Disparities in clinical and demographic characteristics among Asian/Pacific Islander and Non-Hispanic White newly diagnosed lung cancer patients

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Abstract
Purpose Racial disparities persist among lung cancer patients but have not been adequately studied among Asian/Pacific Islander (API) subgroups, which are heterogeneous. This study compared clinical and demographic characteristics at diagnosis of API subgroups and NHW patients.

Methods NHW and API adults diagnosed with lung cancer were identified from the Surveillance, Epidemiology, and End Results database (1990–2015). API was divided into eight subgroups: Chinese, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Vietnamese, Asian Indian/Pakistani, and Other. Multivariable multinomial logistic regression models were used to assess adjusted associations of clinical and demographic factors with API/subgroups.

Results There were 522,702 (92.6%) NHW and 41,479 (7.4%) API lung cancer patients. API were less likely to be diagnosed at the age of ≥ 80 years (ORadj 0.53, 95% CI 0.48–0.58 for ≥ 80 vs. ≤ 39 years) than NHW. However, Japanese patients were more often diagnosed at ≥ 80 years compared to other ethnic subgroups. API were less often female (ORadj 0.85, 95% CI 0.83–0.86), and unmarried (ORadj 0.71, 95% CI 0.68–0.74); however, among API, Japanese, Hawaiian/Pacific Islander, Korean, and Vietnamese were more often unmarried, compared to Chinese patients. API were more frequently diagnosed at stage IV, compared to stage I (ORadj 1.31, 95% CI 1.27–1.35). API had significantly less squamous cell carcinoma (ORadj 0.54, 95% CI 0.52–0.56, compared to adenocarcinoma); among API, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, and Vietnamese more often presented with squamous cell histology (range: ORadj[Other] 1.24, 95% CI 1.09–1.41; ORadj[Hawaiian/Pacific Islander] 2.47, 95% CI 2.22–2.75).

Conclusion At diagnosis, there are significant differences in demographic and clinical characteristics between NHW, API, and API subgroups. Treating API patients as a single population may overlook biological, environmental, and behavioral differences that might be beneficial in designing prevention strategies and treatment.

Keywords Lung cancer · Racial disparities · Asian/Pacific Islanders · Minority populations · Administrative database

Introduction

Lung and bronchial cancers are among the leading causes of cancer death in the USA [1–3]. The standard of care for treating lung cancer and its subsequent prognosis is highly dependent on tumor histology and stage. In fact, the mainstay treatment for early-stage, non-small cell lung cancer (NSCLC) is surgery, which can be curative for many patients. As small cell lung cancer (SCLC) is often detected at later stages it is generally treated with chemotherapy and/or radiotherapy with a lower survival compared to NSCLC. Despite a decrease in the incidence of lung cancer in recent years, racial disparities in disease stage at diagnosis, tumor histology, treatment, and survival continue to persist [4, 5]. Disparities by race have been well documented among Non-Hispanic Whites (NHW), Blacks/African Americans, and Hispanics [1, 3, 5–8]. However, few studies have thoroughly assessed these differences in Asian Americans/Pacific
Among API patients, lung and bronchial cancers remain a significant concern. While Surveillance, Epidemiology, and End Results (SEER) age-adjusted lung and bronchial cancer incidence from 2000 to 2018 shows that API have lower rates than whites, the decrease over time is less pronounced in API than in whites [14]. As one of the fastest growing populations in the USA, API display immense heterogeneity, especially with regard to country of origin, cultural diversity, health behaviors, health outcomes, lifestyle, and socioeconomic status [9, 10]. This heterogeneity is likewise seen in how the burden and type of lung and bronchial cancer are distributed across the API ethnic subgroups [1, 9, 11]. For example, Chang et al. reported that Japanese patients with NSCLC in California had significantly worse overall and disease-specific survival rates compared to their Chinese counterparts [12]. Despite the heterogeneity across ES, API patients are frequently treated as one group in research, primarily due to small sample size restrictions [10].

The goal of this study was to assess differences in demographic and clinicopathologic characteristics at lung or bronchial cancer diagnosis between API, ES, and NHW patients. This study drew upon data for NHW and API patients diagnosed with lung or bronchial cancer between January 1, 1990 and December 31, 2015 from the SEER Program. The primary aims of this analysis were to identify racial disparities at the time of diagnosis and to determine whether these disparities persisted after adjusting for confounders.

**Methods**

**Data source and study population**

SEER is a program funded by the National Cancer Institute (NCI) that compiles cancer incidence and mortality information from population-based registries, which cover approximately 35% of the population of the USA [15]. The database provides data on patient demographics, primary cancer diagnoses, tumor morphology, cancer stage at diagnosis, treatment, and vital status [16]. The dataset is public and de-identified and therefore, the study was deemed exempt from institutional review.

