

A Comparison Study of Clinicopathologic Characteristics of Southern California Asian American Non-small Cell Lung Cancer (NSCLC) Patients by Smoking Status

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Background: We previously reported that Asian ethnicity is a favorable prognostic factor for overall survival (OS) in non-small cell lung cancer (NSCLC) patients independent of smoking status. However, Asian ethnicity represents a diverse and heterogeneous population. In this report, we compared the clinicopathologic characteristics of Asian American NSCLC patient subgroups by smoking status.

Methods: Clinicopathologic characteristics of the five major Asian American NSCLC patient subgroups diagnosed between 1991 and 2005 from three Southern California counties were analyzed. Prognostic factors for OS were evaluated by Cox multivariate analysis.

Results: One thousand one hundred twenty-four NSCLC patients were analyzed: Filipino American (37.0%), Vietnamese American (32.8%), Japanese American (11.8%), Chinese American (11.7%), and Korean American (6.7%). A total of 25.7% of these patients were never smokers. With the exception of Japanese American, most of Asian American were native born. Median age of never smokers was marginally younger than ever smokers (66 years versus 68 years, respectively, $p = 0.0507$). The proportion of never smokers who were women was 72.7% and ranged from the lowest among Korean American women (66.7%) to the highest among Japanese American women (84.2%). Among female patients, Vietnamese American patients had the highest proportion of being never smokers (65.5%). Significantly more never smokers (60.9%) than ever smokers (47.9%) presented with stage 4 disease. There was no statistical significant difference in OS between never smokers and ever smokers (11 versus 10 months; $p = 0.3040$). Tumor-related factors (stage and histologic differentiation) and treatment (surgery and chemotherapy) were independent prognostic factors for survival.

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Conclusions: We found no statistical significant difference in clinicopathologic features or survival outcome between individual Asian American subgroup when analyzed according to smoking status.

Key Words: Non-small cell lung cancer, Asian American, Filipino American, Vietnamese American, Chinese American, Japanese American, Korean American, Never smoker, California Cancer Registry, Prognostic factors.

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Although tobacco-related lung cancer mortality is the number 1 cause of cancer death globally, deaths from lung cancer patients who were never smokers accounts for the seventh most common cancer cause of death globally.¹ Lung cancer in never smokers is commonly adenocarcinoma histology, predominantly occurs in women, presents with advanced stage, harbors mutations in the epidermal growth factor receptor (EGFR) but not *K-ras*, and possesses different mutation profiles in the p53 tumor suppressor gene (transversions in smokers and transitions in never smokers).^{2–4} Lung cancer in never smokers also responds better to chemotherapy and has better survival outcome.^{5–7} There is a remarkable regional variation in the proportion of lung cancer patients who are never smokers. Never smokers with lung cancer are found in greater proportion among Asians, especially Asian women.^{2,3} Lung cancer is the most common cancer cause of mortality for the five most populous Asian American subgroups (Chinese American, Vietnamese American, Filipino American, Japanese American, and Korean American) in the United States.⁸ Lung cancer is also the most common cancer cause of mortality for the same five subgroups in California except for Vietnamese American women.⁹ We have shown that Asian American ethnicity is an independent favorable prognostic factor after factoring in smoking status in a multivariate analysis among non-small cell lung cancer (NSCLC) patients in Southern California.¹⁰ However, Asian Americans are extremely diverse with respect to country of origin, socioeconomic status (SES), time since immigration, language spoken, religion practiced, and many other characteristics that affect health outcome. Studies have shown that different Asian American subgroups in the United States have different cancer burdens, that individual Asian American subgroups should be monitored separately, and that presenting one statistical estimate for Asian Americans does not accurately depict cancer burden of any different Asian subgroup.^{8,9} Further-

more, although Asian American may have lower lung cancer risk when compared with whites, the lung cancer risk is different among different Asian American subgroups.¹¹

In 2007, the U.S. census bureau estimated that California is home to 4.5 million Asian Americans (34% of the total Asian American population in the United States). In this report, we describe and compare clinicopathologic characteristics and survival outcomes of the five most common Asian American NSCLC patient subgroups (Filipino American, Vietnamese American, Japanese American, Chinese American, and Korean American) in three counties of Southern California.

