The Impact of Ethnic Subgroups on Tumor Stage at Diagnosis, Treatment Received, and Long-Term Survival Among Asian Adults With Hepatocellular Carcinoma

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Background & aims: Hepatocellular carcinoma (HCC) outcomes among Asians may differ by the Asian ethnic subgroup. We aim to evaluate the impact of the Asian ethnic subgroup on HCC tumor stage, treatment received, and overall survival among US adults. **Methods:** Using the 2004–2012 Surveillance, Epidemiology, and End Results U.S. cancer registry, we retrospectively evaluated disparities in HCC tumor stage at diagnosis, HCC treatment received, and overall survival among Asian adults, stratified by Asian ethnic subgroups. Multivariate regression models evaluated the independent impact of Asian ethnic subgroups on the HCC tumor stage at diagnosis, treatment received, and overall long-term survival. **Results:** Among 8160 Asians with HCC, Southeast Asian (SEA) patients accounted for 26% of all HCC, followed by Chinese (CH) (22%), and Filipinos (FP) (14.0%) patients. Japanese (JP) patients were significantly older than those of the other subgroups (mean 71.1, SD 10.8, $P < 0.01$). When evaluating HCC stage, FP patients were less likely to have localized HCC and less likely to have HCC within the Milan criteria than CH HCC patients. When evaluating HCC treatment, pacific islanders (PI), FP and SEA patients were significantly less likely to any receive HCC treatment than CH patients. Overall five-year HCC survival was highest among CH HCC patients (33.1%) and lowest among FP (19.9%) and JP patients (22.0%). **Conclusion:** Among Asians with HCC in the US, significant disparities among Asian ethnic subgroups exist. More advanced disease was seen among FP patients, less HCC treatment was seen among FP and SEA patients, and significantly higher mortality was seen among FP, SEA, and JP patients with HCC. (J CLIN EXP HEPATOL 2019;9:182–190)

Hepatocellular carcinoma (HCC) is a significant cause of morbidity and mortality in the US.^{1–3} Five-year survival rates in the US remain poor at less than 30% despite advances in HCC treatment.^{3–6} Early detection with screening and surveillance programs among high risk patients has been shown to improve treatment and survival outcomes.^{4,6–9}

Race- and ethnicity-specific disparities in HCC epidemiology and outcomes have been previously reported, which may reflect underlying liver disease etiology.^{10–14} These previous studies have demonstrated that Asians with HCC generally have higher rates of HCC treatment and higher overall survival than other race/ethnic groups.^{10,12,14} The major risk factors for development of HCC include liver disease from chronic hepatitis B virus infection (HBV), chronic hepatitis C virus infection (HCV), alcoholic liver disease, and nonalcoholic fatty liver disease (NAFLD).^{3,15} In the US, HCV and NAFLD are the leading causes of HCC, whereas HBV is the primary etiology of HCC in Asian-Pacific regions.^{16–18} The higher incidence of chronic HBV in Asians is a contributing factor for Asians having the highest incidence of HCC in the US.^{4,10} Asian men have approximately 12 times the incidence rate of liver cancer when compared with Caucasian men, and liver cancer is among the top five cancers among Asian men in the US.¹⁹ Despite having significantly higher incidence of HCC, previous studies have reported disparately lower

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Abbreviations: CH: Chinese; FP: Filipino; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; JP: Japanese; KR: Korean; NAFLD: nonalcoholic fatty liver disease; PI: Pacific Islander; SA: South Asian; SEA: Southeast Asian; SEER: Surveillance, Epidemiology, and End Results; TACE: transarterial chemoembolization

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likelihood of receiving liver transplantation among Asians in the US than non-Hispanic whites.^{20,21}

Recent trends have shown that Asians in the US have the highest overall five-year survival compared with blacks, Hispanics, and non-Hispanic whites.¹⁰ However, Asians are not a homogenous group and comprised various ethnic subgroups. In addition to different risk factors, Asian ethnic subgroups may have differences in underlying genetics or disease characteristics that affect HCC outcomes. Using data from the Surveillance, Epidemiology, and End Results (SEER) US cancer registry, we aim to evaluate the impact of the ethnic subgroup on HCC outcomes among Asian adults, with a focus on HCC stage at diagnosis, treatment received, and overall survival.