For this study, the SEER*Stat software [17] was used to query the SEER 18 Registries for all patients diagnosed with lung or bronchial cancer in 1990–2015 (n = 1,011,282). NHW and API adults (≥ 18 years) with a microscopically confirmed first or only primary diagnosis of lung or bronchial cancer and a reporting source other than autopsy or death certificate were included (n = 575,126). Cases were excluded if their clinical classification was unclear for at least one of the following reasons: tumor histology labeled as either unspecified malignant neoplasm or sarcoma, no primary tumor present at diagnosis, malignant cells present only in secretions, or a mismatch between patient stage and stage-dependent treatment. These patients represented < 2% of the sample. This resulted in a cohort of 564,181 cases (Fig. 1).

Lung and bronchial cancer patients were analyzed as a single category. Although lung cancer anatomically arises in the lung parenchyma compared to the lumen of a bronchia for bronchial cancer, both cancers share the same set of histologies, TNM staging criteria, and histology/stage-specific treatment guidelines. The study population was divided according to race into NHW and the overall API groups. Based on prior research, API patients were further divided into eight major ethnic subgroups (ES) as follows: Chinese, Japanese, Filipino, Hawaiian/Pacific Islander (including Hawaiian, Samoan, Pacific Islander, Tongan, Fijian, Guamanian, Micronesian, Polynesian, Melanesian, Chamorro, Tahitian, Kampuchean, and New Guinean), Korean, Vietnamese, Asian Indian/Pakistani, and Other (which composed of Laotian, Hmong, Thai, and Other/Unknown API) [11].

**Covariates**

Variables of interest included age at diagnosis, sex, marital status, TNM stage, and histology. TNM stage was classified using the third (1990–2003) and sixth (2004–2015) editions of the American Joint Cancer Committee on Cancer [18]. Histology was categorized as adenocarcinoma, squamous cell, large cell, other specified non-small cell (which includes carcinoid tumors, adenoid cystic, mucoepidermoid, adenosquamous, and large cell neuroendocrine carcinomas), non-small cell—not otherwise specified (NOS), and small cell carcinomas according to the guidelines by the International Agency for Research on Cancer [19].

**Statistical analysis**

NHW and the overall API patients were compared across all demographic and clinicopathologic characteristics using $\chi^2$ tests. Multivariable logistic regression was used to assess the adjusted associations of all covariates with race (API vs. NHW) by odds ratios (OR) with corresponding 95% confidence intervals (CI). A multivariable multinomial logistic regression was performed to assess the adjusted associations between these characteristics and race for all eight API ES with Chinese as the reference group.

Multivariable analyses were adjusted for age at diagnosis, sex, marital status, TNM stage, and histology. In order to account for changes over time, models were also adjusted for year of diagnosis as the following five sub-periods: 1990–1994, 1995–1999, 2000–2004, 2005–2009, and 2010–2015. Multivariable analyses were conducted on the
subset of patients with complete data for the included variables. Because 11.9% of patients had missing stage, a missing category for stage was created to keep these patients.

All analyses were conducted using SPSS version 26. The $p$-value < 0.05 was considered statistically significant. When the 95% CI of adjusted OR did not cover the critical value, 1.0, there was sufficient evidence to support the significant difference from the reference.

**Results**

There were 564,181 patients included in the study: 522,702 (92.6%) NHW and 41,479 (7.4%) API patients (Table 1). Compared to NHW patients, the overall API group was significantly more likely to be ≤ 39 years and 40–49 years, more often male, married, diagnosed at stages III and IV, and more likely to have adenocarcinoma histology (all $p$-value < 0.0001).

Within the overall API population, there were 9,860 (23.8%) Chinese, 5,832 (14.1%) Japanese, 10,002 (24.1%) Filipino, 4,178 (10.1%) Hawaiian/Pacific Islander, 2,928 (7.1%) Korean, 4,041 (9.7%) Vietnamese, 1,522 (3.7%) Asian Indian/Pakistani, and 3,116 (7.5%) Other API patients (Table 2). The API ES were significantly different on all variables (all $p$-value < 0.0001). Japanese and Chinese patients were significantly more likely to be diagnosed at age ≥ 80 years compared to other ES (24.1% and 20.9% ≥ 80 years, compared to 8.4–15.2% for other ES), while Asian Indian/Pakistani, Filipino, and Vietnamese patients were the least likely to be female (32.4%, 37.2% and 34.9%, compared to 41.1–47.2% for all other ES). Chinese patients were the most likely to be married (70.4%), while Hawaiian/Pacific Islanders were the least (53.3%). Korean and Hawaiian patients were the most likely to have squamous cell carcinoma (21.8% and 21.4%). While all API ES were more likely to be diagnosed at stage III and IV compared to NHW patients, Vietnamese and Asian Indian/Pakistani patients were the most likely to present at stage IV (49.4% and 47.7%, compared to 42–46.5% for all other ES).

