

A Decade-old Change in the Screening Rate for Hepatocellular Carcinoma Among a Hepatitis B Virus-infected Population in Korea

Hee Yeon Kim¹, Chang Wook Kim¹, Jong Young Choi¹, Chung-Hwa Park¹, Chang Don Lee², Hyeon Woo Yim³

¹Department of Internal Medicine, Division of Hepatology, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea

²Department of Internal Medicine, Division of Hepatobiliary, International St. Mary's Hospital, Incheon 22711, Republic of Korea

³Department of Preventive Medicine, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea

Abstract

Background: Evaluating a change in the screening rate for hepatocellular carcinoma (HCC) is critical for understanding screening implementation, and whether targeted population groups are receiving proper screening. This study examined recent nationwide changes in HCC screening use among hepatitis B virus (HBV)-infected populations after the introduction of the Korean National Cancer Screening Program and predictors of screening adherence.

Methods: We analyzed 165 and 276 participants ≥ 40 years of age who were hepatitis B surface antigen-positive from 2001 (14,936 participants) to 2010–2011 (9159 participants) Korea National Health and Nutrition Examination Surveys, respectively. Demographic data, socioeconomic factors, and HCC screening use were collected by means of self-reported questionnaires.

Results: The rate of HCC screening within the previous 2 years increased significantly from 17.5% in 2001 to 40.3% in 2010–2011 ($P < 0.0001$). The rate of HCC screening use increased from 2001 to 2010–2011 in all study populations. Subjects who had a higher income status and were aware of their infection were more likely to have undergone recent HCC screening.

Conclusions: This study showed a substantial increase in HCC screening in high-risk HBV-infected subjects from 2001 to 2010–2011. However, the HCC screening participation rate remained suboptimal despite the introduction of the nationwide screening program. Efforts should be made to identify high-risk individuals and increase attendance at HCC screening events among high-risk groups.

Key words: Carcinoma; Health Surveys; Hepatitis B; Hepatocellular; Surveillance

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth and seventh most commonly diagnosed cancer in males and females, respectively, and the third leading cause of cancer mortality worldwide. The incidence and mortality rates for HCC are similar because most HCC patients are diagnosed at an advanced stage, highlighting the importance of early HCC detection in the application of potentially curable treatment options.^[1] Hepatitis B virus (HBV) is the major risk factor for HCC^[2] and early detection of HCC through surveillance of high-risk populations improves HCC mortality.^[3] Therefore, national practice guidelines recommend regular HCC surveillance for high-risk HBV-infected persons.^[4,5]

In Korea, the Korean Association for the Study of the Liver and the National Cancer Center jointly developed guidelines

for HCC screening in 2001 recommending that high-risk adults with HBV infection should undergo surveillance for HCC using ultrasonography and alpha-fetoprotein (AFP) every 6 months.^[6] Based on this recommendation, the Korean government introduced nationwide HCC screening as a part of the organized National Cancer Screening Program (NCSP) for lower income levels in 2003. The NCSP

Address for correspondence: Dr. Chang-Wook Kim, Department of Internal Medicine, Division of Hepatology, College of Medicine, The Catholic University of Korea, 222, Banpo-daero, Seocho-gu, Seoul, 06591, Republic of Korea
E-Mail: cwkim@catholic.ac.kr

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provides a biannual ultrasonography and AFP test for males and females ≥ 40 years of age that were hepatitis B surface antigen (HBsAg)-positive, had hepatitis C infection, or liver cirrhosis. In the beginning, the NCSP supplied Medicaid recipients and National Health Insurance (NHI) beneficiaries in the lower 30% income bracket with free HCC screening services. In 2006, the NCSP provided participants in the lower 50% income bracket with HCC screening services free of charge.^[7] In addition to these national HCC screening programs, ultrasonography and AFP testing are performed in outpatient clinics or private health promotion centers across Korea.

Based on the advantages of early HCC detection, it is crucial to investigate the rate of adherence to HCC screening to understand how HCC surveillance tests are being implemented in high-risk groups in Korea. Previous studies have reported that the rate of adherence to HCC surveillance was low.^[8-10] Although a nationwide organized screening program has been provided in Korea since 2003, no study to date has investigated changes in adherence rates to HCC screening in practice.

