Research Article

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Survival following Non–Small Cell Lung Cancer among Asian/Pacific Islander, Latina, and Non-Hispanic White Women Who Have Never Smoked

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Abstract

Background: Lung cancer is the leading cause of cancer death among U.S. Asian/Pacific Islander (API) and Latina women despite low smoking prevalence. This study examined survival patterns following non–small cell lung cancer in a population-based sample of lung cancer cases from the San Francisco Bay Area Lung Cancer Study (SFBALCS).

Methods: Women diagnosed with lung cancer from 1998 to 2003 and 2005 to 2008 and identified through the Greater Bay Area Cancer Registry were telephone-screened for eligibility for the SFBALCS. The screener data were linked to the cancer registry data to determine follow-up. This analysis included 187 non-Hispanic (NH) white, 23 U.S.-born Latina, 32 foreign-born Latina, 30 U.S.-born API, and 190 foreign-born API never-smokers diagnosed with lung cancer and followed through 2008.

Results: All-cause survival was poorer among APIs [HR = 1.7 (95% CI: 1.0–2.8) among U.S.-born APIs and HR = 1.2 (95% CI: 0.9–1.5) among foreign-born APIs] and Latinas [HR = 2.1 (95% CI: 1.2–3.6) among U.S.-born Latinas; HR = 1.4 (95% CI: 0.9–2.3) among foreign-born Latinas] relative to NH whites. These survival differences were not explained by differences in selected sociodemographic or clinical factors.

Conclusions: Further research should focus on factors such as cultural behaviors, access to or attitudes toward health care, and genetic variations as possible explanations for these striking racial/ethnic differences.

Impact: Latina and API female never-smokers diagnosed with lung cancer were up to two times more likely to die than NH whites, highlighting the need for additional research to identify the underlying reasons for the disparities and heightened clinical awareness. *Cancer Epidemiol Biomarkers Prev; 20(3); 545–54. ©2011 AACR.*

Introduction

Lung cancer is the leading cause of cancer death both worldwide (1) and in the United States (US) (2). Among US Asian/Pacific Islander (API) and Latina women, lung cancer is also the leading cause of cancer death; however, this disease burden is particularly striking in light of the fact that more than 80% of API and Latina women have never smoked cigarettes (3). Even though trends in lung cancer incidence are predominantly dictated by patterns of tobacco smoking, there remains a substantial proportion of non–smoking-associated lung cancer that is not attributable to either firsthand or secondhand smoke exposure (4–6). Other possible risk factors for lung cancer include exposure to cooking fumes, radon, arsenic, heavy metals, certain viruses, steroid hormones, and genetic susceptibility, although few of these have been confirmed (4–6). An estimated 20% of lung cancer in U.S. women now occurs among never-smokers (7). However, in Asia, this proportion is as high as 80% (8), and the same may be true of U.S. Asian women (9). The exceptionally high burden of non–smoking-associated lung cancer among U.S. Asian and possibly also Latina women is a health disparity that has received little attention. In particular, few studies of lung cancer survival have paid notice to this sizeable group of patients, in whom survival patterns and clinicopathologic characteristics (6) may differ from those in ever-smokers.

Therefore, given the predominance of lung cancer among Asian and Latina women who have never smoked, we focused this study on better understanding

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the survival patterns in this specific group. Taking advantage of the availability of patient-reported data on smoking status and secondhand smoke exposure, this study examined the impact of demographic and clinical factors on survival patterns following a first primary diagnosis of non–small cell lung cancer (NSCLC) in a population-based sample of lung cancer cases from the San Francisco Bay Area Lung Cancer Study (SFBALCS).

