Ethnicity as a Predictive Factor for Hepatocellular Carcinoma Screening among Patients in Hawaii

Catherine L. Ly, BA; Linda L. Wong, MD

Objectives: Although hepatocellular carcinoma (HCC) surveillance is associated with mortality reduction, it continues to be underutilized. The failure to conduct screening tests is a significant factor in the late diagnosis of hepatocellular carcinoma when curative interventions may not be feasible. Reasons for these low surveillance rates are unclear and need to be elucidated.

Design, Setting, Patients: This retrospective study reviewed 616 cases of HCC from a hepatobiliary surgery office in Hawaii for age, sex, ethnicity, birthplace, residence, education, employment, insurance, and obesity to determine their influence on HCC screening.

Main Outcome Measures: HCC screening.

Results: Of the 616 cases, only 132 patients (21.4%) had undergone screening. Although the majority of patients were male, those who were screened were more likely to be female ($P=.0082$). However, multivariate analysis found ethnicity to be the sole determinant of screening ($P<.0005$). Koreans were more likely than Whites to have had screening, whereas Japanese, Pacific Islanders, and Filipinos were less likely. Age >60 years, sex, American birthplace, urban residence, high school completion, employment status, insurance, and BMI>35 kg/m^2 were not predictors of screening.

Conclusions: Of the sociodemographic factors, ethnicity was important in predicting screening. Further research is needed to understand the reasons for these ethnic differences and to develop targeted interventions to improve hepatocellular carcinoma surveillance utilization rates. (*Ethn Dis*. 2014; 24[3]:376–381)

Key Words: Early Detection of Cancer, Health Care Disparities, Hepatocellular Carcinoma, Liver Neoplasms, Mass Screening

From Department of Surgery, University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii (CLL, LLW); and University of Hawaii Cancer Center, Honolulu, Hawaii (LLW).

Address correspondence to Linda L. Wong, MD; 550 South Beretania Street, Suite 403; Honolulu, Hawaii 96817; 808.523.5033; 808.528.4940 (fax); hepatoma@aol.com.

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide and is one of the few cancers that is increasing in both incidence and mortality.[1,2] Surveillance strives to reduce mortality through the repeated application of screening tests in patients who are considered at high risk for HCC, such as those who have viral hepatitis or chronic liver disease.[3,4] These tests aim to detect HCC at an early stage that would allow for the effective use of potentially curative interventions such as transplantation, resection, or radiofrequency ablation.[5,6]

The American Association for the Study of Liver Diseases (AASLD) recommends surveillance with ultrasound examination every 6 months.[7] Despite these guidelines, studies have shown that utilization rates for HCC surveillance are low. In a systemic literature review, the pooled surveillance rate was 18.4%, with significantly higher rates in patients followed in subspecialty gastroenterology clinics and lower rates in non-Caucasians and those of low socioeconomic status.[8] In another study of patients with a prior diagnosis of cirrhosis, only 17% received regular surveillance, while 38% received inconsistent surveillance.[9] Singal et al found that although there are multiple points of failure in the surveillance process, the most common is the failure to order screening tests at all.[10] Specific reasons as to why screening is not performed are unclear.

According to the National Cancer Institute, Asians/Pacific Islanders have the highest incidence rate for cancer of the liver and intrahepatic bile duct compared to other races (22.1 per 100,000 for men and 8.5 per 100,000 for women).[1] Being of Asian/Pacific Islander race has been shown to be predictive of long-term survival in some studies, but this population continues to have the highest mortality rate (14.5 per 100,000 men and 6.1 per 100,000 women).[1,11–13] Improving rates of surveillance within this high risk population would likely lead to significant outcomes, so part of our study seeks to understand if there are better ways to target this group of people. Several studies have examined HCC screening practices in this population, but few have sought to identify differences among the ethnic subgroups within the Asian/Pacific Islander race.[14–16] This racial category encompasses a diverse group of people with differences in culture, time since immigration, socioeconomic status, religion, and other factors that may affect health care decisions, so it is not surprising that there would be differences in cancer screening practices that may be generally based on ethnic subgroup.[17–20] As a result, our study differentiates between the ethnic subgroups rather than viewing them as a one group. Understanding the possible differences between these groups may lead to targeted interventions that may be more effective than those focused on Asians/Pacific Islanders as a single entity or those simply directed toward the general population.