This study used data from the second and fifth Korea National Health and Nutrition Examination Surveys (KNHANES), which is a nationally representative, cross-sectional survey. We analyzed screening rates for HCC among the HBV-infected Korean population after the introduction of the nationwide HCC screening program and assessed factors related to HCC screening adherence.

METHODS

Study population

This study used the second KNHANES (KNHANES II) data collected during 2001 and fifth KNHANES (KNHANES V) data collected from 2010 to 2011. The KNHANES is a series of nationally representative, cross-sectional health and nutrition examination surveys conducted by the Korean Centers for Disease Control and Prevention since 1998. It uses a complex, stratified, multistage probability sample representative of the Korean population. The procedures for selecting the sample and conducting the interviews and examinations have been described elsewhere.^[11]

Consistent with current Korea NCSP recommendations, we restricted the analysis to adults ≥ 40 years of age at the time of the interview. There were 14,936 individuals who participated in KNHANES II and 9159 who participated in KNHANES V who met the age criteria; 3763 and 8145, respectively, of these participants, were tested for HBsAg. Of these, 176 and 285 participants in KNHANES II and V, respectively, were infected with HBV. Among these populations, we excluded participants who reported a personal history of HCC ($n = 4$ in KNHANES V) or did not answer questions on compliance to HCC screening tests ($n = 11$ and 5 in KNHANES II and V, respectively). In the final analysis, we included 165 and 276 participants ≥ 40 years of age who were HBsAg-positive from KNHANES II and V, respectively [Figure 1].

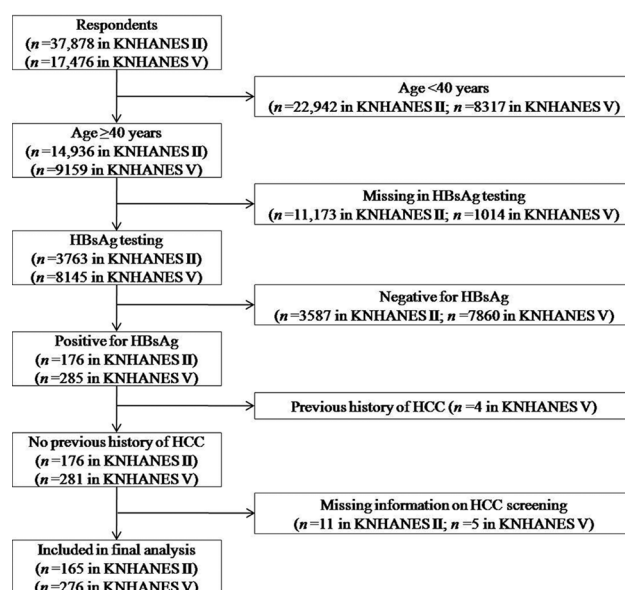


Figure 1: Flowchart of the study population selection. KNHANES: Korea National Health and Nutrition Examination Surveys.

All participants provided informed consent, and the protocol was approved by the Institutional Review Board of the Korea Centers for Disease Control.

Data collection

HBsAg was measured using enzyme-linked immunosorbent assays in KNHANES II (CODA; Bio-Rad, Hercules, CA, USA), and an electrochemiluminescence immunoassay (Modular E-170; Roche Diagnostics, Mannheim, Germany) in KNHANES V. All other parameters were determined from the self-reported questionnaires.

The primary outcome variable was whether HCC screening had been conducted. In KNHANES II, participants were asked, “Have you had a screening test for HCC within the last 2 years?”; possible responses were “yes,” “no,” and “do not know.” In KNHANES V, participants were asked, “When was the last time you had HCC screening test?”; possible responses were “never,” “ ≤ 6 months ago,” “ >6 months and ≤ 1 year ago,” “ >1 year and ≤ 2 years ago,” “ >2 years ago,” and “do not know.” To standardize the major outcome variable, participants who had undergone HCC screening test within the previous 2 years were considered to have undergone recent HCC screening.

