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Endoscopic history and provider characteristics influence gastric cancer survival in Asian Americans

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Abstract

Gastric carcinoma (GC) disproportionately affects Asian Americans. We examined whether history of upper gastrointestinal endoscopy was associated with lower stage at GC diagnosis among Asian Americans and whether origin of providers influenced referral for endoscopy. We employed SEER-Medicare data on Asian Americans diagnosed with GC in 2004–2013 (n=1,554). Stage distribution, gastrointestinal conditions at diagnosis, and history of endoscopy were compared between Asian ethnic groups. Multivariable logistic regression adjusting for age, sex, poverty level, tumor location and histology was used to examine the association of ethnicity and endoscopic history with stage I disease at diagnosis of GC. Koreans were more likely to be diagnosed with Stage I, T1a GC and have prior history of endoscopy, compared to other Asian ethnicities (24% vs. 8% for Stage I, T1a; 40% vs. 15% for endoscopy). Patients with primary care providers of concordant ethnic origin were more likely to have history of endoscopy. Asian American GC patients with history of endoscopy were more likely to be diagnosed with GC at stage I disease (adjusted OR = 3.07, 95% CI 2.34, 4.02). Compared to other Asian Americans, Koreans were diagnosed with GC at earlier stages owing to common history of endoscopy, which was more often undergone by patients with primary care providers of concordant ethnic origin. Overall, upper gastrointestinal endoscopy was associated with early detection of GC in Asian Americans.

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Author contribution:

CYJ conceived of the study design and acquired data; YCL, SK conducted statistical analyses; CYJ, YCL, SJK, BW, SK, KMW, RWH analyzed and interpreted results; CYJ drafted the manuscript; CYJ, SJK, BW, KMW, RWH provided critical revisions to the manuscript for important intellectual content.

Conflicts of interest: None

Introduction

Asians are the fastest growing minority population in the U.S. and carry a disproportionate burden of gastric cancer (GC) in the U.S., with incidence rates more than 50% greater than that of non-Hispanic Whites [1]. Among Asian subgroups, Koreans face an even higher incidence of GC, estimated at 20–40 cases per 100,000 persons per year [2], comparable to colorectal cancer rates in the general U.S. population [3]. While clear consensus guidelines for colorectal cancer screening are established, we lack evidence-based guidelines for GC control in high risk groups residing in the U.S. [4] This is in spite of economic analyses that demonstrate that screening for GC is cost-effective in persons with sufficiently high lifetime risk of GC [5, 6].

Belief in the value of GC screening varies by provider's race, with Asian providers most frequently responding that screening for GC should be recommended in select populations [7]. Asian providers may have been trained abroad and thus be influenced by policies in Korea and Japan, where upper gastrointestinal series test for GC screening in adults over the age of 40 have led to significant decrease in GC mortality [8, 9]. They may have a lower threshold for recommending endoscopy, understanding the race-specific risk of GC in Asians. National GC screening programs have contributed to higher 5-year survival (50–70%) with GC in Korea and Japan [10], much greater than the average 5-year survival reported in the U.S. (31%) [3]. Indeed in the U.S., Asian GC patients who were born in Asia were more likely to be diagnosed at stage I cancer than non-Asians GC patients [11]. It is unknown whether this is due to more vigilant care by Asian providers.

There is a current knowledge gap in understanding the influence of endoscopic history in patients ultimately diagnosed with GC. To address this question, we examined pre-diagnostic history of endoscopy in Asian Americans ultimately diagnosed with GC, to evaluate their association with diagnosis with early stage of GC. We then explored the influence of the primary care provider characteristics and presenting symptoms on referral for endoscopic examination. Ultimately, we evaluated survival outcomes within Asian subgroups to ascertain if practice differences translate to benefit.

Methods

Data

The Surveillance, Epidemiology and End Results (SEER) tumor registries collate data on incident cancer cases in 30% of the U.S. population, from whom national cancer incidence statistics are derived [12]. Linkage of SEER to Medicare claims on inpatient and outpatient procedures and diagnoses offers unique population-based source of information on patterns of care before and after diagnosis that can be used for epidemiological and health services research [13, 14]. For the purposes of the current analyses, we extracted pathology and diagnosis data on GC cases from SEER, and comorbidity, procedures, provider encounters data from Medicare claims. SEER-Medicare data pertaining to GC cases were obtained and analyzed as a limited data set without direct identifiers. The study was conducted in accordance with the U.S. Common Rule. The Institutional Review Board of Cedars-Sinai Medical Center approved this study. Informed consent was waived for this study of existing

records without direct identifiers. The data that support the findings of this study are available from Information Management Services Inc (IMS). Restrictions apply to the availability of these data, which were used under license for this study. Data are available from IMS through the process delineated in this link https://healthcaredelivery.cancer.gov/seermedicare/obtain/requests.html, with approval from National Cancer Institute.

Study population

We identified primary gastric carcinoma cases who were 65 years or older at the time of diagnosis and were reported to SEER between 2004–2013. Cases reported through death certificates or autopsy, or cases that were not confirmed by histology, laboratory test or visual inspection were excluded. Histology codes for gastric carcinoma are presented in Supplementary Material Table S1. Non-primary gastric cancer cases, *in situ* (stage 0) cases, and non-carcinoma cases were also excluded. Finally, persons enrolled in Medicare HMO, or person who had not been enrolled in Medicare Part A (inpatient care coverage), and Medicare Part B (outpatient care coverage) for at least 36 months prior to GC diagnosis were excluded given that their claims history may not be complete. Supplementary Table S2 compares the selected population to the population excluded due to non-continuous Medicare membership and age of diagnosis. Of the selected population, we analyzed persons who were classified as Asian by race according to the Medicare demographic data. Asian patients were further categorized by major subethnic groups, Japanese, Korean, Chinese, Filipino, Vietnamese. Ethnic groups with case count of less than 100 were combined with Asians without specifications on ethnicity.

