-risk populations could assist healthcare professionals to develop more effective intervention methods for early detection. As 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 healthcare practitioners and community health promotion leaders should pursue an active role to implement and utilize 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, as well as 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; this calls for the widely implementation and adaptation of electronic health record systems in China. Further studies conducted in multiple diverse areas in China are warranted.
Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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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. [PubMed: 25651787]
3. Chen WQ, Zheng RS, Zhang SW. Liver cancer incidence and mortality in China, 2009. Chin J Cancer 2013;32:162–169. [PubMed: 23489585]
4. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. J Cancer Res Clin Oncol 2004;130:417–422. [PubMed: 15042359]
5. Kudo M, Han KH, Kokudo N, et al. Liver cancer working group report. Jpn J Clin Oncol 2010;40(suppl 1):i19–i27. [PubMed: 20870915]
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;2:31–39. [PubMed: 24159594]
7. Zeng H, Zheng R, Guo Y, et al. Cancer survival in China, 2003–2005: a population-based study. Int J Cancer 2015;136:1921–1930. [PubMed: 25242378]
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. [PubMed: 24691105]
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;56:793–796. [PubMed: 22689409]
10. Bruix J, Sherman M. Management of hepatocellular carcinoma: An update. Hepatology 2011;53:1020–1022. [PubMed: 21374666]
11. Dong ZW. 中国癌症筛查及早诊早治指南 [The guidelines for the screening and early diagnosis and treatment of cancer in China]. 北京: 北京大学医学出版社 [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;21:793–799. [PubMed: 22374994]
13. Chang TS, Wu YC, Tung SY, et al. Alpha-fetoprotein measurement benefits hepatocellular carcinoma surveillance in patients in cirrhosis. Am J Gastroenterol 2015;110:836–844. [PubMed: 25869392]
14. Attwa MH, El-Etreby SA. Guide for diagnosis and treatment of hepatocellular carcinoma. World J Hepatol 2015;7:1632–1651. [PubMed: 26140083]
15. He WJ, Xu MY, Xu RR, et al. Inpatients’ knowledge about primary liver cancer and hepatitis. Asian Pac J Cancer Prev 2013;14:4913–4918. [PubMed: 24083767]
16. Chao J, Chang ET, So SK. Hepatitis B and liver cancer knowledge and practices among healthcare and public health professionals in China: a cross-sectional study. BMC Public Health 2010;10:98. [PubMed: 20184740]

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 (KNCCSS) 2005–2009. BMC Cancer 2011;11:257. [PubMed: 21682886]

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. [PubMed: 23843976]

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;36:357–364.

22. Wang S, Liu L, Li L, Liu J. Comparison of Chinese inpatients with different types of insurance before and after the 2009 healthcare reform. BMC Health Serv Res 2014;14:443. [PubMed: 25267508]

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;50:120–133. [PubMed: 26583266]

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;52:132–141. [PubMed: 20578139]

26. Wang C, Chen V, Yu V, et al. Poor adherence and low persistency rates for hepatocellular carcinoma surveillance in patients with chronic hepatitis B. Medicine 2016;95:e4744. [PubMed: 27583921]

27. Khalili M, Guy J, Yu A, et al. Hepatitis B and hepatocellular carcinoma screening among Asian Americans: survey of safety net healthcare provider. Dig Dis Sci 2011;56:1516–1523. [PubMed: 21046247]

28. Chen YW, Liu CC, Perng DS. Perceptions about preventing hepatocellular carcinoma among patients with chronic hepatitis in Taiwan. World J Gastroenterol 2013;19:3459–3465. [PubMed: 23801839]

29. Singal AG, Volk ML, Rakoski MO, et al. Patient involvement in healthcare is associated with higher rates of surveillance for hepatocellular carcinoma. J Clin Gastroenterol 2011;45:727–732. [PubMed: 21602704]

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. [PubMed: 20831903]

31. Madhoun MF, Fazili J, Bright BC, Baker T, Roberts DN, Bronze MS. Hepatitis C prevalence in patients in hepatocellular carcinoma without cirrhosis. Am J Med Sci 2010;339:169–173. [PubMed: 20087166]

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;26:139–145. [PubMed: 12102148]

34. Wang JH, Mandelblatt JS, Liang W, Yi B, Ma II, Schwartz MD. Knowledge, cultural, and attitudinal barriers to mammography screening among nonadherent immigrant Chinese women: ever versus never screened status. Cancer 2009;115:4828–4838. [PubMed: 19645031]

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;16:404–411. [PubMed: 17682242]
36. Ferketich A, Wewers ME, Kwong K, et al. Smoking cessation interventions among Chinese Americans: the role of families, physicians, and the media. Nicot Tob Res 2004;6:241–248.