In addition to ethnicity, other sociodemographic factors may contribute to the likelihood of screening as well.[12,13] Ultimately, we sought to identify overall determinants of HCC screening in an attempt to guide efforts to improve surveillance utilization rates.

Methods

Patients

This is a retrospective analysis of a database consisting of 819 cases of

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HCC referred to a group of surgeons specializing in hepatobiliary surgery from 1993 to 2012. This group is affiliated with the only clinic dedicated to liver diseases and the only liver transplant center in the State of Hawaii, and is the only referral center for liver diseases and surgery for the American territories of the Pacific Basin, including American Samoa, Guam, Saipan, and the Marshall Islands. Overall, these surgeons see 60–70% of HCC cases in the state.

These cases of HCC were diagnosed histologically by percutaneous biopsy, liver biopsy at the time of surgery, or by examination of the resected liver. Before 2010, according to the United Network for Organ Sharing policy, patients without histologic confirmation were included if they had a history of chronic liver disease, in addition to a mass of at least 2 cm in size seen on two imaging studies (ultrasound, computed tomography [CT] scan, or magnetic resonance imaging [MRI]), and one of the following: 1) a vascular blush seen on CT scan or MRI; 2) alpha fetoprotein (AFP) greater than 200 ng/mL; or 3) an arteriogram confirming the tumor. Since 2010 and consistent with the AASLD guidelines, patients without histologic confirmation were included if they had a contrast-enhanced study demonstrating a tumor larger than 1 cm with hypervascularity in the arterial phase and washout in the portal vein or delayed phase. If the findings were not typical, a second contrast-enhanced study or biopsy was utilized for diagnosis confirmation.[7,21]

Sociodemographic data was collected through clinical interviews and included age, sex, ethnicity, birthplace, current residence, education, employment status, medical insurance, and body mass index (BMI). Age was divided into two categories, aged $\leq$60 years and $>$60 years. Ethnicity was self-reported and categorized as White, Black, Hispanic, Chinese, Filipino, Japanese, Korean, Southeast Asian, Pacific Islander, or mixed. Patients were considered to be Southeast Asian if they were Burmese, Cambodian, Indonesian, Laotian, Malaysian, Thai, Hmong, or Vietnamese. If patients identified with more than one ethnicity, they were recognized as mixed. However, patients of mixed race who were greater than 50% Pacific Islander were categorized as Pacific Islander. Blacks and Hispanics were ultimately excluded due to small numbers (n=4 and n=10, respectively). Whites were used as the population of reference.

Because a significant proportion of the population in Hawaii are immigrants and a number of patients were foreign nationals who sought medical care in the United States, birthplace was considered and noted as either in the United States or foreign. Current residence was based on zip code, which allowed for categorization into Honolulu vs non-Honolulu residence as a surrogate for urban vs rural. The non-Honolulu residence group included non-Hawaii residents and foreigners who did not report a home address in Honolulu. The distinction between home residence may be significant because Honolulu is the state's capital and the location of most major hospitals and physicians as well as the only dedicated liver transplant and treatment facility in the Pacific Basin. Those who do not live in Honolulu typically require travel if evaluation is needed.

High school completion was recorded if the patient had successfully passed the General Educational Development test (GED) or finished 13 years of education. Similarly, employment status was noted as either employed or unemployed. Unemployed patients included those who were on disability, retired, homemakers, unemployed but looking for work, and those who had never been employed. Medical insurance was categorized as government insurance (Medicare, Medicaid, or Veterans Administration) or private insurance.

Measured weight and height were determined to calculate BMI, which may be considered as a surrogate marker for socioeconomic status in some instances.[22] It is also important to note that BMI $\geq$35 kg/m^2 is a relative contraindication to liver transplantation at this center.

The cases of HCC detected through screening were noted. This was viewed in the context of patients who had what was considered to be a screenable disease, such as any viral hepatitis, cirrhosis, or other chronic liver disease. Although the liver center at our institution had recommended screening with AFP and ultrasound every 6 months for such patients, a uniform screening protocol was not employed in this study. Referring physicians utilized AFP and/or imaging in the form of ultrasound, CT, or MRI at intervals ranging from 3 to 12 months. Hepatocellular carcinoma was deemed to be found on screening if the referring physician stated that screening was done or if the patient had an imaging test completed within the prior 3 to 12 months.