Covariates

We extracted data on patient demographics, stage of disease, histology and anatomic location of the tumor through SEER data. The 7th edition of American Joint Committee on Cancer (AJCC) staging system was used to determine the stage of disease and Stage I patients were further classified into T1a and T1b stage. Symptoms and risk factors of GC were extracted from Medicare claims within 6 months of the GC diagnosis. These included unintended weight loss, late onset or refractory dyspepsia, iron-deficiency or pernicious anemia, advanced or multifocal gastric intestinal metaplasia, epigastric pain, dysphagia, blood in stool, hereditary cancer syndromes, *Helicobacter pylori* (*H. pylori*) infection, and peptic ulcers. To evaluate endoscopic history (>18 months), we extracted data on administration and timing of procedures commonly or historically used to detect gastric lesions or mass: esophagogastroduodenoscopy (EGD), endoscopic ultrasound (EUS), upper gastrointestinal series, abdominal computed tomography. We chose 18 months as the threshold to ascertain healthcare unaffected by recent development of symptoms due to GC, and also to capture a population who may be following a biennial surveillance schedule for gastric cancer, as screening upper GI endoscopies are not distinguishable from diagnostic endoscopies based on ICD codes. We also extracted frequency of endoscopies per person-year of Medicare membership among those with at least 60 months of Medicare enrollment prior to GC diagnosis, a sufficient observation period to detect repeat endoscopies. Because *H. pylori* infection is a strong risk factor for GC, we also extracted data on *H. pylori* testing by Current Procedural Terminology (CPT) codes on healthcare claims >18 months prior to GC diagnosis. CPT codes for *H. pylori* breath, serological or urine testing include: 78267,

78268, 83009, 83013, 83014, 86677, 87338, 87339. We also noted whether biopsy was performed at the time of the endoscopic procedures. The corresponding ICD9/10 or CPT codes are listed in Supplementary Material Table S3 and Table S4. Missing data on categorical variables were summarized as 'unknown'. The lack of an indicator or procedure in Medicare claims history was assumed to mean that the patient did not have history of that indicator/procedure.

Provider Characteristics

We determined the primary care provider of the patient by ascertaining the physician with a specialty in general practice, family medicine, internal medicine, osteopathic manipulative therapy, pediatric medicine, geriatric medicine, or preventive medicine who had the most numerous encounters with the patient prior to GC diagnosis based on Medicare claims history [15]. In the case of a tie for the highest number of encounters, the provider that cared for the patient most recently was assigned as a primary care provider. The provider's birth month and year, sex, place of training (U.S. or foreign country) and place of birth were recorded from the American Medical Association provider files.

Statistical Analyses

We first compared the distributions of patient demographics and pathologic characteristics of tumors between specific Asian ethnicities. We then examined clinical symptoms, risk factors identified within 6 months of cancer diagnosis and diagnostic procedures performed within 6 months of the cancer diagnosis between Asian sub-populations. To account for multiple comparisons of clinical indicators, we used a method of Benjamini and Yekutieli with a false discovery rate of 5% when comparing distribution of multiple clinical indicators between Korean ethnicity and the other ethnicities [16]. To understand patterns of usual care not affected by GC, procedure history more than 18 months prior to GC were also compared between sub-populations. Given that likelihood of endoscopy may be influenced by varying burden of comorbid conditions in the different ethnic populations, we also compared history of endoscopy with biopsy by ethnicity restricting to those with history of symptoms or signs that might warrant an endoscopy. Comparison of distribution of categorical variables were conducted by chi-square test, and that of continuous variables were conducted by Wilcoxon rank sum test. Pair-wise comparisons were made to the most populous sub-population (Japanese), but also to Koreans, whose clinical manifestations and stage of diagnosis were markedly different from other sub-populations.

The primary endpoint was stage I disease at diagnosis versus all other stages including 'unknown' stage. Covariates considered included ethnicity, age, sex, residence in big metropolitan areas, neighborhood poverty index, histology, and history of endoscopy. A logistic regression model was employed to examine associations of stage I disease at diagnosis with covariates. All covariates were included in the multivariable model and multicollinearity was assessed with variance inflation factor. Unknown categorical data were included in the model as its own category.

A secondary endpoint was overall survival (OS) defined as time from GC diagnosis to death. Persons who did not die were censored on December 31st 2014. Survival differences

between ethnicities and within each ethnicity by procedure history were conducted by log-rank test, and median survival was estimated by Kaplan-Meier methods [17]. Univariate and multivariable analyses of OS were further conducted using Cox proportional hazards regression models to examine effects of ethnicity and endoscopic history in relation to OS [18]. All variables considered were included in the model. The proportional hazards assumption was assessed graphically and analytically with scaled Schoenfeld residuals [19]. Violation of the proportional hazards assumption was addressed by use of a stratified Cox regression model.

We summarized the provider birthplace by concordance with the race and ethnic origin of the patients at the level of the patient. For example, for Japanese GC cases, we categorized into patients treated by providers born in Japan, born in other Asian countries, born in U.S. or born elsewhere. We compared patient-provider ethnic concordance by chi-square test. We then examined whether a patient's endoscopy history varied by provider's place of birth and place of training (U.S. vs. foreign). All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, North Carolina) with two-sided tests and a significance level of 0.05.

Results

Study population

We identified 1,554 Asian American cases among 13,171 total primary gastric carcinoma cases with ≥36 months of continuous Medicare membership prior to GC diagnosis (Supplementary Material Figure S1). Of these, 366 were Japanese, 352 were Korean, 350 were Chinese, 179 were Vietnamese, 147 were Filipino, 56 were of other Asian ethnicities, and 104 did not have specific information on ethnicity. The latter two groups were combined as 'Other Asian' group. Demographic, clinical and survival statistics on these populations are described in Table 1. Median age at diagnosis within each ethnicity ranged from 77 to 80 and males comprised 50.3% to 61.4% of the cases depending on ethnicity. More than 35% of Koreans lived in neighborhoods of higher poverty index (20–100% of the population below federal poverty level) a prevalence that was higher than that any other Asian sub-populations ($p<0.05$ for all pair-wise comparisons). Except for Japanese patients, the majority of the Asian population resided in large metropolitan areas with population size of one million or greater. Most patients resided in the Western SEER Regions, which comprise of California, Hawaii, New Mexico, Seattle and Utah. Stage 1, T1a prevalence (24.0%) at diagnosis was notably higher in Koreans compared to that in other subpopulations (6.4% −12.9%, $p<0.05$ for all pair-wise comparisons). Conversely, Stage IV prevalence was lowest among Koreans (16%) compared to other populations (25.3–30.2%, $p<0.05$ for all pair-wise comparisons). Further breakdown of the TNM stage distribution of the gastric cancer cases are presented in Supplementary Table S5. On pathologic assessments, most patients had intestinal type gastric adenocarcinomas located in the non-cardia regions of the stomach. Presence of tumors in the cardia region was highest in Filipinos (16.3%) and lowest in Koreans (6.0%). Median survival from time of diagnosis to death was longest for Koreans (34 months) and shortest for Filipino patients (11 months).