**Demographics**

In the multivariable analysis comparing overall API to NHW patients (Table 3), API patients were less likely to be diagnosed at older age groups, compared to ≤ 39 years. They were also less likely to be female (OR$_{adj}$ 0.85, 95% CI 0.83–0.86). When compared to NHW patients, the API population was significantly less likely to be never or previously married at the time of diagnosis (OR$_{adj}$ [Never Married] 0.71, 95% CI 0.68–0.74; OR$_{adj}$ [Previously Married] 0.60, 95% CI 0.58–0.61).
Associations varied when comparing individual ES to Chinese patients (Table 4). Compared to Chinese patients, Filipino, Hawaiian/Pacific Islander, Vietnamese, Asian Indian/Pakistani, and Other were significantly less likely to be ≥ 80 years at the time of diagnosis (range of effects: ORadj [Asian Indian/Pakistani] 0.11, 95% CI 0.08–0.15 for ≥ 80 vs. ≤ 39 years; ORadj [Filipino] 0.60, 95% CI 0.47–0.77 for ≥ 80 vs. ≤ 39 years). Japanese patients did not follow this trend and were more likely to be diagnosed with lung or bronchial cancer in all older age groups, compared to ≤ 39 years.

Filipino, Hawaiian/Pacific Islander, Vietnamese, and Asian Indian/Pakistani patients were significantly less likely to be female compared to Chinese patients (range of effects: ORadj [Asian Indian/Pakistani] 0.58, 95% CI 0.52–0.67; ORadj [Hawaiian/Pacific Islander] 0.87, 95% CI 0.80–0.94). Korean and Other patients did not have any significant difference in sex compared to Chinese patients, while Japanese patients were more likely to be female (ORadj [Japanese] 1.12, 95% CI 1.04–1.20).

Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Vietnamese, Asian Indian/Pakistani, and Other patients were significantly more likely to be previously married than currently married (range of effects for previously married: ORadj [Asian Indian/Pakistani] 1.17, 95% CI 1.002–1.37; ORadj [Hawaiian/Pacific Islander] 2.95, 95% CI 2.69–3.24). Japanese, Hawaiian/Pacific Islander, Korean, Vietnamese, and Other patients were also more likely than Chinese patients to be never married. Asian Indian/Pakistani patients were significantly less likely to be never married (ORadj [Asian Indian/Pakistani] 0.76, 95% CI 0.61–0.95).

### Clinicopathologic characteristics

Overall, API patients were significantly more likely to be diagnosed at stages III and IV compared to NHW patients.
Table 2  Demographics of Asian/Pacific Islander patients diagnosed with lung or bronchial cancer ($n = 564,181$)