METHODS

Study Design and Population

We retrospectively evaluated Asian adults (age ≥ 20 years) with HCC using data from the 2004–2012 SEER US cancer registry, a population-based cancer registry that includes data from 18 regions in the US and represents about 28% of the US population. Asian ethnic subgroup classifications included Chinese (CH), Japanese (JP), Korean (KR), Filipino (FP), Southeast Asian (SEA), South Asian (SA), and Pacific Islander (PI). The SEA group includes Kampuchean, Laotian, and Vietnamese. The SA group includes Asian Indian or Pakistani. The PI group includes Guamanian, Native Hawaiian, Samoan, and Tongan. HCC cases in SEER were identified using the International Classification of Disease for Oncology.²²

HCC stage was assessed using the SEER historic staging system, which describes the extent of disease but not necessarily prognosis.²² Localized stage is defined as tumor involvement of a single lobe of the liver. Regional stage is defined as tumors involving more than one lobe via contiguous growth of a single lesion, extension to adjacent structures (diaphragm, extrahepatic biliary system, or gallbladder), or spread to regional lymph nodes. The distant stage is defined as tumors that have metastasized, extended growth to nearby organs (pancreas, pleura, or stomach), or spread to distant lymph nodes. In addition to SEER staging, we also evaluated HCC based on whether the tumor met the Milan criteria (single lesion less than 5 cm or no more than 3 lesions each less than 3 cm) with no extrahepatic or vascular involvement using tumor characteristics as supplied by SEER, which affects eligibility for liver transplantation.

HCC treatment categories were based on SEER's site-specific surgery variables including no treatment, locoregional therapy, surgical resection, and liver transplantation (22). Locoregional therapy included photodynamic therapy, electrocautery, cryosurgery, laser, percutaneous ethanol injection, and heat-radiofrequency ablation.

Transarterial chemoembolization (TACE) is relatively new in the SEER registry and was not well evaluated in our study, given our study period spans a period that included concerns about data inconsistency and underreporting of TACE therapy.

Statistical Analysis

Baseline demographics were stratified by Asian ethnic subgroups and presented as proportion (%) and frequency (N) and compared using chi-square testing for categorical variables and analysis of variance for continuous variables. There were a portion of Asian adults whose ethnic subgroup was unknown and were included in analysis. Furthermore, owing to missing values for some of the variables and outcomes analyzed, the total sample size may be different across comparisons. HCC tumor stage at diagnosis was stratified by the Asian ethnic subgroup and compared using chi-square methods. Multivariate logistic regression models evaluated the impact of Asian ethnic subgroups on the HCC tumor stage at diagnosis. Similarly, predictors of receiving HCC treatment (any HCC treatment vs. no treatment) were evaluated with multivariate logistic regression models. We further stratified our treatment analysis by patients with HCC SEER localized stage and patients with HCC within the Milan criteria, given that stage of disease at diagnosis directly affects treatment eligibility. Furthermore, we performed a subanalysis specifically focusing on predictors of receiving surgical resection and liver transplantation. Overall, five-year HCC survival was evaluated using Kaplan–Meier methods and stratified by Asian ethnic subgroups. Multivariate Cox proportional hazard models were used to evaluate the impact of Asian ethnic subgroup on overall five-year HCC survival. All statistical analyses were performed with Stata, version 14 (Stata Corp, College Station, TX). Statistical significance was met with a two-tailed P -value < 0.05 . The study was reviewed and determined to be exempt by the Alameda Health System Institutional Review Board because human subjects were not involved, as per the US Department of Health and Human Services guidelines, and the SEER database is publicly available without individually identifiable private information.