Presenting symptoms and recent procedures

Distribution of risk factors, signs or symptoms of GC presenting within 6 months of diagnosis are presented in Table 2. Koreans were less likely to have blood in stool as compared to Japanese, Chinese, or Vietnamese cases (false discovery rate $p<0.05$ for all pairwise comparisons). Koreans were more likely to have a diagnosis of late onset or refractory dyspepsia or peptic ulcer disease compared to Japanese, Filipino or Other Asian, and also more likely to have a diagnosis of peptic ulcer than Japanese and Chinese patients (Table 2) Most patients, although variable by ethnicity (79%−93%), had a diagnostic endoscopy with biopsy within 6 months of the GC diagnosis. In contrast to this, testing for *H. pylori* was not common (8.2% to 12.9% by sub-population) within 6 months of GC diagnosis. (Table 2)

History of abdominal procedures

Prior to GC diagnosis (>18 months), Koreans had an exceptionally high prevalence (40%) of previous endoscopy with biopsy, as compared to other Asian subpopulations (9.5% to 19%). Among persons who underwent endoscopy, biopsy rates varied by ethnicity. Among Koreans, only 7% of those with a history of endoscopy prior to GC development had not undergone biopsy, whereas 31% of Japanese patients with a history of endoscopy went through the procedure without a biopsy. In contrast, history of abdominal CT was relatively similar across the sub-populations (9.5% to 13%). *H. pylori* testing prior to GC diagnosis was also common among Korean (34%) and Vietnamese (27%) groups, as compared to other Asian sub-populations (6.2% to 14.7%). (Table 3)

Among persons with a history of unintended weight loss, an alarm feature for cancer for any person, there were still diverging history of endoscopy with biopsy by Korean (80%) vs. non-Korean ethnicity (50%, $p=0.002$). Also, among persons with history of dyspepsia, a milder gastrointestinal condition, history of endoscopy with biopsy was more prevalent among Korean (68%) vs. non-Korean GC patients (48%, p=006). (Table S6)

When the rate of endoscopy with biopsy per time spent in Medicare membership were compared between Koreans and non-Koreans among those *with prior endoscopy with biopsy*, the rates were similar for both groups (0.40 per person-year in Koreans, and 0.41 per person-year in non-Koreans, $p=0.73$).

Association of endoscopy history with Stage I diagnosis

Distribution of stage I disease at diagnosis of GC is presented by endoscopic history within sub-ethnic groups in Table 3. Within each ethnic group, percent of stage I diagnosis is higher for patients with a history of endoscopy with biopsy (39%−54%), as compared to persons with no abdominal procedures conducted (21%−37%) (Table 3), also as compared to persons with history of endoscopy without biopsy (0–46%), and those with history of abdominal CT without endoscopy (14–27%). Of note, Korean patients with no known history of endoscopy or abdominal CT, still had higher prevalence of stage I disease (37%), as compared to the rest of the Asian American patients with gastric cancer (19%−24%, $p<0.0001$).

We examined the association of demographic factors, histology, and endoscopy with biopsy with Stage I disease at diagnosis of GC combining all Asian ethnic groups. (Table 4) In univariate analysis, we found that Koreans were more likely to be diagnosed at stage I (OR = 2.44, 95% CI 1.79, 3.34), as compared to Japanese (reference group) and that history of endoscopy with biopsy was strongly associated with stage I diagnosis (OR = 3.52, 95% CI 2.73, 4.55). These associations remained significant in the multivariable model, adjusting for age, sex, neighborhood socioeconomic measures, and histology: OR for Korean ethnicity 2.00, 95% CI 1.38, 2.89, OR for endoscopy with biopsy 3.07, 95% CI 2.34, 4.02. (Table 4) Of note, the ORs for Korean ethnicity was attenuated in multivariable analysis, indicating that the association is partially explained by endoscopic history.

Association with overall survival

We examined the association of ethnicity, age, sex, residence in big metropolitan areas, neighborhood poverty index, tumor location, histology, and stage with overall survival (OS) and present the findings in Supplementary Table S7. In the univariate analysis, Koreans showed significantly increased OS (HR=0.62, 95% CI 0.52–0.74) and Filipinos showed lower OS (HR=1.20, 95% CI 0.98–1.48) as compared to Japanese. After adjustment for age, sex, metropolitan residence, neighborhood poverty level, tumor location and histology, Koreans still showed better OS (HR=0.69, 95% CI 0.57–0.84) and Filipinos showed lower OS (HR = 1.26, 95% CI 1.01–1.57). With further adjustment for history of endoscopy with biopsy, which was associated with higher OS (HR = 0.61, 95% CI 0.52–0.72), the relative hazard of death for Koreans increased to HR=0.78, 95% CI 0.64–0.95. When the model was fully adjusted for stage of disease at diagnosis, the survival advantage for Koreans disappeared (HR = 0.96, 95% CI 0.77–1.19), while excess risk of mortality in Filipinos remained (HR = 1.36, 95% CI 1.07–1.73).

Other factors associated with poor OS included diffuse (HR = 1.33, 95% CI 1.11–1.59) or indeterminate (HR = 1.49, 95% CI 1.19–1.86) histology as compared to intestinal types of tumors. As expected, those with T1a and T1b tumors and no lymph node involvement had considerably lower hazard of mortality (HR = 0.11, 95% CI 0.08–0.14, HR =0.11, 95% CI 0.08–0.15) as compared to patients with stage IV diagnosis.