37. Kan Q, Wen J, Xue R. Discrimination against people with hepatitis B in China. Lancet 2015;386:245–246. [PubMed: 26194522]

38. Meng Q, Zhang J, Yan F, Hoekstra EJ, Zhou J. One country, two worlds – the health disparity in China. Glob Public Health 2012;7:124–136. [PubMed: 21981140]

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;58:1157–1160. [PubMed: 23111632]

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;13:172–179. [PubMed: 24813175]
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 Value |
|------------------------------|---------------------------------|------------------------------------------|-------------------------------------|---------|
| Age group (year)             |                                 |                                          |                                     | 0.57    |
| 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                       |                                 |                                          |                                     | 0.12    |
| Male                         | 117 (66.5)                      | 70 (74.5)                                | 64 (78.1)                           |         |
| Female                       | 59 (33.5)                       | 24 (25.5)                                | 18 (22.0)                           |         |
| Residence                    |                                 |                                          |                                     | 0.003 *|
| Urban                        | 160 (90.9)                      | 71 (86.6)                                | 71 (75.5)                           |         |
| Rural                        | 16 (9.1)                        | 11 (13.4)                                | 23 (24.5)                           |         |
| Household registration       |                                 |                                          |                                     | 0.003 *|
| Urban                        | 145 (82.4)                      | 67 (81.7)                                | 61 (64.9)                           |         |
| Rural                        | 31 (17.6)                       | 15 (18.3)                                | 33 (35.1)                           |         |
| Education level              |                                 |                                          |                                     | <0.0001 *|
| 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)       |                                 |                                          |                                     | <0.001 *|
| <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               |                                 |                                          |                                     | 0.17    |
| 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               |                                 |                                          |                                     | 0.027 *|
| Yes                          | 45 (25.6)                       | 19 (23.2)                                | 11 (11.7)                           |         |
| No                           | 131 (74.4)                      | 63 (76.8)                                | 83 (88.3)                           |         |
| Hepatitis duration (year)    |                                 |                                          |                                     | 0.050   |
| 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             |                                 |                                          |                                     | 0.017 *|
| Yes                          | 78 (44.3)                       | 27 (32.9)                                | 26 (27.7)                           |         |

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|                      | Routine Screening (N=176) N (%) | Irregular Screening Interval (N=82) N (%) | Incomplete/No Screening (N=94) N (%) | P Value |
|----------------------|---------------------------------|------------------------------------------|--------------------------------------|---------|
| No                   | 98 (55.7)                       | 55 (67.1)                                | 68 (72.3)                            | 0.78    |
| **Comorbidity**      |                                 |                                          |                                      |         |
| 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)                            | <0.0001 * |

* Statistical significance at P <0.05
## 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 Value                                                | OR (95% CI)                                 | P Value                                                |
| **Gender**                  |                                             |                                                        |                                          |                                                        |
| Male                        | 1.56 (0.81, 3.00)                           | 0.18                                                   | Reference                                 | Reference                                              |
| Female                      |                                              |                                                        | 0.85 (0.41, 1.78)                          | 0.66                                                   |
| **Education level**         |                                             |                                                        |                                          |                                                        |
| Middle school or below      | Reference                                   | Reference                                              | Reference                                 | Reference                                              |
| High school                 | 2.80 (1.45, 5.41)                           | 0.002 *                                                | 2.72 (1.36, 5.46)                         | 0.005 *                                                |
| College or above            | 3.94 (1.67, 9.27)                           | 0.002 *                                                | 2.62 (1.02, 6.73)                         | 0.045 *                                                |
| **Family history**          |                                             |                                                        |                                          |                                                        |
| No                          | Reference                                   | Reference                                              | Reference                                 | Reference                                              |
| Yes                         | 2.86 (1.28, 6.40)                           | 0.011 *                                                | 2.51 (1.08, 5.82)                         | 0.033 *                                                |
| **Cirrhosis status**        |                                             |                                                        |                                          |                                                        |
| No                          | Reference                                   | Reference                                              | Reference                                 | Reference                                              |
| Yes                         | 2.39 (1.28, 4.46)                           | 0.007 *                                                | 1.40 (0.71, 2.76)                         | 0.33                                                   |
| **Knowledge score**         | 1.47 (1.30, 1.67)                           | <0.0001 *                                              | 1.18 (1.04, 1.35)                         | 0.013 *                                                |