Participants were also asked, “Have you ever been diagnosed with HBV infection by a doctor or a health professional?” Subjects who answered positively to this question were defined as those who were self-aware of HBV infection. Data were also collected on demographic and socioeconomic factors (e.g., age, gender, urbanity, marital status, education, household income, health insurance, smoking, and alcohol consumption) relevant to HCC screening.

Two categorical levels for education attainment were used based on the highest level of education achieved by the respondent: High school or higher, and less than high school. Household income was divided into four groups on the basis of monthly

income quartile. With regard to health insurance, subjects were categorized into “NHI beneficiary” or “medical aid beneficiary.” Subjects were categorized into current smokers, past smokers, and nonsmokers. Three categorical groups for alcohol amount were used: Light drinking (<10 g/d for women, <20 g/d for men), moderate drinking (10–20 g/d for females, 20–40 g/d for males), and heavy drinking (\geq 20 g/d for females, \geq 40 g/d for males).

Statistical analysis

Statistical analyses were performed using SAS software (version 9.3, SAS Institute, Cary, NC, USA), which incorporates sample weights and adjust the analyses for the complex sample design of the survey. The survey sample weights, which were calculated taking into consideration the sampling rate, response rate, and age/gender proportion of the reference population (2000 and 2005 National Census Registry, respectively), were used in all analyses to produce estimates representative of the noninstitutionalized civilian Korean population considering a complex, stratified, multistage probability sampling design.

The prevalence and 95% confidence interval (CI) of HBV infection aged \geq 40 years were estimated according to the baseline characteristics. The HCC screening rate within 2 years and 95% CI for each survey year were calculated using cross-tabulation. Differences in the proportion of participants who had HCC screening in each survey were analyzed using the Chi-square test (PROC SURVEYFREQ procedure). To identify risk factors for adherence to an HCC screening program, the crude and adjusted odds ratios (ORs) were calculated using logistic regression (PROC SURVEYLOGISTIC procedure). The covariates for the adjusted OR calculation were household income, smoking status, awareness of HBV infection, and survey year. These variables were obtained statistically significant variables by univariate logistic regression. A $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline characteristics of the participants \geq 40 years of age with hepatitis B virus infection

There were 165 and 276 participants \geq 40 years of age infected with HBV in 2001 and 2010–2011, respectively. The weighted seroprevalence of HBV infection was 4.3% in 2001, and 3.8% in 2010–2011. Table 1 shows the demographic characteristics of these participants. The baseline distribution of the study population was broadly similar between survey years, with the exception of educational attainment, household income, smoking status, and alcohol intake.

Rates of recent hepatocellular carcinoma screening tests within 2 years

Table 2 shows changes in rates of HCC screening use between 2001 and 2010–2011. The proportion of study participants with HBV infection reporting an HCC screening test within the previous 2 years increased significantly from 17.5% in 2001 to 40.3% in 2010–2011 ($P < 0.0001$). An increased rate

of HCC screening tests from 2001 to 2010–2011 was also observed in the entire study population.

Factor influencing hepatocellular carcinoma screening tests among hepatitis B virus-infected participants \geq 40 years of age

The results of the multivariable logistic regression models for factors associated with the adherence to HCC screening tests are reported in Table 3. Following adjustments for household income, smoking status, awareness of HBV infection, survey year, and individuals in higher income quartiles were more likely to have undergone recent HCC screening (third quartile: Adjusted OR = 3.03, 95% CI: 1.27–7.23; fourth quartile: Adjusted OR = 2.49, 95% CI: 1.08–5.73). Self-awareness of HBV infection was positively related to recent HCC screening (adjusted OR = 2.74, 95% CI: 1.40–5.38). Survey year 2010–2011 was associated with a significantly higher rate of recent HCC screening (adjusted OR = 3.37, 95% CI: 1.95–5.81).