| Variable                  | Chinese ($n = 9,860$) | Japanese ($n = 5,832$) | Filipino ($n = 10,002$) | Hawaiian/Pacific Islander ($n = 4,178$) | Korean ($n = 2,928$) | Vietnamese ($n = 4,001$) | Asian Indian/Pakistani ($n = 1,522$) | Other ($n = 3,116$) | $p$-value |
|---------------------------|------------------------|------------------------|--------------------------|-----------------------------------------|----------------------|--------------------------|-------------------------------------|-------------------|-----------|
| Age (years)               |                        |                        |                          |                                          |                      |                          |                                     |                   |           |
| ≤ 39                      | 146 (1.5)              | 31 (0.5)               | 134 (1.3)                | 59 (1.4)                                | 32 (1.1)             | 109 (2.7)                | 65 (4.3)                            | 80 (2.6)          | <0.0001   |
| 40–49                     | 536 (5.4)              | 135 (2.3)              | 505 (5.0)                | 322 (7.7)                               | 160 (5.5)            | 370 (9.2)                | 123 (8.1)                           | 232 (7.4)         |           |
| 50–59                     | 1,442 (14.6)           | 540 (9.3)              | 1,656 (16.6)             | 937 (22.4)                              | 462 (15.8)           | 826 (20.4)               | 273 (17.9)                          | 589 (18.9)        |           |
| 60–69                     | 2,457 (24.9)           | 1,453 (24.9)           | 3,203 (32.0)             | 1,392 (33.3)                            | 898 (30.7)           | 1,162 (28.8)             | 464 (30.5)                          | 829 (26.6)        |           |
| 70–79                     | 3,217 (32.6)           | 2,268 (38.9)           | 3,146 (31.5)             | 1,116 (26.7)                            | 930 (31.8)           | 1,091 (27.0)             | 454 (29.8)                          | 914 (29.3)        |           |
| ≥ 80                      | 2,062 (20.9)           | 1,405 (24.1)           | 1,358 (13.6)             | 352 (8.4)                               | 446 (15.2)           | 483 (12.0)               | 143 (9.4)                           | 472 (15.1)        |           |
| Sex                       |                        |                        |                          |                                          |                      |                          |                                     |                   |           |
| Male                      | 5,622 (57.0)           | 3,234 (55.5)           | 6,286 (62.8)             | 2,451 (58.7)                            | 1,724 (58.9)         | 2,629 (65.1)             | 1,029 (67.6)                        | 1,646 (52.8)      | <0.0001   |
| Female                    | 4,238 (43.0)           | 2,598 (44.5)           | 3,716 (37.2)             | 1,727 (41.3)                            | 1,204 (41.1)         | 1,412 (34.9)             | 493 (32.4)                          | 1,470 (47.2)      |           |
| Marital status            |                        |                        |                          |                                          |                      |                          |                                     |                   |           |
| Married/domestic partner  | 6,944 (70.4)           | 3,477 (59.6)           | 6,924 (69.2)             | 2,225 (53.3)                            | 1,995 (68.1)         | 2,763 (68.4)             | 1,120 (73.6)                        | 1,953 (62.7)      | <0.0001   |
| Never married             | 724 (7.3)              | 604 (10.4)             | 728 (7.3)                | 533 (12.8)                              | 256 (8.7)            | 452 (11.2)               | 104 (6.8)                           | 362 (11.6)        |           |
| Previously married        | 1,911 (19.4)           | 1,612 (27.6)           | 2,102 (21.0)             | 1,281 (30.7)                            | 583 (19.9)           | 690 (17.1)               | 241 (15.8)                          | 685 (22.0)        |           |
| Unknown                   | 281 (2.8)              | 139 (2.4)              | 248 (2.5)                | 139 (3.3)                               | 94 (3.2)             | 136 (3.4)                | 57 (3.7)                            | 116 (3.7)         |           |
| TNM stage                 |                        |                        |                          |                                          |                      |                          |                                     |                   |           |
| I                         | 1,501 (15.2)           | 934 (16.0)             | 1,484 (14.8)             | 579 (13.9)                              | 440 (15.0)           | 629 (15.6)               | 261 (17.1)                          | 520 (16.7)        | <0.0001   |
| II                        | 302 (3.1)              | 229 (3.9)              | 332 (3.3)                | 125 (3.0)                               | 108 (3.7)            | 120 (3.0)                | 44 (2.9)                            | 106 (3.4)         |           |
| III                       | 2,490 (25.3)           | 1,627 (27.9)           | 2,575 (25.7)             | 1,185 (28.4)                            | 805 (27.5)           | 976 (24.2)               | 351 (23.1)                          | 749 (24.0)        |           |
| IV                        | 4,491 (45.5)           | 2,447 (42.0)           | 4,673 (46.7)             | 1,870 (44.8)                            | 1,253 (42.8)         | 1,998 (49.4)             | 726 (47.7)                          | 1,148 (46.5)      |           |
| Unknown                   | 1,076 (10.9)           | 595 (10.2)             | 938 (9.4)                | 419 (10.0)                              | 322 (11.0)           | 318 (7.9)                | 140 (9.2)                           | 293 (9.4)         |           |
| Histology                 |                        |                        |                          |                                          |                      |                          |                                     |                   |           |
| Adenocarcinoma            | 5,737 (58.2)           | 2,580 (44.2)           | 5,415 (54.1)             | 1,727 (41.3)                            | 1,374 (46.9)         | 2,452 (60.7)             | 834 (54.8)                          | 1,803 (57.9)      | <0.0001   |
| Squamous cell             | 1,295 (13.1)           | 1,187 (20.4)           | 1,657 (16.6)             | 893 (21.4)                              | 638 (21.8)           | 504 (12.5)               | 240 (15.8)                          | 421 (13.5)        |           |
| Large cell                | 986 (10.0)             | 643 (11.0)             | 862 (8.6)                | 450 (10.8)                              | 237 (8.1)            | 281 (7.0)                | 85 (5.6)                            | 215 (6.9)         |           |
| Other specified malignant carcinoma | 238 (2.4) | 158 (2.7) | 255 (2.5) | 112 (2.7) | 63 (2.2) | 98 (2.4) | 78 (5.1) | 96 (3.1) |           |
| Non-small cell, NOS       | 911 (9.2)              | 513 (8.8)              | 894 (8.9)                | 370 (8.9)                               | 231 (7.9)            | 428 (10.6)               | 143 (9.4)                           | 315 (10.1)        |           |
| Small cell                | 693 (7.0)              | 751 (12.9)             | 919 (9.2)                | 626 (15.0)                              | 385 (13.1)           | 278 (6.9)                | 142 (9.3)                           | 266 (8.5)         |           |
(ORadj 1.31, 95% CI 1.27–1.36 for stage III vs. stage I; ORadj 1.31, 95% CI 1.27–1.35 for stage IV vs. stage I) (Table 3). They were also more likely to be diagnosed with adenocarcinoma and less likely to present with a histology of squamous cell, small cell, or large cell carcinoma (compared to adenocarcinoma: ORadj[squamous] 0.54, 95% CI 0.52–0.56; ORadj[small cell] 0.40, 95% CI 0.39–0.41; ORadj[large cell] 0.71, 95% CI 0.69–0.74).