RESULTS

Patient Characteristics

Among 8160 US Asian adults with HCC, 72.2% were male, and the largest ethnic groups comprised SEA (26.0%), CH (22.5%), and FP (13.9%) (Table 1). Overall, 37% of Asian HCC patients were aged 70 years or older at time of diagnosis. JP HCC patients were the oldest at time of HCC diagnosis, with mean age of 71.2 years, whereas PI and SEA patients were younger, with mean age of 61.7 years and 62.2 years, respectively.

Table 1 Characteristics of the Study Cohort.

Variables	Chinese (CH)		Japanese (JP)		Korean (KR)		Filipino (FP)		Southeast Asian (SEA)		South Asian (SA)		Pacific Islander (PI)		P-Value
	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)	Frequency (N)	
Patient characteristics															
Total	22.5	1836	8.6	702	10.5	854	13.9	1140	26.0	2122	1.6	134	7.5	609	
Female	26.6	489	48.7	342	30.7	262	27.1	309	23.4	496	19.4	26	23.8	145	<0.001
Male	73.4	1347	51.3	360	69.3	592	72.9	831	76.6	1626	80.6	108	76.2	464	
Married	76.3	1361	57.7	392	72.8	605	71.7	794	69.9	1416	72.8	91	61.3	349	<0.001
Insurance status															
Commercial/medicare	67.6	803	92.2	404	58.2	308	74.1	572	53.2	786	62.4	58	67.7	266	<0.001
Medicaid	28.5	339	5.3	23	33.3	176	21.5	166	42.7	631	24.7	23	25.9	102	
Uninsured	3.9	46	2.5	11	8.5	45	4.4	34	4.1	60	12.9	12	6.4	25	
Age															
<50 years	12.1	222	2.6	18	11.4	97	11.6	132	13.3	283	9.0	12	12.2	74	<0.001
50–59 years	21.1	387	15.8	111	25.5	218	22.5	257	28.9	614	29.1	39	33.0	201	
60–69 years	24.8	456	17.1	120	28.2	241	25.8	294	28.5	605	35.8	48	29.2	178	
70 years and older	42.0	771	64.5	453	34.9	298	40.1	457	29.2	620	26.1	35	25.6	156	
Age (mean ± SD)	65.2 ± 12.8		71.2 ± 10.8		63.8 ± 11.9		65.0 ± 12.6		62.2 ± 12.1		63.2 ± 10.9		61.7 ± 11.7		<0.001
HCC characteristics															
HCC tumor stage															
SEER localized	56.5	918	56.5	352	51.6	400	48.8	515	54.6	1063	43.8	53	48.7	263	<0.001
SEER regional	30.2	491	30.9	193	33.4	259	33.3	352	31.8	619	28.1	34	33.2	179	
SEER distant	13.2	215	12.5	78	15.1	117	17.9	189	13.6	264	28.1	34	18.2	98	
HCC within Milan criteria	37.2	682	37.9	266	42.2	360	31.6	360	39.7	842	31.3	42	32.0	195	<0.001
HCC treatment															
No treatment	64.9	1187	65.2	457	67.0	572	76.0	865	70.1	1487	61.2	82	73.4	446	<0.001
Locoregional	12.3	235	15.7	110	11.4	97	7.9	90	12.0	255	11.2	15	10.7	65	
Surgical resection	17.0	311	12.0	84	15.9	136	11.4	130	14.2	300	11.9	16	8.9	54	
Liver transplantation	4.3	79	4.3	30	4.9	42	3.3	37	2.7	57	13.4	18	2.6	16	
Tumor size (mean ± SD)	6.59 ± 6.09		6.13 ± 5.55		6.10 ± 4.62		7.69 ± 7.06		6.40 ± 4.93		7.00 ± 7.81		7.21 ± 7.50		<0.001
Number of tumors (mean ± SD)	1.12 ± 0.37		1.23 ± 0.50		1.12 ± 0.34		1.12 ± 0.37		1.08 ± 0.30		1.12 ± 0.41		1.12 ± 0.37		<0.001

HCC, hepatocellular carcinoma; SEER, Surveillance, Epidemiology, and End Results; SD, standard deviation.