Patient-provider in ethnicity and endoscopic history

We examined the distribution of provider birthplace for each subpopulation. Majority of Koreans (81%) and Vietnamese (68%) were treated by providers of concordant origin (e.g. Korean patients by providers born in Korea). On the other hand, only a minority of Japanese patients were treated by providers born in Japan (10%) and rather were treated by providers born in the U.S (68%). Approximately 60% of Chinese and Filipinos were treated by Asian providers, of whom more than half were of concordant origin as the patient. (Figure 1)

History of biopsy-included endoscopy was compared by provider birthplace. For each sub-population, persons whose primary care provider was of concordant origin were more likely to have a history of biopsy-included endoscopy as compared to patients whose provider was of different origin. The difference was more notable for Koreans (47% vs 33%), Japanese (24% vs. 18%) and Vietnamese patients (20% vs. 12%, Figure 2). Among Korean patients

treated by providers born in Korea, we further examined endoscopic history by place of training (U.S. vs. foreign). History of endoscopy did not vary by place of provider training (52% trained in the U.S. vs. 45% trained abroad, p=0.31).

Discussion

Differential outcomes for gastric cancer between Asian and non-Asian patients are well described [11, 20]. However, examination of outcomes and practice patterns in Asian subgroups within the United States is understudied. In this analysis of more than 1,500 gastric cancer cases among Asian American Medicare enrollees, we found substantial differences in stage of diagnosis and survival by specific Asian ethnicity. Koreans were more likely than any other sub-populations to be diagnosed with Stage I, T1a tumors, the earliest form of GC, leading to large survival advantage for this population. They were also less likely to be diagnosed with alarm features of GC, such as unintended weight loss and blood in stool. The high prevalence of Stage I T1a tumors in Korean is significant, given that it is the most curable form of GC, and also typically found when asymptomatic patients undergo screening [21].

Earlier stage of diagnosis among Koreans is consistent with previous analyses of cancer registry data in Asian Americans with GC [22, 23]. Our study delves into the role of prior endoscopic history, ethnicity and primary care providers in explaining the differences in stage at diagnosis. Based on our findings, we hypothesize that a) Korean patients likely have a lower threshold for asking for an endoscopy referral, as they may be influenced by practices abroad where upper GI endoscopy is common, b) Korean patients may be receiving care beyond the context of Medicare that allows earlier detection of gastric cancer and c) Korea-born primary care providers, owing to increased cultural awareness, have lower threshold for endoscopic referral and that referred patients are more likely to follow through with endoscopy. In support of the first hypothesis, we observed that Korean patients whose providers were not born in Korea also had more common history of endoscopy than other ethnicities who were treated by doctors of discordant ethnic origin. In support of the second hypothesis, we observed that Korean patients who had no endoscopic history were still more likely to be diagnosed at earlier stages than non-Korean Asian patients who also had no endoscopic history. South Korea has as a thriving medical tourism industry, with overseas Koreans being the primary users, attracted by lower costs, quality of care, convenient scheduling with one-stop comprehensive exams, including gastric cancer screening [24]. The third hypothesis is supported by our observation that Korean patients whose providers were born in Korea were more likely to have history of endoscopy as compared to Korean patients treated by those not born in Korea. Korean primary care providers may perceive referral for endoscopy as being culturally competent, a quality that is linked to higher patient satisfaction [25]. Because screening upper endoscopies are not distinguishable from diagnostic endoscopies by procedure codes, we are unable to attribute the divergent practice patterns to screening for early detection, such as occurs in Korea where upper GI endoscopies with biopsy are recommended every two years [8, 9]. The literature points to contrasting provider perspectives on the values of gastric cancer screening by provider ethnicity in the U.S. Asian providers, more than providers of other races, most frequently report that screening for GC should be recommended in specific minority populations [7].

When presented with a case study of a recently immigrated Korean male in his 60's without symptoms, over 90% of Korean geriatricians who practice in the U.S. responded they would recommend GC screening test on a 1–2 year frequency, as opposed to only 30% of U.S. born geriatricians, who recommended a frequency of 3–5 years [26]. However, when we examined rate of endoscopy by ethnicity among those who had ever received endoscopy with biopsy, we saw no difference in the rates of endoscopy per observation period by ethnicity. Therefore, we attribute the higher prevalence of history of endoscopy in Koreans to lower threshold to referral when presented with suggestive symptoms, rather than repeat screening endoscopy. Furthermore, we believe that cultural sensitivity, more than training, likely drives referral patterns, since endoscopic referral did not vary by place of training among Korean doctors.

Biopsy during endoscopy offers a chance to discover lesions, such as intestinal metaplasia, that may not be visible to the naked eye of an endoscopist [27]. We found that upper GI endoscopy was not always accompanied by biopsy and likelihood of omission of biopsy varied by patient ethnicity. Among Koreans, only 7% of those with a history of endoscopy prior to GC development had not undergone biopsy, whereas 31% of Japanese patients with a history of endoscopy went through the procedure without a biopsy, a potential missed opportunity for early GC detection. Our study highlights the need to include biopsy when conducting endoscopic examinations.

We also found that history of *H. pylori* testing prior to GC development was more common among Korean and Vietnamese patients than in other sub-populations. Both groups of patients are primarily managed by primary care providers of concordant origin from South Korea or Vietnam, respectively. *H. pylori* seroprevalence is relatively high in Korea (54%, excluding persons with history of *H. pylori* eradication treatment) [28] and in Vietnam (75% in the general population) [29]. Korea and Vietnam are well-known to be a countries of high GC incidence (36/100,000 person-years, 24/100,000 person-years, respectively) [30, 31]. Experts strongly endorse *H. pylori* eradication as a method of GC reduction in these countries [31, 32] which, in combination with the high concordance of patient-provider ethnicity, may explain the more prevalent history of *H. pylori* testing in this population. However, given the long latency period of *H. pylori*-associated GC, it is unclear whether testing for *H. pylori* over the age of 65 would help to prevent GC [33].

We observed an important health inequity among Filipinos, who experienced lower survival even after adjustment for neighborhood socioeconomic level and prognostic factors at diagnosis. This is consistent with a previous investigation of Asians Americans with GC who underwent gastric surgery [22]. Filipinos have markedly higher prevalence of obesity than other Asian ethnicities [34], and among GC cases studied in this study, Filipinos were most likely to be diagnosed with cardia-type of GC, a type of GC consistently associated with obesity and obesity-related illnesses [35]. Greater burden of obesity may render surgical intervention more challenging, and recurrence more likely. Whether obesity explains the inequity in GC survival is remains to be investigated.