These associations varied when examining API ES (Table 4). Japanese, Asian Indian/Pakistani, and Other patients were significantly less likely to be diagnosed at stage IV compared to Chinese patients (range of effects for stage IV vs. I: ORadj[Asian Indian/Pakistani] 0.83, 95% CI 0.71–0.98; ORadj[Other] 0.87, 95% CI 0.77–0.98). Asian Indian/Pakistani patients were also less likely to present with stage III disease in comparison to Chinese patients (stage III vs. I: ORadj 0.81, 95% CI 0.68–0.97). Filipino, Hawaiian/Pacific Islander, Korean, and Vietnamese did not significantly differ from Chinese patients in terms of stage at diagnosis.

Among API ES, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Asian Indian/Pakistani, and Other were significantly more likely than Chinese patients to present with squamous and small cell histology, compared to adenocarcinoma (range of effects for squamous cell carcinoma: ORadj[Other] 1.24, 95% CI 1.09–1.41; ORadj[Hawaiian/Pacific Islander] 2.47, 95% CI 2.22–2.75; range of effects for small cell carcinoma: ORadj[Filipino] 1.36, 95% CI 1.22–1.52; ORadj[Hawaiian/Pacific Islander] 3.01, 95% CI 2.65–3.42). Japanese and Hawaiian/Pacific Islander patients were more likely to present with a histology of large cell carcinoma (range of effects for large cell carcinoma: ORadj[Japanese] 1.23, 95% CI 1.10–1.38; ORadj[Hawaiian/Pacific Islander] 1.52, 95% CI 1.33–1.74). For Vietnamese patients, there was no significant difference in histology compared to Chinese patients. A sensitivity analysis conducted on the subset of patients with complete staging information had similar results for all variables (data not shown).

A sensitivity analysis of patients from registries available for the full timeframe stratified by five sub-time periods was conducted to examine changes in the observed associations over time (Tables S1–S8). API patients became a larger proportion of lung cancer patients over time (Table S1). API patients continue to be significantly more likely to be diagnosed at stages III and IV compared to NHW patients (Table S2). However, there was variation in the odds ratios of diagnosis at stage III and IV compared to stage I over the five sub-periods (ORadj[Stage III] 1.58, 95% CI 1.40–1.78 and ORadj[Stage IV] 1.40, 95% CI 1.25–1.58 in 1990–1994; ORadj[Stage III] 1.31, 95% CI 1.25–1.58 in 2010–2015). The major change for histology was in the odds ratio of NSCLC, NOS, compared to adenocarcinoma.

Among API ES, increases were seen over time in the proportion of Filipino (except for 2010–2015), Korean, Vietnamese, Asian Indian/Pakistani, and Other patients (Table S3). Japanese patients were significantly less likely to be diagnosed at stage III and IV compared to Chinese patients (Table S3), although this difference was only significant during 1995–1999 (Table S5). Asian Indian/Pakistani patients were less likely to be diagnosed at stage IV in 1995–2009 (Table S7). In 2010–2015, Korean patients were significantly less likely to be diagnosed at stage IV, while Other API patients were less likely to present with stage III and stage IV disease (Table S8).
Table 4  Adjusted associations of clinical and demographic characteristics with Asian/Pacific Islander ethnic subgroups, compared to Chinese patients ($n=40,269$)