Statistics

All analyses were performed using SPSS statistical software. Of the 819 cases in the database, 630 were selected with the exclusion of cases in which sociodemographic data collection was incomplete. The further exclusion, due

Table 1. Age, sex, birthplace, and residence by ethnicity

Ethnicity	Age >60 Years		Male		Born in the United States		Rural Residence	
	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Chinese	63.5	2.26 (1.27–4.06)	73.0	.52 (.26–1.03)	36.5	.01 (.004–.05)	25.7	.13 (.07–.25)
Filipino	54.5	1.56 (.90–2.68)	80.7	.80 (.39–1.62)	30.0	.01 (.003–.04)	75.0	1.14 (.62–2.10)
Japanese	62.0	2.11 (1.30–3.43)	70.4	.45 (.25–.82)	79.4	.10 (.03–.32)	54.2	.45 (.27–.74)
Korean	50.0	.73 (.38–1.40)	52.6	.10 (.05–.21)	8.3	.002 (.0002–.01)	21.0	.08 (.03–.18)
Mixed	80.0	.87 (.36–2.07)	72	.49 (.18–1.32)	96	.60 (.06–5.97)	64.0	.67 (.27–1.66)
Pacific Islander	31.2	.59 (.34–1.03)	81.7	.85 (.42–1.72)	56.0	.03 (.009–.11)	69.9	.88 (.49–1.58)
Southeast Asian	52.0	1.40 (.60–3.31)	76.0	.60 (.22–1.69)	0		24.0	.12 (.04–.32)
White	43.5	1.0	84.0	1.0	97.6	1.0	72.5	1.0

to small *n*, of those who were self-identified as Black or Hispanic resulted in a total of 616 cases for analysis.

Each sociodemographic factor was analyzed by ANOVA to evaluate for significant differences among the ethnicities. All percentages were calculated based on available data; those without specific sociodemographic data were not included in the respective calculations. In addition, Fisher's exact test of factors was used to identify significant factors in those who were screened compared to those who were not screened among all patients with a screenable disease. Univariate analysis was conducted to assess the individual predictive value of age, sex, ethnicity, birthplace, current residence, education, employment status, medical insurance, and BMI. Multivariate analysis was subsequently completed to determine overall predictive factors.

Results

A total of 616 patients were evaluated, including 468 males and 148 females with a mean age of 61.5 years (range 22–88 years). The distribution of ethnicity was as follows from largest to smallest *n*: Japanese, 142; White, 131; Pacific Islander, 93; Filipino, 88; Chinese, 74; Korean, 38; Southeast Asian, 25; and mixed, 25. As seen in Table 1, slightly more patients were aged >60 years (321 patients, 52.1%). There were significant differences among the ethnicities, with Japanese and Chinese patients more likely to be >60 years. Although HCC was more common in males in all ethnicities, the male predominance was less prominent in Japanese and Korean patients compared to Whites.

A majority of patients (364, 59.1%) was born in the United States. Table 1 demonstrates that Japanese, Pacific Islanders, Filipino, Chinese, and Koreans were more likely than Whites to be born in a foreign country or territory. At the time of interview, a greater proportion of patients resided outside of Honolulu (352 patients, 57%). Japanese, Chinese, Koreans, and Southeast Asians were more likely than Whites to live in Honolulu, which is considered a surrogate for urban residence.

More patients reported having a high school degree or a GED (349 patients, 56.7%). Table 2 shows that Pacific Islanders, Filipinos, Koreans, Southeast Asians, and mixed patients were less likely than Whites to have completed high school. Only 67 patients (10.9%) were unemployed at the time of the interview. Employment status did not vary significantly between ethnicities. Overall, 292 patients (47.4%) had some type of government insurance. Filipinos were less likely to be government-insured compared to Whites, whereas Pacific Islanders and Southeast Asians were more likely to be government-insured.