One of the major limitations of our data is that birthplace of the patients was not available. Whereas previous release of SEER data included birthplace (foreign vs. U.S.), the more

recent public release of SEER data (2015 onwards) has excluded birthplace, making it challenging to make inference on whether endoscopic history varied by *patient* birthplace, which has a direct influence on risk of *H. pylori* infection and consequent risk of GC. Another limitation was that there was no self-identified race or ethnicity data on providers, thus, we had to rely on birthplace of provider to infer their ethnic origin. It is possible that U.S. born providers who are of Asian descent may follow a practice similar to that of providers born in Asia but were not classified according to their ethnic origin. Furthermore, we were not able to distinguish screening endoscopy from diagnostic endoscopy. The distinction is critical in understanding whether conducting endoscopy not indicated by symptoms leads to early detection of GC. Also, procedures conducted overseas, often undertaken by Koreans who have access to national health insurance in their country of origin [24], would not have been reflected in the Medicare claims. This means that the true frequency of upper GI endoscopy is even higher in the Korean population than observed in this study. In addition, we lacked biological data on *H. pylori* infection or body mass index, which would have helped explained the etiology or prognosis of GC. We examined several indicators that may have prompted endoscopic examinations, but these are not all comprehensive, and recognize that other reasons may have prompted endoscopies. In particular, we lacked smoking history and family history of gastric cancer that strongly influences the risk of GC as well as surveillance for GC. Moreover, our survival analysis may be influenced by lead-time bias, in which survival may appear to be longer in patients with endoscopic history purely because the disease was found earlier in the pathogenesis and therefore had greater period of observation (lead-time) and not because subsequent early intervention would have led to better outcomes. To overcome this bias, future studies comparing gastric cancer mortality in persons receiving endoscopy vs. those not receiving endoscopy among persons at risk for gastric cancer are warranted. Finally, because our follow-up period did not reach 5-years for a considerable portion of our study population, we were not able to compute 5-year survival, a standard metric for assessing cancer outcomes.

Our study clearly demonstrates that among Asian Americans the chance of early detection is markedly increased in populations who have been receiving vigilant care via upper GI endoscopy with biopsy and *H. pylori* testing. Consequent survival trends in these populations exceed that of unselected GC populations in the U.S. Our findings support current guideline set forth by American Society for Gastrointestinal Endoscopy: "*Endoscopic screening for GC in first generation U.S. immigrants from high-risk regions may be considered for those aged 40 years, particularly if there is a family history of GC in a first-degree relative*." While this study was not limited to patients with gastric intestinal metaplasia (GIM), a histologic precursor to GC, our findings provide evidence for endoscopic screening highlighted as largely lacking in a recently published 'Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia', which recommends against routine use of endoscopic surveillance in the general population with GIM [36]. This notwithstanding, the Guideline does suggest that 'surveillance may be considered based on shared decision-making between patients and providers for patients with family history for gastric cancer or increased background risk for gastric cancer'. Our findings on the association of patient-provide ethnic concordance with endoscopic history informs that such

shared decision-making is already at-play, but could potentially be beneficial to broader populations with greater awareness of GC risk on the part of at-risk patients and their providers. These guidelines point to need for more evidence, especially on what the frequency of screening should be and how high-risk regions are defined. Economic analysis demonstrates that GC screening at the same frequency of colonoscopy in most minorities in the U.S. (Asians, Hispanics, and Blacks) is cost-effective, but not at the frequency of every two years. Collectively these studies support ethnic-specific guidelines for GC screening. Targeted guidelines for cancer prevention and control in the U.S. have shown success in reducing health disparities by ethnicity. For example, hepatitis B screening programs aimed towards Asian immigrants have increased uptake of hepatitis B vaccinations [37, 38], which has demonstrated preventative effect against hepatocellular carcinoma [39].

Despite this evidence, we lack clear consensus guidelines on endoscopic screening for gastric cancer in high risk Asian Americans populations. Also, the American College of Physicians deems upper endoscopy, without the presence of alarm features, like bleeding, or anemia unnecessary [40]. Existing guidelines do not recognize the large heterogeneity in risk of GC, especially in ethnic minorities who would benefit from lower threshold for endoscopic referral. Further research is necessary to precisely identify those at risk for GC who will benefit from routine endoscopic surveillance and our work provides foundational support for ongoing efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Novelty and Impact

It is well-established that Asian Americans in the U.S. are disproportionately affected by gastric cancer. In our study we found that Asian American patients treated by physicians of similar ethnic background are more likely to undergo upper GI endoscopy in the U.S., leading to early detection of gastric cancer and longer survival. Given this, targeted endoscopic screening in Asian Americans should be considered for early detection of GC.