* Statistical significance at P <0.05
Table 3.
A Comparison of Knowledge Score by Sociodemographic and Clinical Characteristics (N = 352)

| Knowledge Score | Mean | SD  | P Value |
|----------------|------|-----|---------|
| **Age group (year)** |      |     | 0.003 * |
| 35–44           | 9.9  | 3.0 |         |
| 45–54           | 9.0  | 2.8 |         |
| 55–65           | 8.6  | 2.7 |         |
| **Gender**      |      |     | 0.73    |
| Male            | 9.0  | 2.9 |         |
| Female          | 9.1  | 2.6 |         |
| **Residence**   |      |     | <0.0001 * |
| Urban           | 9.4  | 2.7 |         |
| Rural           | 7.1  | 2.6 |         |
| **Household registration** |      |     | <0.0001 * |
| Urban           | 9.4  | 2.7 |         |
| Rural           | 7.7  | 2.6 |         |
| **Education level** |      |     | <0.0001 * |
| Middle school or below | 8.0  | 2.6 |         |
| High school     | 8.9  | 2.6 |         |
| College or above| 10.7 | 2.5 |         |
| **Household income (RMB)** |      |     | <0.0001 * |
| <40K            | 7.8  | 2.5 |         |
| 40K-80K         | 9.0  | 2.7 |         |
| 80K-150K        | 9.7  | 2.8 |         |
| >150K           | 10.7 | 2.6 |         |
| **Insurance type** |      |     | <0.0001 * |
| 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** |      |     | 0.48    |
| Yes             | 9.2  | 3.0 |         |
| No              | 9.0  | 2.7 |         |
| **Hepatitis duration (year)** |      |     | <0.0001 * |
| 0–9             | 8.1  | 2.6 |         |
| 10–19           | 9.2  | 2.6 |         |
| ≥20             | 9.6  | 2.9 |         |
| **Cirrhosis status** |      |     | 0.58    |
| Yes             | 9.1  | 3.0 |         |
| Comorbidity | Mean | SD  | P Value |
|-------------|------|-----|---------|
| No          | 9.0  | 2.7 |         |
| 0           | 9.1  | 2.9 |         |
| 1           | 9.2  | 2.8 |         |
| 2           | 8.6  | 2.6 |         |
| ≥3          | 9.0  | 2.8 |         |

* Statistical significance at $P<0.05$
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 Value  |
|-----------------------------|-----------------|---------------|-----|-----------------|----------|
| **Age group (year)**        |                 |               |     |                 |          |
| 35–44 Reference             |                 |               |     |                 |          |
| 45–54                       | −0.98           | 0.38          | (−1.73, −0.24) | 0.010 *  |
| 55–65                       | −1.49           | 0.38          | (−2.24, −0.75) | <0.001 * |
| **Gender**                  |                 |               |     |                 |          |
| Male Reference              |                 |               |     |                 |          |
| Female                      | 0.72            | 0.30          | (0.11, 1.31)   | 0.020 *  |
| **Residence**               |                 |               |     |                 |          |
| Urban Reference             |                 |               |     |                 |          |
| Rural                       | −1.25           | 0.41          | (−2.06, −0.45) | 0.002 *  |
| **Education level**         |                 |               |     |                 |          |
| Middle school or below      |                 |               |     |                 |          |
| High school                 | 0.46            | 0.33          | (−0.18, 1.10)  | 0.16     |
| College or above            | 1.67            | 0.41          | (0.87, 2.47)   | <0.0001 *|
| **Household income (RMB)**  |                 |               |     |                 |          |
| <40K Reference              |                 |               |     |                 |          |
| 40K-80K                     | 0.70            | 0.34          | (0.03, 1.37)   | 0.041 *  |
| 80K-150K                    | 0.65            | 0.44          | (−0.22, 1.51)  | 0.14     |
| >150K                       | 1.48            | 0.51          | (0.48, 2.47)   | 0.004 *  |
| **Hepatitis duration (year)**|                |               |     |                 |          |
| 0–9 Reference               |                 |               |     |                 |          |
| 10–19                       | 0.92            | 0.34          | (0.25, 1.59)   | 0.007 *  |
| ≥20                         | 1.59            | 0.31          | (0.98, 2.21)   | <0.0001 *|

* Statistical significance at P < 0.05