Methods

Cancer cases

Lung cancer cases included in this study were from the SFBALCS, a population-based case–control study for which the original aim was to examine molecular, behavioral, and occupational factors in lung cancer etiology (10). The present study incorporates information from the screening interviews conducted with newly diagnosed lung cancer cases [International Classification of Diseases (ICD)-O-3 C340-C349] living in Alameda, San Francisco, Contra Costa, Santa Clara, or San Mateo counties, diagnosed between September 1998 and March 2003 (phase I) or July 2005 and March 2008 (phase II), and identified through rapid case ascertainment from the Greater Bay Area Cancer Registry, in addition to Alta Bates/Summit Hospital in phase I and Northern California Kaiser Permanente Medical Group in phase II. Because race/ethnicity information is generally not available from pathology records, the primary source for rapid case ascertainment, all cases potentially eligible for the SFBALCS, regardless of race/ethnicity, were contacted by English- and Spanish-speaking interviewers and screened for eligibility on average 4.4 months following diagnosis. For those who were deceased, too ill, or unable to complete the screener, interviewers attempted to conduct the interview with a proxy. The original SFBALCS was approved by the University of California, San Francisco Institutional Review Board (IRB). The present study was approved by the Stanford Medical Center and Cancer Prevention Institute of California IRBs. Informed consent was obtained from the patients.

A total of 8,414 cases from phase I and 4,580 cases from phase II were identified for screening. Of these, 51.5% of females and 48.8% of males completed a screening interview (6,499 cases). Approximately 5% of cases did not complete a screening interview because they were deceased at the time of contact and an interview could not be conducted with a proxy. A total of 788 cases were excluded because they were subsequently determined to be ineligible. Of 2,864 female cases, 504 were never-smokers, defined on the basis of self-reported response to the question: "Have you ever smoked cigarettes, pipes, or cigars?" For the present study, focused on specific ethnic populations, we included only those lifetime nonsmoker women who self-identified as API, Latina, or non-Hispanic (NH) white, for a total of 472 cases. We excluded 1 case with missing month and day of diagnosis and 9 cases diagnosed with small cell lung cancer, for a final sample of 462. We did not include men with lung cancer, as this study specifically focused on women and because of the low proportion of male cases (14% of APIs, 7% of Latinos, and 5% of NH whites) who were never-smokers. Among APIs, 99 (45%) were Chinese, 67 (30.5%) were Filipina, 10 (4.6%) were Japanese, and 44 (20%) were Pacific Islanders or another Asian ethnic group (not specified).

Analytic variables

Patient clinical and sociodemographic factors. Data on patient factors were collected from either the screening interview or the cancer registry. The screening interview included questions on date of birth, place of birth, race/ethnicity, birthplace, and race/ethnicity of mother and father, number of people living in the household, education, usual occupation, health insurance, exposure to household and workplace secondhand smoke, consumption of selected vegetables and fruits, and first-degree family history of lung cancer. Place of birth was used to assign immigrant status as U.S.- or foreign-born. Thirty-eight percent of the screening interviews were conducted with a proxy. Patient and clinical data from the cancer registry included year of diagnosis, age, marital status, residential address at diagnosis, American Joint Committee on Cancer stage 3rd edition (I, II, III, IV, unknown), histologic subtype [bronchioloalveolar carcinoma (BAC), squamous cell, large cell, non-BAC adenocarcinoma, or undifferentiated], first course of treatment (i.e., treatment administered within approximately 4 months following initial diagnosis and including surgical resection, radiation, and chemotherapy), and the hospital that first reported the case to the cancer registry (usually the diagnosing hospital).

Neighborhood and institutional factors. Patients' addresses at diagnosis were geocoded to latitude and longitude for 97.4% of cases; the remaining 2.6% were randomly assigned to a 2000 Census block group value within a ZIP code. Neighborhood socioeconomic status (SES) was then determined using U.S. Census 2000 block group data, as previously described (11). Neighborhood SES was classified into quintiles on the basis of the distribution of the SES index across the state of California and then recategorized into 2 groups because of small sample sizes in the quintiles: lower SES (quintiles 1–4) or high SES (quintile 5).

Hospital utilization data from California's Office of Statewide Health and Policy Development (12) was used to determine the number of beds (as proxy for size) and ownership status of each hospital. We also classified hospitals as teaching or nonteaching on the basis of their affiliation with a university medical school. Using cancer registry data, we computed measures of the percentage of Latino or API cancer patients in each hospital for the same years of diagnoses as the cases in this case series; these characteristics were classified independently of hospital size, ownership status, and teaching status.