HCC Characteristics

For HCC stage, 54.0% of patients had SEER-localized HCC at diagnosis, 31.2% had SEER regional stage, and 14.8% had SEER distant stage (Table 1). Only 37.3% of HCC tumors met the Milan Criteria. Among ethnic subgroups, the CH and JP patients had a higher percentage of SEER-localized HCC, whereas KR had a higher percentage of regional HCC. PI and SA HCC patients had significantly higher rates of SEER distant HCC. Multivariate regression analysis using the CH group as the reference group showed that PI (OR 0.65, 95% CI 0.46–0.92, $P = 0.014$), FP (OR 0.57, 95% CI 0.44–0.76, $P < 0.001$), and SA (OR 0.42, 95% CI 0.24–0.74, $P = 0.003$) were significantly less likely to have SEER-localized disease (Table 2). FP HCC patients were significantly less likely to have HCC within the Milan criteria at time of diagnosis (OR 0.75, 95% CI 0.62–0.91, $P = 0.004$) than CH.

HCC Treatment

An overall 69.2% of Asians with HCC in the US received no treatment, with FP, PI, and SEA patients having higher percentages of no treatment at 76.0%, 73.4%, and 70.1%,

respectively (Table 1). The CH and SA groups were more likely to undergo HCC treatment in this cohort. The most common treatment modality was surgical resection (14.1% of patients). Liver transplantation was received in 3.9% of all patients, with the lowest rates seen in the PI, SEA, FP group (2.6%, 2.7%, and 3.3%, respectively). When stratified by SEER-localized disease, similar trends were observed. For patients with HCC within the Milan criteria, 53.1% did not receive treatment, with higher percentages of no treatment in the FP, SEA, PI group (60.3%, 57.8%, and 57.4%, respectively) (Table 3). Among those that did receive treatment, locoregional therapy was most common (Table 3). Liver transplantation for those with HCC within the Milan criteria was 8.6% overall, with the lowest rates seen in the PI and SEA group. Multivariate regression analysis showed that SEA (OR 0.77, 95% CI 0.64–0.91, $P = 0.003$), PI (OR 0.61, 95% CI 0.46–0.79, $P < 0.001$), and FP (OR 0.54, 95% CI 0.43–0.67, $P < 0.001$) patients with HCC were significantly less likely to undergo treatment than CH patients (Table 2). These same trends were observed when stratified by patients with SEER-localized disease and patients with HCC within the Milan criteria. When evaluating specifically for receipt of surgical resection or

Table 2 Multivariate Regression Mode of HCC Stage at Diagnosis and HCC Treatment Received.

HCC stage at diagnosis									
Variables	HCC localized vs. distant			HCC within Milan criteria vs. outside Milan criteria					
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-Value			
Chinese	1.00	Reference	–	1.00	Reference	–			
Japanese	0.81	0.55–1.17	0.256	0.98	0.78–1.24	0.897			
Korean	0.79	0.57–1.09	0.152	1.15	0.94–1.42	0.181			
Filipino	0.57	0.44–0.76	<0.001	0.75	0.62–0.91	0.004			
Southeast Asian	0.97	0.76–1.25	0.821	1.00	0.85–1.17	1.00			
South Asian	0.42	0.24–0.74	0.003	0.92	0.59–1.42	0.698			
Pacific Islander	0.65	0.46–0.92	0.014	0.86	0.68–1.09	0.218			
Model adjusted for age, sex, year, and insurance status									
HCC treatment received									
Variables	Receipt of any treatment vs. no treatment			Receipt of any treatment vs. no treatment in localized disease			Receipt of any treatment vs. no treatment for HCC within Milan criteria		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Chinese	1.00	Reference	–	1.00	Reference	–	1.00	Reference	–
Japanese	0.80	0.62–1.03	0.085	0.77	0.55–1.06	0.104	0.77	0.54–1.10	0.153
Korean	0.91	0.72–1.15	0.438	0.98	0.73–1.33	0.909	0.84	0.61–1.16	0.298
Filipino	0.54	0.43–0.67	<0.001	0.51	0.38–0.67	<0.001	0.56	0.41–0.76	<0.001
Southeast Asian	0.77	0.64–0.91	0.003	0.72	0.58–0.90	0.004	0.69	0.54–0.88	0.003
South Asian	1.39	0.88–2.21	0.159	3.22	1.50–6.91	0.003	1.77	0.86–3.64	0.123
Pacific Islander	0.61	0.46–0.80	<0.001	0.66	0.47–0.93	0.017	0.65	0.44–0.95	0.024