| Variable                        | Japanese | Filipino | Hawaiian/Pacific Islander | Korean | Vietnamese | Asian Indian/Paki-stani | Other |
|---------------------------------|----------|----------|---------------------------|--------|------------|------------------------|-------|
|                                 | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* | Adjusted OR (95% CI)* |
| **Age (years)**                 |          |          |                           |        |            |                        |       |
| ≤ 39                            | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)                 | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)             | 1.00 (Ref) |
| 40–49                           | 1.35 (0.86–2.10) | 1.01 (0.77–1.32) | 1.53 (1.08–2.15)          | 1.35 (0.88–2.07) | 0.92 (0.69–1.22) | 0.49 (0.34–0.70) | 0.83 (0.60–1.14) |
| 50–59                           | 2.00 (1.32–3.03) | 1.16 (0.90–1.48) | 1.54 (1.11–2.13)          | 1.33 (0.89–2.00) | 0.71 (0.55–0.94) | 0.35 (0.25–0.48) | 0.70 (0.52–0.95) |
| 60–69                           | 3.09 (2.05–4.65) | 1.28 (1.00–1.63) | 1.25 (0.90–1.72)          | 1.47 (0.99–2.20) | 0.58 (0.45–0.76) | 0.34 (0.25–0.47) | 0.58 (0.43–0.78) |
| 70–79                           | 3.58 (2.38–5.37) | 0.93 (0.73–1.18) | 0.68 (0.49–0.94)          | 1.11 (0.75–1.66) | 0.42 (0.32–0.54) | 0.24 (0.17–0.33) | 0.47 (0.35–0.64) |
| ≥ 80                            | 3.47 (2.30–5.23) | 0.60 (0.47–0.77) | 0.29 (0.21–0.41)          | 0.81 (0.54–1.21) | 0.26 (0.20–0.35) | 0.11 (0.08–0.15) | 0.33 (0.24–0.45) |
| **Sex**                         |          |          |                           |        |            |                        |       |
| Female vs. male                 | 1.12 (1.04–1.20) | 0.76 (0.71–0.80) | 0.87 (0.80–0.94)          | 1.00 (0.92–1.10) | 0.63 (0.58–0.68) | 0.59 (0.52–0.67) | 1.05 (0.96–1.14) |
| **Marital status**              |          |          |                           |        |            |                        |       |
| Married/domestic partner        | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)                 | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)             | 1.00 (Ref) |
| Never married                   | 1.90 (1.69–2.14) | 1.02 (0.91–1.13) | 2.15 (1.89–2.43)          | 1.21 (1.04–1.41) | 1.41 (1.24–1.60) | 0.76 (0.61–0.95) | 1.54 (1.34–1.77) |
| Previously married              | 1.54 (1.41–1.68) | 1.39 (1.29–1.50) | 2.95 (2.69–3.24)          | 1.19 (1.06–1.33) | 1.28 (1.16–1.42) | 1.17 (1.00–1.37) | 1.44 (1.29–1.61) |
| **TNM stage**                   |          |          |                           |        |            |                        |       |
| I                               | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)                 | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)             | 1.00 (Ref) |
| II                              | 1.17 (0.97–1.42) | 1.01 (0.85–1.20) | 0.84 (0.66–1.06)          | 1.11 (0.86–1.42) | 0.88 (0.70–1.12) | 0.75 (0.53–1.06) | 0.97 (0.76–1.24) |
| III                             | 0.91 (0.82–1.01) | 1.02 (0.93–1.12) | 1.01 (0.89–1.14)          | 1.04 (0.91–1.20) | 0.94 (0.83–1.06) | 0.81 (0.68–0.97) | 0.90 (0.79–1.03) |
| IV                              | 0.85 (0.77–0.94) | 1.01 (0.93–1.10) | 0.90 (0.81–1.02)          | 0.91 (0.80–1.03) | 0.96 (0.85–1.07) | 0.83 (0.71–0.98) | 0.87 (0.77–0.98) |
| Unknown                         | 0.64 (0.56–0.73) | 0.86 (0.77–0.97) | 0.74 (0.63–0.86)          | 1.01 (0.85–1.20) | 0.88 (0.75–1.04) | 0.88 (0.70–1.12) | 1.00 (0.84–1.19) |
| **Histology**                   |          |          |                           |        |            |                        |       |
| Adenocarcinoma                  | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)                 | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref)             | 1.00 (Ref) |
| Squamous                        | 1.93 (1.75–2.12) | 1.33 (1.22–1.45) | 2.47 (2.22–2.75)          | 2.15 (1.91–2.41) | 0.98 (0.87–1.11) | 1.39 (1.18–1.64) | 1.24 (1.09–1.41) |
| Large cell                      | 1.23 (1.10–1.38) | 0.93 (0.83–1.03) | 1.52 (1.33–1.74)          | 1.11 (0.94–1.31) | 0.85 (0.73–0.99) | 0.88 (0.69–1.13) | 1.11 (0.94–1.31) |
| Other specified malignant carcino-ma | 1.68 (1.36–2.08) | 1.11 (0.92–1.33) | 1.54 (1.21–1.95)          | 1.07 (0.80–1.43) | 0.90 (0.71–1.15) | 1.87 (1.42–2.48) | 1.15 (0.89–1.48) |
| Non-small cell, NOS             | 1.29 (1.14–1.46) | 0.96 (0.87–1.07) | 1.45 (1.26–1.67)          | 1.03 (0.88–1.22) | 1.00 (0.88–1.14) | 1.00 (0.82–1.22) | 1.12 (0.96–1.29) |
| Small cell                      | 2.37 (2.11–2.67) | 1.36 (1.22–1.52) | 3.01 (2.65–3.42)          | 2.42 (2.09–2.79) | 1.00 (0.86–1.17) | 1.58 (1.29–1.93) | 1.46 (1.25–1.71) |

*Chinese patients serve as the reference category. Adjusted for all variables listed and year of diagnosis.
Discussion

In this study, using the SEER database, we examined a cohort of 522,702 NHW and 41,479 API lung and bronchial cancer patients across a 26-year period to identify demographic and clinicopathologic differences at the time of diagnosis. While lung and bronchial cancer has been well documented among the overall API population, individual API ethnic subgroups have not been adequately or extensively studied [10]. Despite growing evidence that the API population is highly heterogeneous, API patients from different ethnic subgroups continue to be studied as a single population entity, thus minimizing any differences in cultural diversity, health practices, lifestyle, health behaviors socioeconomic status, and health outcomes [1, 9–12]. With limited precedent, this is one of the few studies that has examined lung and bronchial cancer among the following heterogeneous API ethnic subgroups: Chinese, Japanese, Filipino, Hawaiian/Pacific Islander, Korean, Vietnamese, Asian Indian/Pakistani, and Other [1, 9–12].