Follow-up data. Cancer registry data are routinely linked to death certificate data. Cause of death was ascertained from the underlying cause of death on the death certificate on the basis of ICD-9 (162.2–162.9) or ICD-10 (C34) codes. Survival time was calculated in months from the date of diagnosis to (i) date of death from any cause (for overall survival), (ii) date of last known contact, or (iii) December 31, 2008 (the end of the study period), whichever occurred earliest. Uncoded cause of death was more common in recent years and reflects cancer registry practices in that the patient is known to be deceased, but the cause of death has not been determined because her record could not yet be linked to death records, such as state vital statistics data or the National Death Index. These causes of death could be updated with future linkages. As a result, more recent deaths (and thus, more recent diagnoses) are more likely to be coded as uncoded cause of death and less likely to be coded as lung cancer deaths. For cases diagnosed between 1988 and 2004, 77% of the deaths were due to lung cancer, 18% other causes, and 4.7% not coded. In contrast, for cases diagnosed between 2005 and 2008, 50% were due to lung cancer, 7% other causes, and 43% not coded. Thus, we have focused our analyses on all causes of death.

Statistical analyses

Multivariate Cox proportional hazards models with separate baseline hazards by stage (stage grouped as shown in Table 1) at diagnosis (thereby adjusting for stage by allowing the form of the underlying hazard function to vary by stage) were used to estimate HR and 95% CI for all-cause–specific mortality. The proportional hazards assumption was assessed by visual inspection of the survival curves [log(−log) of the survival distribution function by log(months)] and by tests for time dependency. Because associations with chemotherapy varied over time (i.e., violated the proportional hazards assumption), we included interactions between time and chemotherapy. All statistical tests were 2-sided, with significance assumed for $P < 0.05$, and all analyses were done with SAS software version 9.1.3. Table cells with fewer than 5 cases are not shown to protect patient confidentiality.

Results

Patients who participated in the SFBALCS screener were slightly (not statistically significant) more likely to be U.S.-born than the general population of lung cancer patients in the cancer registry. Among Latinas, 55.4% of the screened cases were U.S.-born compared with 53.8% among the general patient population; among APIs, 20.5% of screened cases were U.S.-born compared with 16.2% of the general patient population. Participating cases were significantly more likely than the general patient population to be diagnosed with early-stage disease but were similar with regard to race/ethnicity and age at diagnosis.

Among all screened lung cancer cases, nearly 70% of API women, 35% of Latina women, and 10% of NH white women with lung cancer were never-smokers. Although we did not analyze data for NH whites by immigration status, in this sample, 18% of NH whites reported to be foreign-born. Never-smoker Latinas and APIs had a higher proportion of deaths due to any cause and deaths due to lung cancer than NH whites (Table 1). Foreign-born Latinas were more likely to have low education and live in lower SES neighborhoods. Latinas were more likely than other racial/ethnic groups to be never married. Foreign-born Latinas and foreign-born APIs were more likely to have only public health insurance and to report no first-degree family history of cancer. None of the examined tumor characteristics were significantly different among the groups. Foreign-born Latinas and foreign-born APIs were more likely to have been diagnosed in a public hospital, whereas U.S.-born APIs were more likely than all other groups to have been diagnosed in a teaching hospital. Two-year survival rates were higher among NH whites (56.6%) than Latinas and APIs, comparable between U.S.-born (37.7%) and foreign-born Latinas (38.6%), and higher among foreign-born (47.4%) than U.S.-born APIs (39.8%). Overall, 70% of the deaths were due to lung cancer as the underlying cause, 12% were due to an unspecified or uncoded cause of death, 6% were due to a noncancer cause, and the remaining 12% were due to a variety of other causes, listed in the footnote of Table 1. The proportion of deaths due to lung cancer was higher among Latinas and Asians relative to NH whites.