DISCUSSION

Given the considerable burden and overall poor prognosis of HCC,^[1,12] early diagnosis through screening enables curative treatments, and, therefore, has the potential to reduce liver-related mortality.^[3,13,14] It is important to investigate changes in the use of HCC screening to understand how screening is being conducted in practice following the introduction of a nationwide HCC screening program in Korea. This study revealed a significant increase in recent HCC screening from 2001 to 2010–2011. In 2001, only 17.5% of respondents had undergone HCC screening test; however, 40.3% of HBV-infected participants had been screened for HCC within the preceding 2 years in 2010–2011. This substantial increase in HCC screening may be partially explained by NCSP. Since 2003, the Korean government has provided individuals at high-risk for developing HCC for free or with a 90% subsidy for HCC screening services.^[8,15] This organized screening program may contribute to the increase in HCC screening.

However, no prominent increase in HCC screening among individuals with low household income was detected. Moreover, the participation rate of HCC screening in the low-income group remained low, even though screening services were offered free of charge by the NCSP. HCC screening programs are different from those of other solid cancers, such as stomach, breast, cervical, or colorectal cancers, in that they target not a general population but a high-risk population.^[7] Therefore, omission from the target population might cause underuse of HCC screening tests among individuals in the low-income group. The target population for HCC screening in Korea NCSP included individuals aged \geq 40 years with liver cirrhosis, HBV or HCV infection. The NCSP HCC screening program comprises two stages. First, the NCSP identifies the high-risk population for HCC among the lower 50% of NHI beneficiaries by screening a computerized medical claims database stored in the NHI Corporation within the past 2 years. The NCSP also analyzed serologic tests for HBsAg and HCV antibody

Table 1: Baseline characteristics of the participants ≥40 years of age with hepatitis B infection

Variables	KNHANES II (2001)		KNHANES V (2010–2011)		χ^2	P
	% (95% CI)*	Total number†	% (95% CI)*	Total number†		
Overall	4.3 (3.6–5.0)	165	3.8 (3.3–4.3)	276	1.31	0.253
Gender						
Male	46.1 (38.1–54.2)	77	51.0 (43.4–58.6)	128	0.67	0.415
Female	53.9 (45.8–61.9)	88	49.0 (41.4–56.6)	148		
Age						
40–49 years	48.9 (42.3–55.5)	82	38.7 (31.4–46.0)	80	4.63	0.099
50–59 years	30.0 (23.6–36.3)	48	36.3 (29.4–43.2)	95		
≥60 years	21.1 (14.7–27.4)	35	25.0 (19.7–30.2)	101		
Marital status						
Never married	13.7 (8.8–18.5)	23	9.9 (5.8–13.9)	33	1.34	0.247
Married or partnered	86.3 (81.5–91.2)	142	90.1 (86.1–94.2)	242		
Education						
Less than high school	56.9 (48.5–65.2)	94	43.3 (36.1–50.6)	137	5.38	0.020
High school or higher	43.1 (34.8–51.5)	70	56.7 (49.4–63.9)	138		
Household income						
1 st quartile	27.0 (20.3–33.7)	42	13.5 (9.3–17.7)	51	12.58	0.006
2 nd quartile	23.7 (16.7–30.7)	39	30.4 (23.8–37.0)	81		
3 rd quartile	22.6 (16.7–28.5)	35	22.9 (16.9–28.9)	59		
4 th quartile	26.7 (20.0–33.4)	41	33.2 (26.5–39.9)	83		
Health insurance						
National health insurance	97.4 (95.2–99.5)	158	97.7 (95.8–99.6)	269	0.01	0.915
Medicaid	2.6 (0.5–4.8)	5	2.3 (0.4–4.2)	7		
Urbanity						
Urban	72.9 (68.0–77.8)	117	75.9 (68.4–83.5)	205	0.92	0.338
Rural	27.1 (22.2–32.0)	48	24.1 (16.5–31.6)	71		
Smoking						
Nonsmoker	59.3 (52.1–66.4)	98	52.3 (44.5–60.0)	156	9.10	0.011
Past smoker	10.6 (5.8–15.5)	18	23.1 (16.6–29.5)	64		
Current smoker	30.1 (23.0–37.2)	49	24.7 (18.1–31.3)	55		
Alcohol consumption						
No	55.7 (46.9–64.6)	93	33.2 (26.3–40.0)	101	20.41	0.0001
Light	28.5 (21.9–35.2)	46	41.9 (34.9–49.0)	120		
Moderate	10.9 (5.2–16.5)	18	14.8 (9.0–20.6)	33		
Heavy	4.9 (2.2–7.6)	8	10.1 (5.6–14.6)	21		
Awareness of hepatitis B infection						
No	83.7 (77.8–89.5)	138	79.0 (73.0–85.0)	214	1.17	0.279
Yes	16.3 (10.5–22.2)	27	21.0 (15.0–27.0)	62		