There were also significant differences in mean BMI, as demonstrated in Table 2. A total of 118 patients (21.2%) were considered obese with a BMI $\geq$30 kg/m^2. Pacific Islanders were more likely to have a BMI >30 kg/m^2, as well as a BMI >35 kg/m^2. Chinese patients, on the other hand, were less

Table 2. Education, insurance, and BMI by ethnicity

Ethnicity	High School Completion		Government Insurance		BMI >35 kg/m^2		BMI >30 kg/m^2	
	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Chinese	82.0	.46 (.17–1.20)	43.8	.79 (.45–1.41)	2.8	.47 (.10–2.34)	7.0	.26 (.10–.72)
Filipino	60.3	.15 (.07–.35)	24.4	.33 (.18–.60)	6.3	1.10 (.34–3.60)	17.7	.75 (.37–1.54)
Japanese	92.6	1.26 (.46–3.44)	42.6	.75 (.47–1.21)	4.6	.78 (.25–2.40)	13.7	.55 (.29–1.07)
Korean	72.2	.26 (.08–.88)	40.5	.69 (.33–1.45)	3.1	.53 (.06–4.43)	6.3	.23 (.05–1.03)
Mixed	75.0	.4 (.10–.93)	60.0	1.52 (.64–3.64)	17.4	3.42 (.92–12.84)	34.8	1.86 (.71–4.84)
Pacific Islander	67.1	.20 (.09–.46)	68.1	2.17 (1.24–3.79)	21.4	4.44 (1.76–11.19)	51.2	3.65 (1.99–6.69)
Southeast Asian	50.0	.1 (.03–.34)	88.0	7.45 (2.12–26.10)	0		4.0	.15 (.02–1.12)
White	90.9	1.0	49.6	1.0	5.8	1.0	22.3	1.0

Table 3. Participants with HCC found upon screening, by ethnicity

Ethnicity	%	OR (95% CI)
Chinese	24.3	.77 (.40–1.49)
Filipino	11.4	.31 (.13–.66)
Japanese	17.9	.52 (.29–.93)
Korean	50.0	2.40 (1.15–5.05)
Mixed	28.0	.93 (.36–2.42)
Pacific Islander	8.7	.23 (.10–.52)
Southeast Asian	32.0	1.13 (.45–2.85)
White	29.6	1.0

likely to have a BMI >35 kg/m^2. Although 550 patients (89.3%) had a screenable disease, only 132 patients (21.4%) had HCC found on screening. Although the majority of patients were male, those who were screened were much more likely to be female (P=.0082). There were no significant differences in age, current residence, education, medical insurance, or BMI between those who were screened and those who were not. As seen in Table 3, Koreans were more likely than Whites to have had HCC found on screening, whereas Japanese, Pacific Islanders, and Filipinos were less likely.

In a univariate nominal regression model, both ethnicity (P<.0005) and completion of high school (P=.045) were shown to be predictive of screening. However, when a multivariate nominal regression model was utilized, only ethnicity remained as the sole determinant of screening (P<.0005). Age >60 years, sex, birthplace, current residence, high school completion, employment status, medical insurance, and obesity were not significant factors in the multivariate analysis.

In this study, only 21.4% of patients had HCC diagnosed through screening.

DISCUSSION

Although surveillance for HCC has been associated with mortality reduction, it continues to be underutilized.[8,9,23–25] Hawaii not only has the highest mortality rate for cancer of the liver and intrahepatic bile duct in the United States (7.29 per 100,000), but also one of the lowest screening rates.[1,9] In this study, only 21.4% of patients had HCC diagnosed through screening. We did not distinguish between those who received regular vs inconsistent surveillance, so the rate of those who received regular surveillance is likely lower than 20%, which is consistent with previous studies of surveillance rates.[8,9] In order to guide effective strategies to improve surveillance utilization rates, our study sought to understand the determinants of HCC screening.

Among those with a screenable disease, female sex was the only significant difference between those who were screened and those who were not (P=.0082). This is not surprising, considering the prevailing perspective that men are less likely than women to seek out medical care and are more likely to endure physical pain as a demonstration of masculinity.[26] However, other studies have showed conflicting data regarding the influence of sex on whether a patient received screening.[8] In addition, both univariate and multivariate analysis in this study ultimately demonstrated that sex was not predictive of HCC screening.

Completion of high school was shown to be predictive of HCC screening in univariate analysis, but not in multivariate analysis. Education is a potentially important determinant of overall health status due to its influence on subsequent socioeconomic status and knowledge of healthy behaviors. However, education was likely not found to be significant in multivariate analysis as it may be influenced by other sociodemographic factors, such as ethnicity (as related to each culture's value on education) and current socioeconomic status.