Kaplan–Meier curves (Fig. 1) show that for stages I to III, overall survival was consistently better among NH whites, followed by Asians, and then Latinas. For stage IV+ unstaged disease, overall survival over time was similar between NH whites and Asians and poorer among Latinas. Proportional hazards regression shows that overall mortality rates among Latinas and APIs, particularly the U.S.-born, were as much as 2.1 and 1.7 times higher than those among NH white women, after adjusting for other covariates (Table 2). Cases who were separated, divorced, widowed, or of unknown marital status at the time of diagnosis had 1.5-times higher mortality than those who were married. Patients diagnosed with squamous cell carcinoma had 2 times higher mortality than those with large cell, non-BAC adenocarcinoma, or undifferentiated tumors, whereas there were no appreciable differences in mortality between the BAC cases and the large cell/non-BAC adenocarcinoma/undifferentiated cases. Radiation therapy as the first course of treatment was associated with slightly higher mortality, whereas surgery was associated with lower mortality.

Discussion

In California, 87.1% of API women and 83.1% of Latina women have never smoked compared with 56.3% of NH

Table 1. Characteristics of female never-smoker NSCLC NH white, Latina, and API patients diagnosed from 1998 to 2003 and 2005 to 2008, by race/ethnicity and immigration status, SFBALCS ($N = 462$)

Characteristics	NH white ($n = 187$)		Latina				API			
			U.S.-born ($n = 23$)		Foreign-born ($n = 32$)		U.S.-born ($n = 30$)		Foreign-born ($n = 190$)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Year of diagnosis										
1998–2003	119	63.6	10	43.5	26	81.3	23	76.7	126	66.3
2005–2008	68	36.4	13	56.5	6	18.8	7	23.3	64	33.7
Age at diagnosis										
Mean (SD)	70.2	(13.1)	65.6	(11.7)	64.4	(14.6)	70.0	(11.7)	66.7	(13.6)
<70	78	41.7	12	52.2	20	62.5	12	40.0	107	56.3
70+	109	58.3	11	47.8	12	37.5	18	60.0	83	43.7
Education[a]										
≤High school	84	45.2	13	56.5	23	74.2	12	42.9	99	54.1
Some college or more	102	54.8	10	43.5	8	25.8	16	57.1	84	45.9
Unknown/[missing ($n = 11$)]										
Neighborhood SES[b]										
Lower (statewide quintiles 1–4)	67	35.8	9	39.1	25	78.1	9	30.0	104	54.7
High (statewide quintile 5)	120	64.2	14	60.9	7	21.9	21	70.0	86	45.3
Marital status[a]										
Never married	15	8.0	5	21.7	9	28.1	–[d]	–	19	10.0
Married	100	53.5	10	43.5	9	28.1	18	60.0	111	58.4
Sep/div/wid/[unknown ($n = 8$)][c]	72	38.5	8	34.8	14	43.8	10	33.3	60	31.6
Type of health insurance[a]										
Public	20	11.1	–	–	10	38.5	6	20.7	73	43.5
Private	99	54.7	10	43.5	15	57.7	12	41.4	74	44.0
Both	62	34.3	10	43.5	–	–	11	37.9	21	12.5
No insurance/unknown/[missing ($n = 35$)]										
First-degree[e] relative with cancer[a]										
None	70	38.0	10	43.5	22	73.3	12	42.9	106	58.2
Any	114	62.0	13	56.5	8	26.7	16	57.1	76	41.8
Unknown/[missing ($n = 15$)]										
Smoke exposure at home (years with another smoker)[f]										
None	45	24.9	57	22.7	11	37.9	8	29.6	68	39.1
1—20	67	37.0	10	45.4	10	34.4	12	44.4	71	40.8
21+	69	38.1	7	31.8	8	27.6	7	25.9	35	20.1
Unknown/[missing ($n = 29$)]										
Smoke exposure at work[g]										
None	96	61.9	9	50.0	21	77.8	7	33.3	98	64.1
Any	59	38.1	9	50.0	6	22.2	14	66.7	55	36.0
Unknown/[missing ($n = 88$)]										
AJCC stage at diagnosis										
I/II	67	35.8	6	26.1	6	18.8	13	43.3	47	24.7
III	43	23.0	–	–	13	40.6	5	16.7	41	21.6
IV/[unstaged ($n = 19$)]	77	41.2	13	56.5	13	40.6	12	40.0	102	53.7
Histologic subtype										
Large cell/non-BAC adenocarcinoma/undiff	141	75.4	21	91.3	26	81.3	24	80.0	166	87.4
Squamous cell	13	7.0	–	–	–	–	–	–	6	3.2
BAC	33	17.7							18	9.5
Chemotherapy										
None/[unknown ($n = 12$)]	115	61.5	11	47.8	20	62.5	20	66.7	97	51.1