PATIENTS AND METHODS

Population

This is a retrospective data analysis from the Cancer Surveillance Programs of Orange, San Diego, and Imperial counties in Southern California databases covering an area with estimated population of 6.0 million. The five most populous Asian American NSCLC patients in the three counties (Filipino Americans, Vietnamese Americans, Japanese Americans, Chinese Americans, and Korean Americans) who were diagnosed between 1991 and 2005 and had complete follow-up data up to December 2007 were included in the study. Tumor site was abstracted as previously described.¹² American Joint Committee on Cancer (AJCC) stage rather than Surveillance, Epidemiology, and End Results (SEER) summary stage (local, regional, or distant) was assigned to individual patients. For the period 1991–2002, AJCC stage was abstracted from existing AJCC codes and derived from SEER extent of disease codes where tumor, node, metastasis data were missing, as done previously.¹⁰ For patients diagnosed between 2003 and 2005, SEER-AJCC summary staging was used. Demographic data including age, ethnicity, gender, marital status, surgery, radiation, and chemotherapy given during the first course of therapy were abstracted using SEER codes. Ethnicity data and marital status were obtained using California Cancer Registry (CCR) codes. Radiation therapy and surgical techniques were abstracted using SEER codes. Chemotherapy given during the first course of therapy was ascertained using CCR codes. The measurement of SES used in this analysis was a composite measure using CCR and census data as previously described.¹²

Smoking status was abstracted using a customized text mining program in SAS 9.2 (SAS Institute, Inc., Cary, NC) that examines text files of individual patient records as previously described.^{10,13} Patients with any documented history of smoking were classified as “ever smokers.” Patients with documentation of no smoking history were classified as “never smokers.” Patients lacking documented information on smoking history were excluded from this analysis.

Statistical Analyses

Comparisons of demographic, clinical, and pathologic variables were made for NSCLC patients, using Pearson χ^2 statistic for nominal variables and Student *t* test for continuous variables. Univariate survival rate analyses were estimated using the Kaplan-Meier method, with comparisons made between groups by the log-rank test. Cox proportional

hazards modeling using time since diagnosis were performed. All statistical analyses were conducted using SAS 9.2 statistical software (SAS Institute, Inc.). Statistical significance was assumed for a two-tailed *p* value less than 0.05.

Ethical Considerations

This research study was approved by the University of California Irvine Institutional Review Board (2007-6078).

RESULTS

Characteristic of Asian American NSCLC Patients

Between 1991 and 2005, a total of 1124 patients from Southern California were analyzed, comprising the five major Asian American NSCLC patient subgroups having complete follow-up data and known smoking status. Two hundred eighty-nine patients (25.7%) were never smokers. There were 575 patients with unknown smoking status were excluded from the analysis. The distribution of Asian American subgroups among those with unknown smoking status was similar to the distribution of Asian American subgroup with known smoking status reported in this study.

Period of Diagnosis

The proportion of Asian American NSCLC patients who were never smokers increased significantly with time: 16.5% (1991–1995), 25.7% (1996–2000), and 31.2% (2001–2005) ($p_{\text{trend}} < 0.0001$). Among female patients, the proportion of NSCLC patients who were never smokers also increased significantly (37.0%, 48.7%, and 59.5%, respectively, $p_{\text{trend}} = 0.0009$). The proportion of male NSCLC patients who were never smokers also increased, but the trend was not significant (9.1%, 11.7%, and 11.9%, respectively, $p_{\text{trend}} = 0.3598$). The proportion of never smokers within individual Asian American subgroup by period of diagnosis were plotted in Figures 1A (all patients), B (male), and C (female). Among individual Asian American subgroup, the trend of increasing proportion of never smokers was significant for Vietnamese American patients as a whole (16.7%, 22.8%, and 39.7%, respectively, $p_{\text{trend}} < 0.0001$) and for female Vietnamese American patients (40.0%, 46.3%, and 89.1%, respectively, $p_{\text{trend}} < 0.0001$). On the other hand, the proportion of female Filipino American NSCLC patients who were never smokers remained constant throughout the three periods of diagnosis (52.6%, 56.4%, and 54.1%, respectively, $p_{\text{trend}} = 0.9956$).

Age at Diagnosis

The median age of diagnosis of never smokers (66 years) was lower than that of ever smokers (68 years), and the difference was borderline significant ($p = 0.0507$) (Table 1). Female never smokers were significantly younger than female ever smokers (65 versus 69 years, $p = 0.0111$) (Table 1).

Histology

Significantly, more never smokers were diagnosed with adenocarcinoma (59.2%) than ever smokers (41.8%). Similarly, the proportion of bronchioloalveolar carcinoma diagnosed in never smokers was 8.7% compared with 3.4% in ever smokers. The proportion of squamous cell carcinoma

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