Trends and Disparities in Incidence and Survival Outcomes for Lung Neuroendocrine Tumors in California

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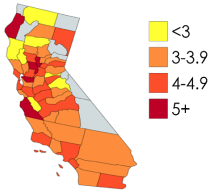
Introduction

- Typical and atypical lung neuroendocrine tumors (NETs) are a relatively rare, heterogeneous group of cancers with a wide spectrum of clinical behavior and limited data regarding risk factors.
- Similar to other primary NET sites, the incidence of lung NETs appears to have increased over the last 40 years.[1-3]
- Rising incidence contrasts with the declining incidence of non-small cell and small cell lung carcinomas, which are largely smoking related, and suggests distinct underlying risk factors.[4]
- Little is known about the epidemiology of lung NETs and whether there are differences in incidence or survival by sex, race/ethnicity, and residence in rural vs urban areas.
- Our group has previously demonstrated substantial geographic variation in the incidence of gastroenteropancreatic (GEP)-NETs in California **(Figure 1)**; unknown if similar variation exists for lung NETs.

Figure1 : Age-adjusted incidence rates of GEP-NETs in CA, 2011-2015



Objectives

- To characterize the burden of lung NETs (typical or atypical histology) in California.
- To compare incidence (**Aim 1**) and overall survival (**Aim 2**) of lung NETs in California and evaluate for differences by patient sociodemographic and geographic characteristics, along with tumor characteristics, year of diagnosis, and first treatment.

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Research methods

Overall study design:

- Observational, population-based study of adults living in California with an incident diagnosis of a lung NET in the California Cancer Registry (CCR).
- CCR is a uniquely rich data source encompassing nearly all cancer diagnoses within the state in California.
- California is a large, diverse state that is well-suited to answer questions about disparities.

Aim 1: Incidence

Study population:

- Californians age ≥18 years with a new diagnosis of a lung NET from 1992-2017 based on ICD-O-3 codes for histology (typical and atypical NETs) and ICD-10 primary site of lung or bronchus.
- Patients without microscopic confirmation of their disease will be excluded, as will those diagnosed at autopsy or via death certificate only.
- We will also exclude people with high-grade histology (small cell or large cell neuroendocrine carcinoma of the lung) because these represent biologically distinct diseases.

Primary predictors:

- We will analyze existing data from the CCR on 1) sex; 2) race/ethnicity coded per NIH standards; and 3) county of residence, classified as rural versus urban versus suburban for cases of lung NETs.

Outcomes:

- Age-adjusted incidence rates of lung NETs standardized to 2000 United States census population

Statistical methods:

- We will compare AIRs by sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and Asian/Pacific Islander, Native American), and county of residence (categorized as urban, suburban, or rural based on the majority of census tracts) using SEER*Stat and generate age-adjusted IR ratios (IRR).
- To evaluate changes in incidence over time, we will calculate annual percentage change in AIRs using Joinpoint regression.

Research methods, cont.

Aim 2: Overall Survival

Study population:

- Californians age ≥18 years in the CCR with an incident diagnosis of a lung NET from 1992-2017 with a minimum survival follow up of one year.

Predictors:

- 1) Sex; 2) race/ethnicity; 3) county of residence, classified as rural, suburban, or urban; 4) socioeconomic status; and 5) year of diagnosis.

Outcomes:

- All-cause mortality is the primary endpoint for Aim 2. The CCR follows patients until confirmation of their death using linkages to state and national vital statistics databases.
- Cancer site-specific mortality is a secondary endpoint, with the underlying cause of death determined by ICD9/10 codes from death certificates.

Statistical methods:

- Time-to-event survival analysis will be estimated by the Kaplan-Meier method and compared among subgroups by the log-rank test.
- We will use multivariable Cox proportional hazard regression to determine the relative effect of our predictor variables of interest (race/ethnicity, sex, rural vs urban residence, SES, diagnosis year) on both all-cause and lung cancer-specific mortality.
- Models will be adjusted sequentially for possible mediators/confounders including tumor and patient characteristics, neighborhood-level characteristics, first treatment, and diagnosis year.

Preliminary results

- California Department of Public Health has approved the study through their IRB.
- Secure file transfer completed to provide UCSF access to CCR data.
- Data cleaning and descriptive analyses of the study population are ongoing; preliminary demographics of study population in **Table 1.**
- Next steps: complete incidence and survival analyses.
- Long-term goal: identify opportunities to improve care for at-risk groups.

Preliminary results, cont.

Table 1. Demographics of lung NETs in CA from 1992-2017

	Lung NETs	CA 2010
N	5,201	37,334,079
Age at diagnosis, median [IQR]	64 [53, 73]	33 [19,50]
Female, N (%)	3,623 (69.7%)	50.3%
Year of diagnosis		
1992-1999	1,137	
2000-2009	1,972	
2010-2017	2,092	
Race/Ethnicity, N (%)		
NH White	3,852 (74.1%)	37%
NH Black	279 (5.4%)	6%
Hispanic	801 (15.4%)	39%
Asian/Pacific Islander	216 (4.2%)	15%
Native American	25 (0.5%)	1%
Unknown	28 (0.5%)	4%
County Type, N (%)		
Urban	3,700 (71.1%)	73%
Suburban	1,363 (26.2%)	25%
Rural	138 (2.7%)	2%
Marital status, N (%)		
Partnered (married or domestic)	2,953 (56.8%)	
Single (never married, separated, divorced, widowed)	2,101 (40.4%)	
Unknown	147 (2.8%)	
Stage, N (%)		
Localized	3,462 (66.6%)	
Regional	923 (17.8%)	
Distant	629 (12.1%)	
Missing or unknown	187 (3.6%)	
Histology code, N (%)		
8150 (islet cell tumor)	1 (0.02%)	
8240 (typical carcinoid)	4,844 (93.1%)	
8245 (tubular carcinoid)	13 (0.2%)	
8249 (atypical carcinoid)	343 (6.6%)	

*California 2010 census population is provided for reference. CA=California, NH=non-Hispanic

References

1. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, Abdalla EK, Fleming JB, Vauthey JN, Rashid A, Evans DB. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 2008;26:3063-72.
2. Dasari A, Shen C, Halperin D, Zhao B, Zhou S, Xu Y, Shih T, Yao JC. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. *JAMA Oncol* 2017;3:1335-42.
3. Broder MS, Cai B, Chang E, Neary MP. Incidence and prevalence of neuroendocrine tumors of the lung: analysis of a US commercial insurance claims database. *BMC Pulm Med* 2018;18:135
4. Govindan R, Page N, Morgensztern D, Read W, Tierney R, Vlahiotis A, Spitznagel EL, Piccirillo J. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. *J Clin Oncol* 2006;24:4539-44.

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