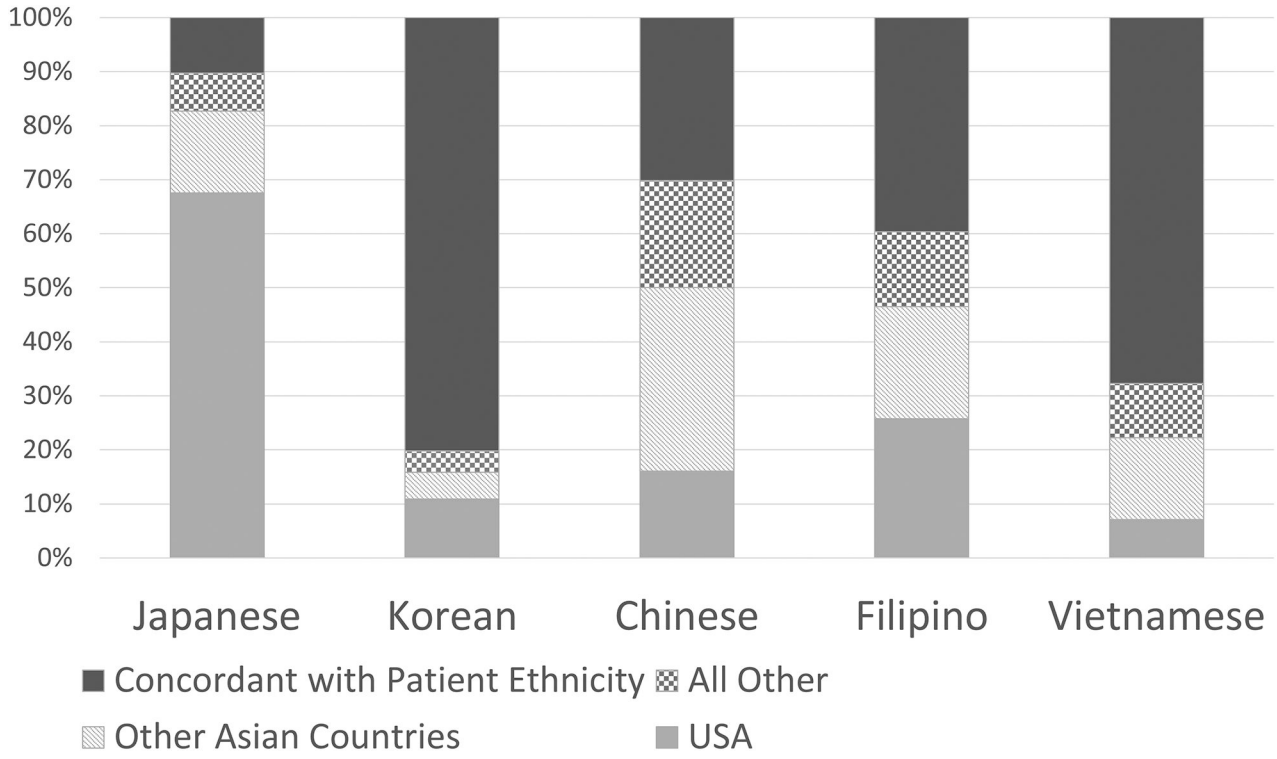

Figure 1.
Distribution of ethnic origin of primary care providers of Asian American gastric cancer patients

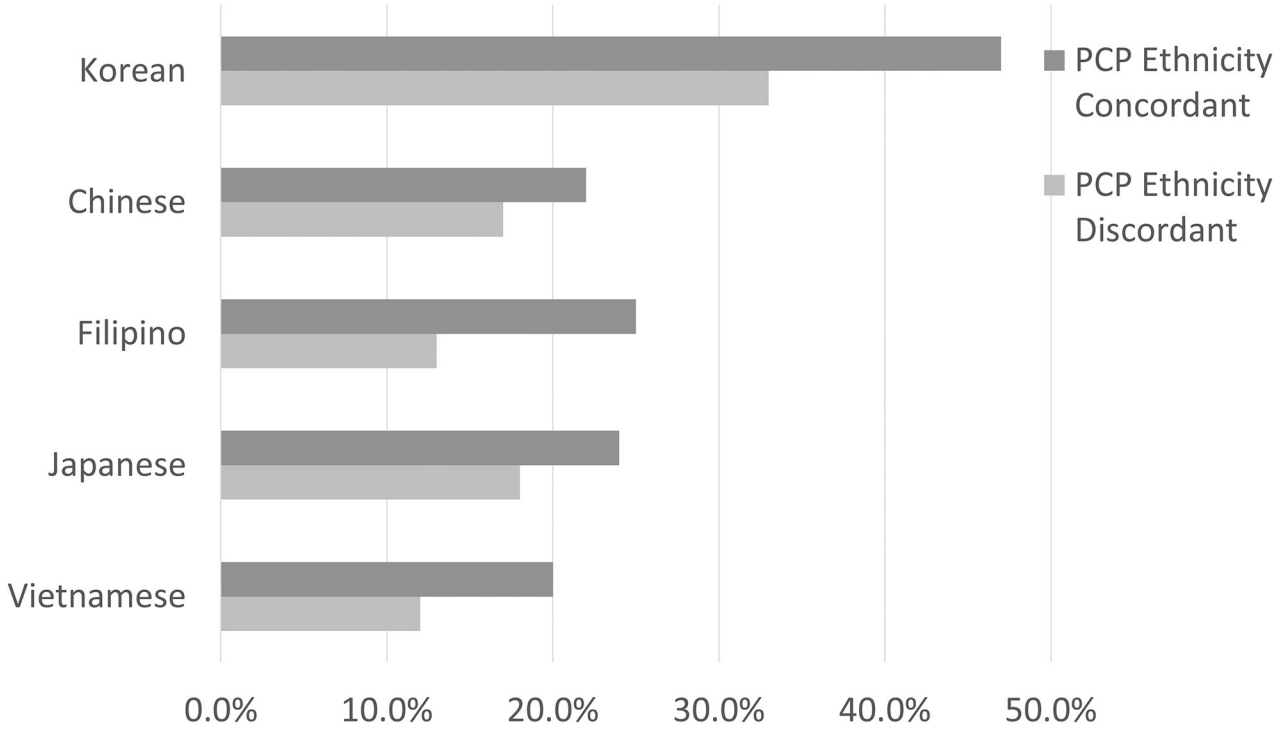

Figure 2.
History of endoscopy with biopsy by concordance in ethnic origin of the primary care providers of Asian American gastric cancer patients

Table 1:

Distribution of demographic factors, stage, histology and median survival of Asian American gastric carcinoma cases represented in SEER 2004 −2013 (N= 1,554)