(Continued on the following page)

Table 1. Characteristics of female never-smoker NSCLC NH white, Latina, and API patients diagnosed from 1998 to 2003 and 2005 to 2008, by race/ethnicity and immigration status, SFBALCS (N = 462) (Cont'd)

Characteristics	NH white (n = 187)		Latina				API			
			U.S.-born (n = 23)		Foreign-born (n = 32)		U.S.-born (n = 30)		Foreign-born (n = 190)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Given	72	28.5	12	52.2	12	37.5	10	33.3	93	49.0
Radiation										
None/[unknown (n = 1)]	122	65.2	17	73.9	19	59.4	19	63.3	117	61.6
Given	65	34.8	6	26.1	13	40.6	11	36.7	73	38.4
Surgery to primary site										
None/[unknown (n = 1)]	108	57.8	17	73.9	25	78.1	15	50.0	133	70.0
Done	79	42.3	6	26.1	7	21.9	15	50.0	57	30.0
Hospital ownership[a]										
Public	75	41.4	10	43.5	17	53.1	15	50.0	113	61.1
Private	106	58.6	13	56.5	15	46.9	15	50.0	72	39.0
Missing (n = 11)										
Hospital teaching status[a]										
Nonteaching	164	87.7	–	–	–	–	246	80.0	131	69.0
Teaching	23	12.3					6	20.0	59	31.1
Hospital total beds										
0–299	108	59.7	14	60.9	20	62.5	12.	40.0	72	38.9
300+	73	40.3	9	39.1	12	37.5	18	60.0	113	61.1
Missing (n = 11)										
≥10% cancer patients seen at hospital are Latino[a]										
Yes	63	33.7	13	56.5	22	68.8	13	43.3	100	52.6
No	124	66.3	10	43.5	10	31.3	17	56.7	90	47.4
≥10% cancer patients seen at hospital are API[a]										
Yes	112	59.9	–	–	26	81.3	22	73.3	166	87.4
No	75	40.1			6	18.8	8	26.7	24	12.6
Proxy interview										
No	143	76.5	19	82.6	16	50.0	19	63.3	90	47.4
Yes	44	23.5	–		16	50.0	11	36.7	100	52.6
Mortality										
Deceased	111	59.4	16	69.6	20	62.5	20	66.7	120	63.2
Lung cancer death	76	40.6	11	47.8	17	53.1	17	56.7	88	53.7
Cause of death (% of deaths)										
Lung cancer	76	67.3	11	68.8	17	85.0	17	85.0	88	73.0
Other cancers	18	15.9		31.2	–	15.0	–	15.0	11	9.1
Other cause[h]	–	–	5						6	5.4
Not coded	14	12.4							15	12.5
2-y survival rates	56.6		37.7		38.6		39.8		47.4	
Median follow-up time, mo	18.3		13.5		10.8		16.9		15.6	

[a]$P < 0.01$.
[b]Neighborhood SES derived from census block group residence at diagnosis.
[c]Separated, divorced, widowed, or unknown status at time of interview.
[d]Cells with fewer than 5 cases are not shown.
[e]First-degree includes parents, brothers, sisters, and children related by blood.
[f]Subject was asked "In your lifetime, how many years in total was there at least one smoker [If smoker: other than yourself] living in your household?"
[g]Subject was asked "How many years in total were you exposed to the tobacco smoke of others in your indoor workplace?"
[h]Other causes include myocardial infarction, pulmonary embolism, other lung disorders, pregnancy complications, dementia, pneumonia, pleural effusion, heart disease, and fall.