Model adjusted for age, sex, year, insurance status, and HCC tumor stage
HCC, hepatocellular carcinoma; CI, confidence interval.

Table 3 HCC Treatment Rates Among Asian Adults With SEER-localized Disease and HCC Within the Milan Criteria.

Variables	No treatment		Locoregional therapy		Surgical resection		Liver transplantation	
	Proportion (%)	Frequency (N)	Proportion (%)	Frequency (N)	Proportion (%)	Frequency (N)	Proportion (%)	Frequency (N)
HCC SEER-localized disease								
Total	54.5	2160	17.7	702	21.8	863	6.0	238
Chinese	47.8	438	19.4	178	26.2	240	6.6	60
Japanese	53.4	188	25.0	88	14.5	51	7.1	25
Korean	49.0	195	18.8	75	25.4	101	6.8	27
Filipino	64.7	330	13.7	70	16.5	84	5.1	26
Southeast Asian	56.7	601	17.9	190	21.4	227	4.1	44
South Asian	31.4	16	19.6	10	19.6	10	29.4	15
Pacific Islander	60.1	158	18.3	48	17.1	45	4.6	12
Other	53.9	189	11.1	39	27.6	97	7.4	26
HCC within the Milan criteria								
Total	53.1	1610	21.0	638	17.3	523	8.6	261
Chinese	46.1	313	23.4	159	21.9	149	8.5	58
Japanese	49.8	132	31.3	83	8.7	23	10.2	27
Korean	50.4	181	19.5	70	20.1	72	10.0	36
Filipino	60.3	216	16.2	58	14.3	51	9.2	33
Southeast Asian	57.8	486	20.0	168	16.5	139	5.7	48
South Asian	31.7	13	22.0	9	9.8	4	36.6	15
Pacific Islander	57.4	112	26.2	51	9.7	19	6.7	13
Other	49.2	119	14.9	36	25.2	61	10.7	26

HCC, hepatocellular carcinoma; SEER, Surveillance, Epidemiology, and End Results.

liver transplantation, JP, KR, SEA, and PI patients were significantly less likely to receive treatment, whereas SA patients were more likely than CH patients with HCC (Table 2).

HCC Survival Outcomes

Overall five-year HCC survival was highest among CH patients (33.1%) and lowest among FP and PI patients (19.9% and 16.3%, respectively) (Table 4, Figure 1). Among those with localized disease, the highest five-year survival rate was seen in the CH group (48.4%), whereas the lowest rates were seen in the PI (25.6%), FP (31.3%), and JP group (31.6%). Among those with HCC within the Milan criteria, the highest five-year survival rate was seen in the CH group (52.4%), whereas the lowest rates were seen in the PI (26.2%), JP (32.9%), and FP group (34.3%). On multivariate Cox proportional hazard models, compared with CH HCC patients, significantly higher mortality was seen in FP (HR 1.57, 95% CI 1.38–1.79, $P < 0.001$), JP (HR 1.48, 95% CI 1.26–1.73, $P < 0.001$), PI (HR 1.47, 95% CI 1.25–1.74, $P < 0.001$), and SEA patients (HR 1.36, 95% CI 1.21–1.52, $P < 0.001$) (Table 5).