*Based on weighted data. †Based on unweighted data. P values are derived from Rao-Scott Chi-square test (PROC SURVEYFREQ procedure). KNHANES: Korea National Health and Nutrition Examination Surveys; CI: Confidence interval.

to identify the high-risk group among Medicaid recipients. The second stage involves active surveillance among these high-risk individuals.^[15] Therefore, individuals with HBV infection who had never undergone a health check-up might be missing from the target population group. Consequently, the opportunity to make use of free HCC screening services would have been lost in this missing population. The lower participation rate among the low-income group may also have been due to their unawareness of HBV infection status, and lack of information regarding the nationwide cancer screening program and the benefits of HCC screening.

We also found that moderate-to-high household income, awareness of HBV infection status, and survey year were associated with increased use of recent HCC screening. The

association between household income and HCC screening in this study was similar to a previous report that participants with higher income were more likely to use HCC screening tests.^[8] In general, individuals with higher household income are more likely to undergo screening for colorectal, gastric, breast, and cervical cancer.^[16] In addition, self-awareness of HBV infection was significantly related to adherence with the HCC screening program. Several reports have shown that awareness of HBV infection significantly affected participation in HCC screening programs.^[8,9,17] In this report, 16.3% of HBV-infected participants aged ≥40 years were aware of their HBV infection status in 2001. However, the rate of infection awareness among HBV carriers ≥40 years of age was 21% in 2010–2011, which was not significantly increased compared to that in 2001. These results imply

Table 2: Rate of recent hepatocellular carcinoma screening within 2 years

Variables	KNHANES II (2001)		KNHANES V (2010–2011)		χ^2	P
	% (95% CI)*	Total number†	% (95% CI)*	Total number†		
Overall	17.5 (12.0–22.9)	29	40.3 (33.2–47.4)	106	23.05	<0.0001
Gender						
Male	23.1 (14.5–31.7)	17	44.5 (33.7–55.3)	53	8.92	0.003
Female	12.6 (5.1–20.1)	12	36.0 (26.5–45.4)	53	11.62	0.001
Age						
40–49 years	24.1 (14.7–33.4)	20	40.1 (27.8–52.4)	30	4.19	0.041
50–59 years	12.1 (2.3–22.0)	6	43.0 (30.9–55.0)	42	10.99	0.001
≥60 years	9.6 (0.0–21.0)	3	36.8 (25.0–48.5)	34	6.85	0.009
Marital status						
Never married	23.2 (6.8–39.6)	5	45.3 (24.1–66.5)	13	2.69	0.101
Married or partnered	16.5 (10.9–22.2)	24	39.8 (32.4–47.3)	93	21.39	<0.0001
Education						
Less than high school	14.4 (7.5–21.3)	14	36.0 (25.6–46.5)	49	10.98	0.001
High school or higher	21.7 (12.8–30.7)	15	43.6 (33.8–53.4)	57	9.47	0.002
Household income						
1 st quartile	12.0 (1.7–22.4)	5	24.6 (12.3–36.8)	15	2.06	0.151
2 nd quartile	11.5 (1.8–21.3)	5	30.3 (18.3–42.3)	25	4.64	0.031
3 rd quartile	19.2 (6.5–32.0)	7	50.6 (35.9–65.3)	28	8.37	0.004
4 th quartile	25.1 (10.5–39.8)	10	46.7 (34.0–59.4)	37	4.29	0.038
Health insurance						
National health insurance	17.5 (11.8–23.1)	28	40.7 (33.5–48.0)	105	22.26	<0.0001
Medicaid	23.9 (0.0–63.3)	1	21.7 (0.0–58.4)	1	0.01	0.934
Urbanity						
Urban	18.5 (11.7–25.3)	21	41.6 (33.3–49.9)	79	16.52	<0.0001
Rural	14.6 (5.9–23.2)	8	36.3 (19.6–53.0)	27	6.10	0.014
Smoking						
Nonsmoker	13.7 (6.4–21.1)	14	35.7 (26.5–45.0)	56	11.09	0.001
Past smoker	47.9 (25.3–70.4)	8	51.3 (36.0–66.6)	30	0.06	0.804
Current smoker	14.0 (5.1–22.8)	7	39.9 (24.9–54.8)	20	9.10	0.003
Alcohol consumption						
No	13.3 (6.0–20.6)	13	42.9 (30.2–55.6)	38	15.52	<0.0001
Light	16.0 (7.1–24.9)	7	37.3 (27.4–47.2)	47	7.90	0.005
Moderate	39.1 (16.4–61.9)	7	38.7 (17.6–59.7)	12	0.001	0.975
Heavy	24.8 (2.8–46.9)	2	47.1 (23.1–71.1)	9	1.821	0.177
Awareness of hepatitis B infection						
No	14.8 (9.3–20.3)	21	35.1 (27.1–43.1)	71	16.17	<0.0001
Yes	31.1 (13.7–48.6)	8	60.0 (45.9–74.2)	35	5.85	0.016