Ethnicity was ultimately identified as the sole determinant of HCC screening in multivariate analysis in this study. Other studies have found that Asians were more likely to have received regular surveillance, but our findings show that those who self-identified as Japanese, Pacific Islander, or Filipino were less likely than Whites to have undergone screening.[9] In contrast, Korean patients were more likely to have had HCC diagnosed following screening. Understanding these differences is critical, especially because Pacific Islanders and Filipinos are more likely to have tumors >5 cm in size and are therefore at risk of poorer prognosis.[20]

The reason for these ethnic differences is likely due to multiple factors, but may be related to cultural attitudes toward cancer and health in general. Various studies have shown that Asians with cultures rooted in Buddhism are likely to have fatalistic views of cancer that discourage adherence to cancer screening guidelines.[27,28] Koreans are presumably included in this group, so the fact that the Korean patients in this study were more likely to have undergone screening is potentially encouraging because it may show that cultural barriers are not necessarily insurmountable obstacles. The higher rate of screening in Koreans is likely related to more effective education of providers who work with this population. Several Korean physicians in our community, who are quite familiar with HCC, have encouraged their high-risk patients to undergo regular surveillance. Higher rates of surveillance among their patients is consistent with studies that have found that utilization rates are related to variation in provider knowledge and attitudes.[8]

One study of the SEER registry found that 80% of Asians/Pacific Islanders were born outside of the United States, so time since immigration may also contribute to a difference in

screening practices.[12] Recent immigrants, which one study classified as those who arrived within the past 10 years, are more likely to experience a significant gap in screening utilization.[29] Individuals from the Republic of Palau, the Federated States of Micronesia, and the Republic of the Marshall Islands, all of whom are classified as Pacific Islanders, are the newest immigrants to Hawaii. Many have had particular difficulty with housing, employment, and adequate access to health care. Therefore, it is not surprising that this population would have lower rates of screening for HCC, as well as for other types of cancer. This also applies to the foreign nationals who traveled to the United States for medical care and who likely did not receive any screening in their home countries. Japanese, Filipinos, and Koreans began immigrating to Hawaii many years ago and while time since immigration may also be significant for some, its influence may be confounded by other factors. Ultimately, future studies are needed to more definitively understand the reasons behind the ethnic differences demonstrated by our study.

Our study is unique in that not only does it separate Asians from Pacific Islanders, it also further categorizes Asians into more distinct ethnic subgroups and considers additional details such as birthplace and other sociodemographic factors for each ethnicity. While many studies continue to combine all Asians and Pacific Islanders into one category, an increasing number of studies, such as those that utilize the SEER (Surveillance, Epidemiology, and End Results) data, also disaggregate the ethnicities. However, to our knowledge, these studies do not include the additional associated details that may highlight further differences between the ethnicities. Our data show there are significant differences within this diverse population in regards to the utilization of HCC screening tests and, presumably, early access to care. These differences must be considered in order to develop more focused efforts toward increasing the rates of surveillance, especially among Pacific Islanders and other ethnicities that have lower rates than would be expected based on their general racial category. It is likely an intervention that would be effective for one ethnic subgroup may not be as effective for another, so further research is needed to understand how to develop the most successful efforts. Consideration of the specific sociodemographic factors that we have found to be associated with each of the ethnicities can help to guide such research.

The limitation of our study lies in its restriction to a single center study in a state with a greater proportion of Asians and Pacific Islanders. Our findings may not necessarily be applicable to all areas of the continental United States, but Asians are the fastest growing minority group in the country and our data may be applied to the development of effective screening programs in those areas with larger populations of Asians and Pacific Islanders.[30] It may also be instructive for such areas to understand that Asians and Pacific Islanders should not be treated as a single entity. Ultimately, our study demonstrates the importance of data collection by individual centers in the effort to understand how to more effectively target particular populations. However, further research in larger center studies or through collaborations between individual centers is required to thoroughly explore the cultural and psychosocial barriers to HCC screening. Future studies may benefit from having information on time since immigration, native language, cultural views and beliefs, and other contributing factors to healthcare access.

CONCLUSION

Our study demonstrates that, while there were significant differences among ethnicities in terms of sociodemographic factors, ethnicity itself was the sole determinant of the use of HCC screening tests. More research is needed to understand the reasons for these ethnic differences and to develop targeted interventions to increase knowledge and awareness among both patients and physicians to ultimately improve surveillance utilization rates, particularly in populations less likely to undergo screening.

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AUTHOR CONTRIBUTIONS

Study design and concept: Ly, Wong
Acquisition of data: Wong
Data analysis and interpretation: Ly, Wong
Manuscript draft: Ly, Wong
Statistical expertise: Wong
Supervision: Wong