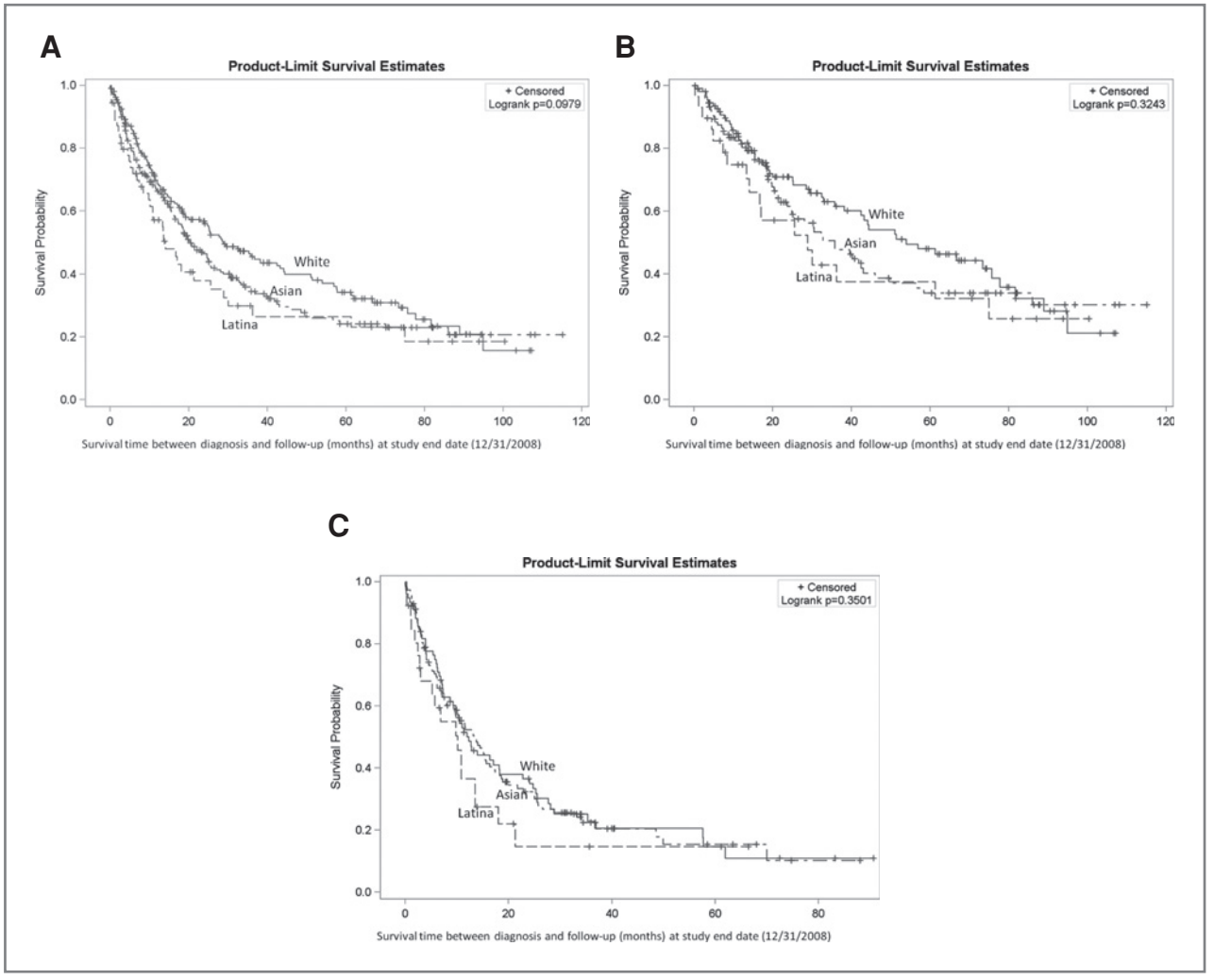

Figure 1. Kaplan–Meier survival curve (all-cause survival) among female never-smoker NSCLC NH white, Latina, and API patients diagnosed from 1998 to 2003 and 2005 to 2008, by race/ethnicity, SFBALCS ($N = 462$). A, all stages combined; B, stages I–III; C, stage IV and unstaged. DX, diagnosis.

white and 65.9% of NH black women (13). It has previously been documented that risks of lung cancer by level of smoking are modified by race/ethnicity (14). We found substantially poorer lung cancer–specific survival among APIs and Latinas, particularly among the U.S.-born, than among NH white women. These survival disparities were not explained by differences in selected sociodemographic or clinical factors, indicating that unmeasured factors associated with race/ethnicity and immigration status, such as cultural behaviors, access to or attitudes toward health care, genetic variation, and/or treatment response, may in part explain these striking differences.