*Based on weighted data; †Based on unweighted data. P values are derived from Rao-Scott Chi-square test (PROC SURVEYFREQ procedure). KNHANES: Korea National Health and Nutrition Examination Surveys; CI: Confidence interval.

that the identification of HBV-infected individuals among the general population group is important for HCC surveillance among HBV-infected persons. Therefore, to increase the low rate of HCC screening use, a national policy should encourage HBsAg screening programs to identify HBV-infected persons, as well as improve patient adherence to HCC screening among HBV-infected individuals.

This study had several limitations. First, causal associations could not be examined due to the cross-sectional design. Second, this study defined recent HCC screening use as that performed within the previous 2 years to make uniform the measurement in the two survey periods. The guidelines released jointly by the Korean Association for the Study of the Liver and the National Cancer Center recommended

regular screening every 6 months on the basis of tumor doubling time.^[6] Therefore, the primary outcome in this study does not represent the recommended HCC screening criteria. Moreover, previous studies reported that the rate of participation in regular HCC screening (every 6 months) was lower compared to that of irregular or lifetime HCC screening.^[8,18] Nevertheless, this study that revealed relatively few participants had undergone recent HCC screening within the previous 2 years. Third, we relied on self-reported data to determine whether a subject had actually been screened and when the screening was performed. Therefore, information and recall bias might have interfered. Self-reporting is likely to overestimate cancer-screening rates.^[19] Therefore, this limitation does not seem to overstate