DISCUSSION

This study identified a large and diverse cohort of Asians across the US with HCC diagnosed between 2004 and 2012 in the SEER database. In this cohort, the majority of HCC was localized at diagnosis, although most did not meet the Milan criteria. The majority of Asians did not undergo HCC treatment, and even so, among those who had HCC within the Milan criteria, only 53.1% underwent any HCC treatment. Only 3.9% of all Asians and 8.6% of Asians with HCC within the Milan criteria underwent liver transplantation. The overall five-year survival rates among the ethnic groups in this cohort remained high when compared with rates in other races in the US.^{4,10} Although the presence of our observed disparities among Asian ethnic subgroups is multifactorial and may reflect race and socioeconomic factors, our study highlights that even among the Asians with HCC in the US, significant disparities in HCC diagnosis and outcomes persist.^{21,23,24}

Although previous studies have evaluated race/ethnicity-specific differences in HCC outcomes, the majority of these studies group Asian ethnicities into one cohort and few have specifically evaluated differences by Asian

Table 4 Overall HCC Survival.

Variables	1-year survival		3-year survival		5-year survival	
	Survival rate	95% CI	Survival rate	95% CI	Survival rate	95% CI
Overall						
Chinese	63.0%	60.5%–65.3%	43.1%	40.4%–45.7%	33.1%	30.3%–35.8%
Japanese	55.6%	51.4%–59.5%	33.2%	29.2%–37.3%	22.0%	18.2%–26.2%
Korean	61.7%	58.0%–65.1%	35.1%	31.3%–38.9%	29.1%	25.3%–33.0%
Filipino	49.4%	46.1%–52.7%	28.3%	25.2%–31.6%	19.9%	16.8%–23.1%
Southeast Asian	55.2%	52.9%–57.6%	32.9%	30.4%–35.3%	23.4%	20.9%–25.9%
South Asian	54.3%	44.4%–63.2%	37.2%	27.4%–47.0%	30.5%	20.2%–41.4%
Pacific Islander	44.9%	40.2%–49.4%	24.0%	19.6%–28.6%	16.3%	12.0%–21.2%
Other	64.1%	59.6%–68.2%	42.7%	37.7%–47.6%	32.7%	27.2%–38.2%
SEER localized						
Chinese	80.7%	77.8%–83.2%	61.3%	57.7%–64.8%	48.4%	44.2%–52.5%
Japanese	71.4%	66.1%–76.1%	46.7%	40.7%–52.5%	31.6%	25.6%–37.8%
Korean	82.7%	78.4%–86.3%	52.6%	46.7%–58.2%	46.1%	39.9%–52.0%
Filipino	67.7%	63.0%–71.9%	43.6%	38.4%–48.6%	31.3%	26.0%–36.7%
Southeast Asian	73.0%	70.0%–75.8%	46.7%	43.0%–50.2%	34.6%	30.8%–38.4%
South Asian	76.8%	60.9%–86.9%	56.2%	38.7%–70.5%	41.6%	23.0%–59.3%
Pacific Islander	62.5%	55.7%–68.6%	37.0%	29.6%–44.3%	25.6%	18.3%–33.5%
Other	79.9%	74.7%–84.1%	59.5%	52.9%–65.5%	46.5%	38.4%–54.2%
Within Milan criteria						
Chinese	84.1%	81.0%–86.8%	65.0%	60.8%–68.9%	52.4%	47.5%–57.2%
Japanese	76.6%	70.8%–81.5%	50.7%	43.8%–57.2%	32.9%	25.9%–40.1%
Korean	79.9%	75.1%–83.9%	54.3%	48.2%–60.0%	48.0%	41.6%–54.0%
Filipino	70.1%	64.7%–74.9%	47.0%	40.8%–52.9%	34.3%	27.7%–41.0%
Southeast Asian	75.4%	72.2%–78.4%	45.7%	41.6%–49.6%	35.3%	31.0%–39.5%
South Asian	80.6%	63.3%–90.3%	57.4%	37.0%–73.3%	44.3%	22.7%–63.9%
Pacific Islander	65.5%	57.6%–72.2%	37.2%	28.5%–45.9%	26.2%	17.4%–35.8%
Other	79.9%	73.7%–84.8%	65.3%	57.4%–72.1%	56.0%	46.5%–64.5%