Few studies have examined survival following a diagnosis of lung cancer among Latina women who have never smoked. The slight survival advantage among foreign-born compared with U.S.-born Latina women is consistent with other studies of cancer mortality (15, 16) and may reflect the "Latino paradox" (17–19), which refers to better health among immigrants despite their being of lower SES. The better survival in foreign-born Latinos could be a result of underascertainment of deaths or loss to follow-up when foreign-born Latinos with cancer return to their native countries and die there. However, prior studies have shown that although the migratory effect may exist to some extent, its magnitude is too small to explain the mortality paradox (20, 21). In our data, loss to follow-up was not significantly different between U.S.- and foreign-born Latinas, suggesting that emigration does not explain our results. Alternatively, this paradox could be due to a true health advantage among Latinos in general due to more favorable health behaviors, use of traditional medicines, and greater extended family support, or it could reflect selective migration of healthier individuals to the United States. The relative importance of these factors would be worth

Table 2. Multivariate HR with 95% CI for associations with overall mortality rates after NSCLC diagnosis in Hispanic and API women never-smokers, 1988 to 2003 and 2005 to 2008, with follow-up through 2008

Characteristic	HR (overall)	95% CI
Age at diagnosis (single year)	1.01	1.00–1.02
Race/ethnicity		
NH white	1.00	
Latina U.S.-born	2.05	1.18–3.55
Latina foreign-born	1.41	0.85–2.33
API U.S.-born	1.69	1.01–2.75
API foreign-born	1.17	0.89–1.54
Marital status		
Married (at diagnosis)	1.00	
Never married	0.83	0.53–1.27
Separated/divorced/ widowed/unknown	1.54	1.17–2.02
Histology		
Large cell/non-BAC adenocarcinoma/undiff	1.00	
BAC	0.72	0.45–1.14
Squamous cell	2.05	1.29–3.26
Radiation		
Not given	1.00	
Given	1.48	1.13–1.92
Surgery		
None	1.00	
Done	0.30	0.20–0.44

NOTE: HRs adjusted for other factors shown in the table including chemotherapy-by-time interaction; separate baseline hazards were estimated by stage at diagnosis (thereby adjusting for stage by allowing the form of the underlying hazard function to vary by stage).

evaluating further with regard to lung cancer survival among Latinas.

Our results for APIs are contrary to those from southern California cancer registry data, showing that survival after NSCLC was better among Asian males and females than other racial/ethnic groups, regardless of smoking status (9, 22, 23). The discrepant findings may be due to gender differences and/or population differences between southern and northern California, as it is known that Asian settlement patterns differ across regions within California (24). For instance, although Chinese comprised 45% of our population, they comprised only 15% of the female never-smoker population in the southern California analysis (25). The differences in findings may also be due to methodologic differences. In the prior analyses, smoking status was inferred on the basis of a text-mining program that abstracted patients' medical record information (9, 22, 23) and nearly 30% of patients were excluded because smoking status could not be determined (9). In contrast, smoking status in our study was based on self-report, which corresponds well with cotinine levels in most populations (26–31), whereas medical records can be inaccurate or lacking in any smoking information at all (32, 33). In the southern California study, the proportions of women with NSCLC who had never smoked were approximately 15% among all races/ethnicities and 55% among Asians. The former proportion is slightly lower than the 20% that we recently documented (7), and the latter proportion is considerably lower than the 70% of API never-smokers in the SFBALCS. These discrepancies suggest that never-smokers may have been disproportionately excluded from the southern California analyses because of missing smoking data in the medical record. Although the survival benefit among Asians relative to NH whites found in the southern California study was independent of smoking status (25), there was likely differential exclusion of Asian never-smokers. It is perhaps more likely that the differences between the two studies are due to the population differences noted earlier and to effect modification by gender, as our effects were noted only among women, who were not evaluated separately in the southern California study. It is worth noting that the method for follow-up was the same in both studies.