Table 3: Regression models for adherence to hepatocellular carcinoma screening

Variables	% (95% CI)*	Total number†	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Gender						
Male	42.5 (32.6–52.4)	70	1			
Female	33.4 (25.0–41.8)	65	0.68 (0.39–1.19)	0.175		
Age						
40–49 years	38.1 (27.2–48.9)	50	1			
50–59 years	40.3 (29.2–51.4)	48	1.10 (0.58–2.10)	0.776		
≥60 years	34.4 (23.5–45.3)	37	0.85 (0.43–1.68)	0.643		
Marital status						
Never married	42.3 (23.6–61.0)	18	1			
Married or partnered	37.6 (30.8–44.3)	117	0.83 (0.37–1.86)	0.650		
Education						
Less than high school	33.3 (24.1–42.4)	63	1			
High school or higher	41.9 (32.8–51.0)	72	1.46 (0.84–2.54)	0.185		
Household income						
1 st quartile	22.3 (12.2–32.5)	20	1		1	
2 nd quartile	28.8 (17.7–39.9)	30	1.49 (0.69–3.21)	0.311	1.28 (0.56–2.94)	0.560
3 rd quartile	47.6 (34.2–61.0)	35	3.33 (1.51–7.35)	0.003	3.03 (1.27–7.23)	0.013
4 th quartile	45.0 (33.2–56.8)	47	3.00 (1.40–6.41)	0.005	2.49 (1.08–5.73)	0.032
Health insurance						
National health insurance	38.4 (31.9–44.9)	133	1			
Medicaid	22.0 (0.0–54.8)	2	0.40 (0.05–3.25)	0.387		
Urbanity						
Urban	39.3 (31.7–46.9)	100	1			
Rural	33.8 (18.8–48.9)	35	0.79 (0.36–1.70)	0.540		
Smoking						
Nonsmoker	33.2 (25.0–41.4)	70	1		1	
Past smoker	51.1 (36.5–65.7)	38	2.08 (1.03–4.21)	0.042	1.78 (0.87–3.65)	0.117
Current smoker	36.7 (23.3–50.1)	27	1.16 (0.58–2.31)	0.683	1.14 (0.55–2.37)	0.725
Alcohol consumption						
No	38.2 (27.3–49.1)	51	1			
Light	35.8 (26.6–45.0)	54	0.88 (0.50–1.57)	0.645		
Moderate	38.7 (19.2–58.2)	19	1.02 (0.40–2.64)	0.964		
Heavy	45.9 (23.1–68.8)	11	1.40 (0.48–4.11)	0.544		
Awareness of hepatitis B infection						
No	32.9 (25.7–40.1)	92	1		1	
Yes	57.7 (44.5–70.9)	43	2.76 (1.46–5.22)	0.002	2.74 (1.40–5.38)	0.003
Survey year						
KNHANES II (2001)	17.5 (12.0–22.9)	29	1		1	
KNHANES V (2010–2011)	40.3 (33.2–47.4)	106	3.54 (2.14–5.85)	<0.0001	3.37 (1.95–5.81)	<0.0001

*Based on weighted data; †Based on unweighted data. Crude and adjusted ORs (95% CIs) were calculated using logistic regression (PROC SURVEYLOGISTIC procedure). OR: Odds ratio; CI: Confidence interval; KNHANES: Korea National Health and Nutrition Examination Surveys.

our finding of underuse of HCC screening among the study population. Fourth, the screening rate for HCC included organized screening programs and opportunistic screening. In Korea, opportunistic screening is widely accessible, in addition to nationwide organized screening programs. Finally, other factors influencing HCC screening use, such as a family history of HCC, or replicative state of HBV, or other co-morbidities, were not investigated.

Despite these limitations, this study had several strengths. First, it was the first to analyze changes in HCC screening rates following the implementation of organized, nationwide HCC screening programs among HBV-infected groups targeted for screening. A substantial increase in HCC screening in HBV-infected individuals following implementation of

the nationwide screening program provides lessons for government's HCC screening policy in areas endemic for HBV. Second, we used data representative of the Korean population. Therefore, we could evaluate the nationwide change in the utilization of HCC screening. Third, we also identified potential factors related to underuse of screening. To improve the efficiency of national HCC screening program and reduce socioeconomic disparities, identification of proper screening targets for active surveillance is a crucial step in HBV-endemic areas. We anticipate that our results might bring about improvements in HCC screening of high-risk individuals.

In conclusion, the rate of adherence to HCC screening within the past 2 years among HBV-infected Korean people