Variable	Category	Japanese	Korean	Chinese	Vietnamese	Filipino	Other Asian
Number of cases (n)		n=366	n=352	n=350	n=179	n=147	n=160
Median Age, interquartile range (Years)		80 (75, 85) **	77 (72, 82) ^^	80 (75, 85) **	79 (74, 85) *	79 (74, 83) *	78 (72, 85) *
Age	65 −74	91 (24.9%) **	141 (40.1%) ^^	80 (22.9%) **	52 (29.1%) *	37 (25.2%) *	51 (31.9%)
	75– 85	191 (52.2%)	163 (46.3%)	190 (54.3%) *	87 (48.6%)	88 (59.9%) *	75 (46.9%)
	> 85	84 (23.0%) *	48 (13.6%) ^	80 (22.9%) *	40 (22.4%) *	22 (15.0%) ^	34 (21.3%) *
Period	2004 – 2008	198 (54.1%)	182 (51.7%)	181 (51.7%)	91 (50.8%)	87 (59.2%)	80 (50.0%)
	2009 – 2013	168 (45.9%)	170 (48.3%)	169 (48.3%)	88 (49.2%)	60 (40.8%)	80 (50.0%)
Male		189 (51.6%) *	216 (61.4%) ^	187 (53.4%) *	90 (50.3%) *	78 (53.1%)	97 (60.6%)
Neighborhood Poverty Index	0% to <5% poverty	110 (30.1%) *	69 (19.7%) ^	90 (25.7%)	20 (11.2%) *^^	35 (24.0%)	58 (36.3%) **
	5% to <10% poverty	107 (29.2%) **	64 (18.2%) ^^	86 (24.6%) *	48 (26.8%) *	37 (25.3%)	41 (25.6%)
	10% to< 20 % poverty	92 (25.1%)	93 (26.5%)	98 (28.0%)	68 (38.0%) *^	44 (30.1%)	34 (21.3%)
	20% to 100 % poverty	57 (15.6%) **	126 (35.6%) ^^	76 (21.7%) ** ^	43 (24.0%) *^	31 (20.6%) **	27 (16.9%) **
Big Metro		164 (44.8%) **	322 (91.5%) ^^	318 (90.9%) ^^	> 172 (> 95%) *^^	105 (71.4%) **^^	134 (83.8%) *^^
SEER Region	Non-West	16 (4.4%) *	37 (10.5%) ^	32 (9.1%) ^	11 (6.2%)	16 (10.9%) ^	42 (26.3%) **^^
	West	350 (95.6%) *	315 (89.5%) ^	318 (90.9%) ^	168 (93.9%)	131 (89.1%) ^	118 (73.8%) **^^
Stage[&]	Stage I: T1A	28 (8.8%) **	74 (24.0%) ^^	30 (11.3%) **	24 (16.0) **C	19 (15.1%) **C	22 (16.7%) **^C
	Stage I: T1B	37 (11.6%) *	54 (17.5%) ^	24 (9.1%) *			
	Stage I: T staging unknown	33 (10.3%)	38 (12.3%)	34 (12.8%)	19 (12.7%)	14 (11.1%)	18 (13.6%)
	Stage II	56 (17.6%)	38 (12.3%)	40 (15.1%)	27 (18.0%)	24 (19.1%)	29 (22.0%) *
	Stage III	73 (22.9%)	54 (17.5%)	64 (24.2%)	42 (28.0%) *	31 (24.6%)	26 (19.7%)
	Stage IV	92 (28.8%) *	50 (16.2%) ^	73 (27.6%) *	38 (25.3%) *	38 (30.2%) *	37 (28.0%) *
Histology[+]	Intestinal	281 (76.7%)	262 (74.4%)	249 (71.1%)	142 (79.3%)	104 (70.8%)	27 (16.9%) ^
	Diffuse	51 (13.9%)	48 (13.6%)	65 (18.6%)	>20 (>10%)	27 (18.4%)	24 (15.0%)

Variable	Category		Japanese	Korean	Chinese	Vietnamese	Filipino	Other Asian
	Indeterminate		34 (9.3%)	42 (11.9%)	36 (10.3%)	<11 (<10%)	16 (10.9%)	27 (16.9%)^
Location	Cardia		42 (11.5%)*	21 (6.0%)^	47 (13.4%)**	15 (8.4%)	24 (16.3%)**	22 (13.8%)*
	Non-Cardia	Body and Fundus	56 (15.3%)	47 (13.4%)	42 (12.0%)	27 (15.1%)	23 (15.7%)	27 (16.9%)
		Pyloric Antrum and Pylorus	128 (35.0%)*	159 (45.2%)^	139 (39.7%)	73 (40.8%)	43 (29.3%)*	59 (36.9%)
		Lesser & Greater Curvature	55 (15.0%)	62 (17.6%)	50 (14.3%)	31 (17.3%)	22 (15.0%)	22 (13.8%)
	Overlapping/Unspecified		85 (23.5%)	63 (18.2%)	72 (20.7%)	33 (18.6%)	35 (23.7%)	30 (18.6%)
Median Survival (in months)			15 (4, 51)##	34 (10, 117)##	13 (4, 47)##	14 (5, 40)##	11 (4, 32)##	16 (5, 49)##

Statistically significant based on chi square test.

^ p <0.05

^^ p<0.001 (Japanese as reference)

* p <0.05

** p<0.001 (Korean as reference)

Statistically significant based on Log Rank test.

# p <0.05

p<0.001 (Japanese as reference)

ǂ p <0.05

ǂǂ p<0.001 (Korean as reference)

[c] Cells with <11 counts were combined, per SEER-Medicare data reporting requirements

[&] Percentage is only calculated by the known

[+] Histology: Intestinal includes: carcinoma (grade I to III), papillary carcinoma, adenocarcinoma (grade I to III). Diffuse includes signet ring cell carcinoma or anything that is grade IV. Indeterminate includes cell type that is not determined, not stated or not applicable

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Table 2.

Presence of symptoms, signs and risk factors at diagnosis (≤6 months) of gastric carcinoma among Asian Americans