Prior literature has demonstrated that the overall API population is younger compared to NHW patients at the time of diagnosis [11, 20, 21]. When API patients were divided according to their ethnic subgroups, this trend was maintained across most ethnicities, but to varying degrees. In particular, Filipino, Hawaiian/Pacific Islander, Vietnamese, and Asian Indian/Pakistani patients were less likely to be ≥80 years at diagnosis, compared to Chinese patients. Trends in age among Japanese patients did not mirror the overall API population. Instead, it was the only ethnic subgroup which was more likely to be diagnosed with lung and bronchial cancer at older age groups. A similarly large study of 849,088 patients with lung cancer from the SEER database showed Hawaiian/Pacific Islander, Vietnamese, and Asian Indian/Pakistani patients had the youngest mean age at diagnosis with Japanese patients having the oldest age at diagnosis [11]. The heterogeneity in age at diagnosis among API patients has significant implications for screening, which has been historically directed toward older patients. In fact, since 2013, United States Preventive Services Task Force (USPSTF) has recommended annual screening with low-dose CT in adults between the ages of 55–80 who had a 30 pack-year smoking history and who currently smoked or had quit within the past 15 years [22]. In 2021, USPSTF further expanded the screening criteria to include adults of ages 50–80 [23]. While this guideline change can increase early detection, API patients may still be more likely to be excluded from early screening strategies.

In addition, our study demonstrated ethnic variations in marital status. This is of particular importance, as this has been previously reported to be a significant predictor of survival among lung cancer patients. While the overall API group was more likely to be married than their NHW counterparts, there was significant variation across all ethnic subgroups. Compared to Chinese patients, Japanese, Hawaiian/Pacific Islander, Korean, and Vietnamese were more likely to be never married. However, Asian Indian/Pakistani patients did not mirror this trend. Rather, it was the only ethnic subgroup that was less likely to be never married. Based on a study of 161,228 small and non-small cell lung cancer patients, compared to unmarried patients, being married and/or widowed at diagnosis were predictors of improved survival at diagnosis, attributed to the benefits of a social support system on health behaviors, access to healthcare, cancer treatment, and overall physical and mental well-being [24]. Taken together, the differences in marital status presented in this study provides insight into potential differences across ethnic subgroups in terms of social support systems, which may subsequently affect survival [24, 25].

The current study also showed that all API patients were more likely than NHW patients to be diagnosed with adenocarcinoma and less likely to present with squamous cell, small cell, or large carcinomas. According to an analysis of lung and bronchial cancer among API patients in California from 1988 to 2003 by Raz et al., API patients, especially those from East and Southeast Asia, have disproportionately higher risk for adenocarcinoma compared to NHW patients despite heterogeneity in the histology among API ES [26]. While the incidence rate of adenocarcinoma among the overall API population is 12.1 per 100,000, the incidence rate is 13.1 among the Chinese, 13.1 among Filipinos, and 17.1 among Vietnamese—the greatest among all API ethnic subgroups [26].

Taken together, the higher burden of adenocarcinoma paired with the younger age at diagnosis among API patients seem to suggest non-smoking-related causes as drivers of lung cancer in this population [29–33]. In fact, the prevalence of smoking among API patients from 2010 to 2013 is 10.9% compared to 24.3% for NHW [34]. The prevalence is especially low among Chinese (7.6%), Asian Indian (7.6%), and Japanese Americans (10.2%) [34]. Koo and Ho have corroborated this, by observing that in Asian populations, a younger age at diagnosis of lung cancer tends to occur...
never-smokers [32]. One possible contributor to these findings might be the higher prevalence of epidermal growth factor (EGFR) mutations observed in the tumors of API patients diagnosed with lung cancer, which has been known an initiator and driver of primarily adenocarcinoma [11, 31, 32, 35–38]. The high rates of adenocarcinoma among Chinese and Vietnamese patients, which was observed in this study, correlates with the high overall EGFR mutation rate in these populations, which is 30.0–50.2% and 40.7–64.2%, respectively [11, 27, 39, 40].