aged ≥ 40 years has more than doubled in 2010–2011 compared to 2001. However, the HCC screening rate among the high-risk group remained suboptimal despite the implementation of a nationwide screening program. Household income and awareness of HBV infection were positively associated with HCC screening in this study population at high-risk for HCC. These results suggest that multiple strategies, including encouragement for HBV-infected persons to attend HCC screening, as well as more efficient identification of HBV-infected subjects unaware of their infection, are urgently needed to maximize the advantages of HCC screening.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61:69-90. doi: 10.3322/caac.20107.
- Beasley RP, Hwang LY, Lin CC, Chien CS. Hepatocellular carcinoma and hepatitis B virus. A prospective study of 22 707 men in Taiwan. *Lancet* 1981;2:1129-33. doi: 10.1016/S0140-6736(81)90585-7.
- Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol* 2004;130:417-22. doi: 10.1007/s00432-004-0552-0.
- European Association for the Study of the Liver; European Organisation for Research and Treatment of Cancer. EASL-EORTC clinical practice guidelines: Management of hepatocellular carcinoma. *J Hepatol* 2012;56:908-43. doi: 10.1016/j.jhep.2011.12.001.
- Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: An update. *Hepatology* 2011;53:1020-2. doi: 10.1002/hep.24199.
- Han KH, Park JW. The usefulness and current status of the screening program for early diagnosis of hepatocellular carcinoma. *J Korean Med Assoc* 2002;45:972-80.
- Yoo KY. Cancer control activities in the Republic of Korea. *Jpn J Clin Oncol* 2008;38:327-33. doi: 10.1093/jjco/hyn026.
- Park B, Choi KS, Suh M, Shin JY, Jun JK. Factors associated with compliance with recommendations for liver cancer screening in Korea: A nationwide survey in Korea. *PLoS One* 2013;8:e68315. doi: 10.1371/journal.pone.0068315.
- Park SH, Heo NY, Park JH, Kim TO, Yang SY, Kim HK, *et al.* Hepatocellular carcinoma screening in a hepatitis B virus-infected Korean population. *Dig Dis Sci* 2012;57:3258-64. doi: 10.1007/s10620-012-2281-6.
- Wong CR, Garcia RT, Trinh HN, Lam KD, Ha NB, Nguyen HA, *et al.* Adherence to screening for hepatocellular carcinoma among patients with cirrhosis or chronic hepatitis B in a community setting. *Dig Dis Sci* 2009;54:2712-21. doi: 10.1007/s10620-009-1015-x.
- The Korean Association for Survey Research. Sampling Design of the KNHANES. Available from: <http://www.knhanes.cdc.go.kr>. [Last accessed on 2013 Jul 28].
- Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: Incidence, mortality, survival and prevalence in 2010. *Cancer Res Treat* 2013;45:1-14. doi: 10.4143/crt.2013.45.1.1.
- Chen TH, Chen CJ, Yen MF, Lu SN, Sun CA, Huang GT, *et al.* Ultrasound screening and risk factors for death from hepatocellular carcinoma in a high risk group in Taiwan. *Int J Cancer* 2002;98:257-61. doi: 10.1002/ijc.10122.
- Ando E, Kuromatsu R, Tanaka M, Takada A, Fukushima N, Sumie S, *et al.* Surveillance program for early detection of hepatocellular carcinoma in Japan: Results of specialized department of liver disease. *J Clin Gastroenterol* 2006;40:942-8. doi: 10.1097/01.mcg.0000225675.14594.d6.
- Lee EH, Han MA, Lee HY, Jun JK, Choi KS, Park EC. Liver cancer screening in Korea: A report on the 2008 National Cancer Screening Programme. *Asian Pac J Cancer Prev* 2010;11:1305-10.
- Park B, Choi KS, Lee YY, Jun JK, Seo HG. Cancer screening status in Korea, 2011: Results from the Korean National Cancer Screening Survey. *Asian Pac J Cancer Prev* 2012;13:1187-91. doi: 10.7314/APJCP.2012.13.4.1187.
- Cho ER, Shin A, Choi KS, Lee HY, Kim J. Factors associated with use of ultrasonography screening for hepatocellular carcinoma among hepatitis B or C carriers. *Cancer Epidemiol* 2010;34:713-6. doi: 10.1016/j.canep.2010.09.003.
- Noh DK, Choi KS, Jun JK, Lee HY, Park EC. Factors associated with attending the National Cancer Screening Program for liver cancer in Korea. *Asian Pac J Cancer Prev* 2012;13:731-6. doi: 10.7314/APJCP.2012.13.2.731.
- Rauscher GH, Johnson TP, Cho YI, Walk JA. Accuracy of self-reported cancer-screening histories: A meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2008;17:748-57. doi: 10.1158/1055-9965.epi-07-2629.