Our study revealed other interesting associations with survival after NSCLC among female never-smokers. Consistent with prior findings in lung (9, 34) and other cancers (35, 36), higher mortality was evident for patients who were widowed, divorced, or separated than for those who were married, even with adjustment for age, indicating that greater spousal social support improves survival. We also observed that first-course radiation therapy was associated with slightly higher mortality, whereas surgery was associated with lower mortality; however, given the known limitations with cancer registry data on treatment, these patterns are likely reflective of residual confounding due to extent of disease.

Regardless of therapy, NSCLC patients who are never-smokers seem to have a small survival benefit compared with those with a smoking history (6), although this pattern is not confirmed in all studies (37). The studies that show better survival among never-smokers may be reflective of a greater number of comorbidities among patients with a history of smoking. In addition, for advanced stage NSCLC, some studies have shown a clear difference in chemotherapy response between smokers and nonsmokers (38), although others have not (39). Clinically important differences in treatment response are seen with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (erlotinib, gefitinib). Higher treatment response rates and better survival have been reported in never-smokers with these drugs than in ever-smokers (40–42). It is likely, however, that never-smoking status is a surrogate for EGFR-activating mutations, as indicated by the results from the IPASS and First-SIGNAL trials of

first-line gefitinib versus chemotherapy for never-smoking Asian patients with advanced stage NSCLC (43, 44). In both studies, only patients with EGFR-activating mutations had a progression-free survival benefit. However, as these are relatively new drug regimens, it is unlikely that they would impact the results seen in our study on the basis of cases diagnosed from 1998 through 2008. Asian race/ethnicity has also been shown to be associated with better survival following NSCLC (45, 46), even adjusted for smoking status and gender (46). However, survival differences across racial/ethnic groups may be modified by smoking status and/or gender, as suggested by our results, which are discordant with those reported from the National Cancer Institute of Canada Clinical Trials Study Group BR.21 (46).

This study has its strengths in being population-based and in its availability of patient-level variables, such as self-reported smoking status and secondhand smoke exposure. The major limitation in this study is the limited sample size, especially after stratification by race/ethnicity and immigrant status, and thus the results should be interpreted with caution. As a result, we were not able to examine survival patterns for detailed API or Latina ethnic groups, which have documented differences in lung cancer survival (45). Self-reported smoking status may be misclassified, possibly to a slightly higher extent among racial/ethnic minorities (47) and among proxy reports (although, in the literature, minorities are not consistently more likely to be misclassified on smoking status than NH whites; refs. 48–50). Even though patients in this study were identified through rapid case ascertainment, patients sometimes were deceased or too ill to participate by the time they were contacted for this study; this is affirmed by the fact that participating patients were more likely to have early-stage disease than the general patient population. The screening interview was conducted in English or Spanish only, therefore possibly restricting participation for subjects who speak a different language; however, participating APIs and Latinas were not significantly more likely to be U.S.-born than the registry patient population. The findings for race/ethnicity may also be impacted by our inability to fully adjust for treatment (51). Our study may also be limited by possible biases in loss to follow-up, such that certain patients, particularly foreign-born APIs and Latinas, may have been more likely to return to their countries of origin upon learning of their serious illness (19, 52, 53). This effect would result in underestimation of the HRs for foreign-born APIs and Latinas. We could not evaluate lung cancer–specific mortality because of how cause of death is coded in the cancer registries. However, given the rapid fatality of this disease and that of deaths of known causes of death, nearly 80% of deaths are due to lung cancer as the underlying cause, it is likely that the racial/ethnic and nativity results will be similar for lung cancer–specific mortality.

In summary, this study identified disparities in survival among API and Latina women never-smokers who have been diagnosed with lung cancer, particularly those who were born in the United States. These disparities present public health and clinical issues of concern, given the large and growing population of never-smokers who present with lung cancer in these racial/ethnic groups. These results highlight the need for additional research to identify the underlying reasons for the disparities and heightened clinical awareness.

Disclosure of Potential Conflicts of Interest

The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California, Department of Health Services, the National Cancer Institute, and the Centers for Disease Control and Prevention or their contractors and subcontractors is not intended, nor should be inferred.

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