Ultimately, the higher portion of adenocarcinoma among the overall API population with significant heterogeneity in lung and bronchial cancer histology among ethnic subgroups has significant implications for treatment, prognosis, and survival. Overall, the higher portion of adenocarcinoma makes the API population more likely to be eligible to receive tyrosine kinase target therapies as part of their treatment regimen. In fact, in 2012, the National Comprehensive Cancer Network recommended that all patients with non-squamous NSCLC histology undergo EGFR mutations and anaplastic lymphoma kinase (ALK) rearrangement testing in order to determine eligibility for tyrosine kinase inhibitors [41]. While the overall 5-year survival for distant NSCLC is 4.5%, treatment with EGFR inhibitors, such as erlotinib or gefitinib, has been associated with a 5-year survival of 14.6% among patients with EGFR-mutant metastatic lung adenocarcinoma [42]. Despite the survival benefit of tyrosine kinase inhibitors, the significant heterogeneity in NSCLC histology among API ethnic subgroups may exclude a significant portion of patients from being eligible for this therapy. This might be especially true for Japanese, Filipino, Hawaiian/Pacific Islander, Korean, and Asian Indian/Pakistani patients, who are more likely than Chinese to be diagnosed with squamous and large cell histology, compared to adenocarcinoma. Furthermore, Japanese and Hawaiian/Pacific Islander patients were more likely to present with SCLC, which has a lower overall 5-year survival rate of 7% compared to 25% for NSCLC [43]. This discrepancy is partly driven by differences in treatment, since surgery for NSCLC, especially at early stages is highly curative, while SCLC is not generally resectable with treatment primarily driven by chemotherapy and/or radiotherapy. The significant heterogeneity in histology among ethnic subgroups suggests that API patients require highly variable treatment, which in turn differentially impacts prognosis and survival. Our findings reinforce the need for the API population to be viewed in greater detail to ensure that disease-specific treatments are appropriately tailored to them.

We also demonstrated that the overall API population was more likely to present with stage III and IV lung cancer compared to NHW patients. However, across the five sub-periods, there was variation in the odds ratios of API patients being diagnosed with stage III or IV disease, compared to stage I, thus implying that late-stage detection for API patients may have shifted. There was also variation among ethnic subgroups across all five sub-periods in stage III and IV presentation of lung cancer. Taken together, these findings might suggest that current US screening guidelines for lung cancer might not be appropriately detecting early-stage (stage I and II) lung cancer across all subgroups of API patients. As reported by Kumar et al., the National Lung Screening Trial (NLST) screening criteria (screening with low-dose computed tomography (CT) among adults between the ages of 55–74 years with at least 30 pack-year smoking history and are currently smoking or have quit within the past 15 years) are valid among Asian patients despite comprising only 2% of the NLST population [44]. However, broadening of the original NLST screening criteria in both age and smoking history as put forth by the current USPSTF guidelines would not increase screening rates among Asian patients, as a significant portion of lung cancer occurs primarily in never or light smokers [44, 45]. Rather, given the high rates EGFR mutation among API patients, EGFR mutation analysis among never and light smokers can be a better alternative, since it might be as sensitive but more specific compared to CT in diagnosing lung cancer [44].

In conclusion, our study is one of the few large population studies that have examined lung and bronchial cancer among eight major API ethnic subgroups in a 26-year time period from 18 US cancer registries. While prior studies have simply assessed the distribution of demographic and clinicopathologic factors across API ethnic subgroups, this is the only study, based on our literature review, which has assessed the adjusted associations of these factors with race. Our study further reinforces the heterogeneity of the API population with lung and bronchial cancer. While analysis of API ethnic subgroups revealed largely similar trends in clinical and demographic factors, compared to the overall API population, there was significant variability among ethnic subgroups when individually studied. In other words, demographic and clinicopathologic characteristics significantly differ across subgroups and none of the eight API ethnicities completely mirrored the overall API population. Ultimately, these findings indicate that treating API patients as a single population may miss crucial biological, environmental, and behavioral differences. Instead, it may be beneficial to view these subgroups separately when developing strategies for prevention and efficacious treatment.

This study should be interpreted within the context of its limitations. This was a retrospective study using a population-based database that only contained pre-selected demographic and clinicopathologic variables. We did not have available data for smoking status, family history of lung and/or bronchial cancer, occupational exposure to carcinogens, and driver mutations. This information would have provided us with increased insight into these populations.
Furthermore, we did not have any information on their place of birth. It is highly likely that a significant portion of the API population was born and raised outside of the USA. This in turn can possibly affect their cultural, lifestyle, and behavioral practices in comparison to their counterparts who were born and primarily raised in the USA. Future research into these factors, as well as differences in survival among API patients is warranted. Despite limitations, this study contributes to our understanding of the heterogeneity of API patients with lung and bronchial cancer and highlights how opportunities for better treatment and prevention strategies may be missed when these patients are treated as a single group.

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Author contributions Study design and conception: all authors. Collection and assembly of data: PB, NA, and ET. Statistical analysis and interpretation: all authors. Manuscript writing and final approval of manuscript: all authors.

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Data availability Data were obtained from the public and de-identified Surveillance, Epidemiology, and End Results (SEER) database. The SEER*Stat software was used to query the SEER 18 registry for all patients diagnosed with lung or bronchial cancer from 1990 to 2015. All analyses were conducted using SPSS version 26. The study was deemed exempt from institutional review at the Icahn School of Medicine at Mount Sinai.

Declarations

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

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