HCC, hepatocellular carcinoma; CI, confidence interval; SEER, Surveillance, Epidemiology, and End Results.

subgroups. Our present study is unique in highlighting disparities between Asian subgroups across the US using SEER data for HCC characteristics, treatment, and survival outcomes. CH patients comprised the second largest group in this cohort, had higher percentage of localized HCC, were the most likely to undergo treatment, and had the highest five-year survival rate. South Asian HCC patients were significantly more likely to receive HCC treatment than CH patients. FP and PI patients had the highest mortality, which was likely a result of these two groups having significantly more advanced disease while being significantly less likely to undergo treatment. SEA patients were the largest group in this cohort and were significantly younger at diagnosis. SEA patients were also among the ethnic groups that were less likely to undergo treatment

and that had the lowest five-year survival rates. Interestingly, JP patients were among those with the lowest survival in this cohort. This finding may be explained by the fact that this group was significantly older and had significantly more primary tumors, but Japan is also unique among East Asian countries in that there is a higher prevalence of HCV-related HCC, whereas for regions such as China, it is predominantly HBV-related HCC.¹⁸ Even after correcting for HCC tumor stage and HCC treatment received, significant disparities in overall HCC survival persisted.

Differences in HBV immunization rates and screening may contribute to the disparities identified in this present study. Ineffective implementation of HBV screening and immunization, especially among HBV endemic regions is

Figure 1 Overall HCC survival among Asian ethnic subgroups. HCC, hepatocellular carcinoma.

Table 5 Predictors of Long-term HCC Survival Among Asians.

Variables	Multivariate model		
	Hazards ratio	95% CI	P-value
Chinese	1.00	–	–
Japanese	1.48	1.26–1.73	<0.001
Korean	1.22	1.05–1.42	0.01
Filipino	1.57	1.38–1.79	<0.001
Southeast Asian	1.36	1.21–1.52	<0.001
South Asian	1.47	1.09–1.98	0.12
Pacific Islander	1.47	1.25–1.74	<0.001

HCC, hepatocellular carcinoma; CI, confidence interval. Model adjusted for age, sex, year, insurance status, HCC tumor stage, HCC treatment.

a missed opportunity for reducing incidence of HBV-associated HCC. Routine screening for chronic HBV in the US was not recommended for immigrants from high-endemic Asian countries until 2008.²⁵ And so, immigration trends of different ethnic groups may affect rates of immunizations and screening for HBV, which then has implications for the development and screening of HCC. Thus, providers play an important role in HBV and HCC management, and prior studies have identified the need to improve screening and vaccination rates.^{25,26} HCC tumor stage at diagnosis is directly affected by the success of HCC surveillance programs, and previous studies have shown suboptimal surveillance in US

patients with HCC.^{6,26,27} Primary care provider attitudes, knowledge, and HCC screening practices have also been previously shown to be suboptimal.^{26,28} Further studies and interventions are warranted to identify barriers to immunization and screening and to target higher-risk groups such as FP, PI, and SEA, given their higher mortality from HCC.