Variable	Category	Japanese	Korean	Chinese	Vietnamese	Filipino	Other Asian
Number of patients		n=366	n=352	n=350	n=179	n=147	n=160
GI Indicator	Unintended weight loss	114 (30.8%) *	60 (17.0%)	69 (19.7%)	36 (20.0%)	30 (20.4%)	44 (27.5%)
	Blood in stool	57 (15.6%) *	19 (5.4%)	57 (16.3%) *	33 (18.4%) *	15 (10.2 %)	20 (12.5%)
	Iron-deficiency/ Pernicious anemia	236 (64.%)	201 (57.1%)	234 (66.9%)	117 (65.4%)	100 (68.0%)	116 (72.5%)
	Abdominal pain, Epigastric	71 (19.4%)	89 (25.3%)	78 (22.3%)	51 (28.5%)	33 (22.4%)	39 (24.4%)
	Late onset dyspepsia / Refractory dyspepsia	28 (7.7%) *	87 (24.7%)	60 (17.1%)	31 (17.3%)	11 (7.5%) *	19 (11.9%) *
	Peptic Ulcer	18 (4.9%) *	76 (21.6%)	32 (9.1%) *	32 (17.9%)	14 (9.5%)	17 (10.6%)
	Advanced/multi-focal Gastric intestinal metaplasia	51 (13.9%)	62 (17.6%)	38 (10.9%)	23 (12.8%)	11 (7.5%)	24 (15.0%)
Abdominal Imaging	Endoscopy with biopsy	325 (88.8%)	327 (92.9%)	317 (90.6%)	159 (88.8%)	116 (78.9%)	141 (88.1%)
	No endoscopy with biopsy	41 (11.2%)	25 (7.1%)	33 (9.4%)	20 (11.2%)	31 (21.1%)	19 (11.9%)
H. Pylori Screening		47 (12.9%)	35 (9.9%)	37 (10.5%)	17 (9.5%)	12 (8.2%)	18 (11.3%)

*Statistically significant with false discovery rate of 5% (Korean as reference)

Dysphagia and *H. Pylo*ri infection are not presented in the table due data <11 counts, per SEER-Medicare data reporting requirements.

Table 3.

History of abdominal imaging and H. pylori testing >18 months prior to gastric carcinoma diagnosis and stage I disease at gastric cancer diagnosis among Asian Americans

Variable	Category	Frequency of endoscopic history (column %)						Stage 1 Frequency (row %)					
		Japanese	Korean	Chinese	Vietnamese	Filipino	Other Asian	Japanese	Korean	Chinese	Vietnamese	Filipino	Other Asian
Number of patients		n=366	n = 352	n = 350	n = 179	n = 147	n = 160	98 (25.8%)	166 (47.1%)	88 (25.1%)	43 (24.0%)	33 (22.4%)	40 (25.0%)
Abdominal Imaging	Endoscopy with biopsy, regardless of CT	46 (12.6%) **	141 (40.1%)	61 (17.4%) **	25 (14.0%) **	14 (9.5%) **	30 (18.8%) **	25 (54.3%) ##	91 (64.5%) ##	24 (39.3%) ##	11 (44.0%) ##	--	12 (40.0%) ##
	Endoscopy without biopsy, regardless of CT	21 (5.7%)	11 (3.1%)	48 (13.7%)	24 (13.4%)	24 (16.3%)	25 (15.6%)	13 (21.3%)	15 (31.3%)	14 (29.2%)	--	--	--
	Abdominal CT only	40 (10.9%)	37 (10.5%)										
	None	259 (70.8%) **	163 (46.3%)	241 (68.9%) **	130 (72.6%)	109 (74.2%) **	105 (65.6%) **	60 (23.2%)	60 (36.8%)	50 (20.7%)	27 (20.8%)	21 (19.3%)	25 (23.8%)
H. pylori testing	Tested	23 (6.3%) **	119 (33.8%)	52 (14.9%) **	49 (27.4%)	17 (11.6%) **	19 (11.9%) **	10 (43.5%)	65 (54.6%)	16 (30.8%)	14 (28.6%)	--	--
	Not tested	343 (93.7%) **	233 (66.2%)	298 (85.1%) **	130 (72.6%)	130 (88.4%) **	141 (88.1%) **	88 (25.7%)	101 (43.3%)	72 (24.2%)	29 (22.3%)	--	--

Statistically significant based on chi-square test.

* p <0.05

** p<0.001 (Korean as reference)

Statistically significant based on chi-square test.

# p<0.05,

p<0.001 (no abdominal imaging as reference)

Table 4.

Association of demographic factors and endoscopic history with stage I diagnosis of gastric cancer in Asian Americans

Variable	Category	N	Number of patients (%) or median (IQR) with Stage I at diagnosis	Univariate OR (95% CI)	Adjusted OR (95% CI)
Ethnicity	Japanese	366	98 (26.8%)	Reference	Reference
	Korean	352	166 (47.2%)	2.44 (1.79, 3.34)	2.00 (1.38, 2.89)
	Chinese	350	88 (25.1%)	0.92 (0.66, 1.28)	0.92 (0.63, 1.34)
	Vietnamese	179	43 (24.0%)	0.87 (0.57, 1.31)	0.92 (0.58, 1.46)
	Filipino	147	33 (22.5%)	0.79 (0.50, 1.24)	0.87 (0.55, 1.40)
	Other Asian	160	40 (25.0%)	0.91 (0.60, 1.40)	0.90 (0.57, 1.43)
Age, Median in years (IQR)		79 (74, 84)	79 (73, 84)	1.00 (0.98, 1.01)	1.01 (0.99, 1.02)
Sex	Male	857	259 (30.2%)	Reference	Reference
	Female	697	209 (30.0%)	0.99 (0.80, 1.23)	1.08 (0.86, 1.36)
Big metropolitan area	Metropolitan	1,216	372 (30.6%)	Reference	Reference
	Rural or small metro	338	96 (28.4%)	0.90 (0.69, 1.17)	1.13 (0.82, 1.56)
Neighborhood poverty index	0% to < 5% poverty	382	117 (30.6%)	Reference	Reference
	5% to < 10% poverty	383	107 (27.9%)	0.88 (0.64, 1.20)	0.86 (0.62, 1.19)
	10% to < 20% poverty	429	115 (26.8%)	0.83 (0.61, 1.13)	0.75 (0.54, 1.04)
	20% to 100% poverty	360	131 (36.3%)	1.28 (0.94, 1.73)	1.05 (0.75, 1.46)
Histology	Intestinal	1,147	362 (31.6%)	Reference	Reference
	Diffuse	242	63 (26.0%)	0.76 (0.56, 1.04)	0.83 (0.60, 1.15)
History of Endoscopy w/ Biopsy	Indeterminate	165	43 (26.1%)	0.76 (0.53, 1.11)	0.69 (0.47, 1.02)
	Absence	1,237	300 (24.3%)	Reference	Reference
	Presence	317	168 (53.0%)	3.52 (2.73, 4.55)	3.07 (2.34, 4.02)

Abbreviation: IQR, interquartile range.