Our present study is in line with prior reports. Using data from the California Cancer Registry for HCC outcomes among patients in California, Stewart et al²⁴ observed lower likelihood of receiving HCC treatment among Laotians/Hmong, Cambodians, and FP, than significantly higher likelihood of HCC treatment among CH, JP, KR, and Vietnamese HCC patients than white patients. Significantly higher mortality was also observed in Laotian and Cambodian HCC patients. Wong et al²⁹ evaluated HCC patients in Hawaii from 1992 to 2009, observing that FP patients were less likely to have HCC within the Milan criteria, FP and PI patients had fewer liver transplants, and FP patients had lower survival than whites. The authors note that these Asian subgroups have higher rate of high-risk behaviors including smoking, alcohol abuse, and high-fat diet, all of which may affect candidacy for liver transplantation. Access to care and insurance coverage were also identified as barriers resulting in more advanced disease at diagnosis. Our present study of US national data observed similar trends, with more advanced disease at presentation, lower likelihood of HCC treatment, and significantly higher mortality in FP patients with HCC.

Although all the patients in our study were of Asian race/ethnicity, the assumption that all patients had monoinfection with chronic HBV has limitations. For example, chronic HCV is also a common etiology of chronic liver disease in JP populations and certain SEA populations. Furthermore, we did not have adequate data to evaluate the possibility of concurrent alcoholic liver disease or NAFLD, both of which can occur independently or concomitantly among patients with underlying chronic HBV.

Although our study provides a large national estimate of HCC among US Asians, certain limitations of the SEER database need to be acknowledged. The SEER database does not include etiology of HCC, and while we estimate that the majority of Asian HCC in the US is secondary to chronic HBV, the inability to evaluate specifically for etiology of liver disease limits the generalizability of our findings. This is particularly important to note as the epidemiology and outcomes of HCC may be affected by underlying liver disease. Although majority of patients who develop HCC have cirrhosis, HBV patients can develop HCC without clinical cirrhosis, and the presence and severity of cirrhosis can affect clinical outcomes in HCC. However, SEER does not include variables that allow accurate assessment of cirrhosis or hepatic functional status. The current database does not provide specific data to assess or compare the severity of liver disease such as laboratory characteristics that would allow one to calculate the model for end-stage liver disease score or the Child-Pugh-Turcotte score. Furthermore, patients' performance status was not readily available in the dataset for inclusion in our analysis. Thus, these limitations need to be accounted for when interpreting our study results as these potential confounders can affect treatment decisions and overall survival outcomes. As previously mentioned, certain locoregional therapies such as TACE are not well captured in the SEER database and may be underreported. Thus, patients who may have been categorized as not receiving any HCC-directed therapy may have actually received locoregional therapies that were not recorded. Furthermore, as previously mentioned, other potential risk factors such as alcohol and drug use or the presence of other comorbidities were not available for inclusion in our analyses. Other demographic data that were missing are immigration status, immigrant generation (for example, first versus second generation), and number of years in the US, which could impact HCC surveillance and access to care.

In summary, there are health disparities among Asians in the US diagnosed with HCC; however, Asians are a heterogeneous group. In this study, disparities in HCC characteristics, treatment, and survival were observed in specific Asian ethnic subgroups. More advanced disease was seen among FP patients, lower rates of HCC treatment was seen among FP and SEA patients, and significantly higher mortality was seen among FP, SEA, and JP patients with

HCC. The etiology of these disparities is multifactorial and influenced by disease etiology, differing comorbidities as risk factors for disease, and socioeconomic factors. Further investigation into understanding contributing factors is needed so that targeted programs can promote more equitable outcomes. The implications of these findings highlight the need for greater awareness of HCC disparities even among different subgroups of Asian patients. Raising awareness of these disparities is key to implement effective programs to improve HCC management, from appropriate screening, early tumor diagnosis, and access to potentially curative therapies.

CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

Justin Yu, Taft Bhuket, Benny Liu, Jennifer Wang, and Robert J. Wong contributed in analysis and interpretation of data; critical revision of the manuscript for important intellectual content; approval of the final draft submitted. Jennifer Wang and Robert J. Wong contributed in study concept and design. Robert J. Wong contributed in acquisition of data; statistical analysis; and study supervision.

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