Introduction

- Well-differentiated lung neuroendocrine tumors (NETs) are a heterogeneous group of cancers with varying clinical behavior.
- Little is known about the epidemiology of lung NETs or predictors of survival beyond disease-related factors like histology (typical vs atypical) and stage.
- We investigated associations between sociodemographic, clinicopathologic, geographic, and treatment factors with survival for patients with lung NETs in the diverse state of California.

- CCR is a uniquely complete data source encompassing nearly all cancer diagnoses within the state.

Objectives

- To compare overall survival of patients with lung NETs in California and evaluate for survival differences by sociodemographic and geographic characteristics, along with clinicopathologic and treatment factors.

Research methods

Study Design

- Population-based, prospective study of Californians with an incident diagnosis of a lung NET in the California Cancer Registry (CCR).

Study population:

- Californians age ≥18 years in the CCR with an incident diagnosis of a lung NET (typical or atypical histology) from 1992-2017.
- Cases selected based on ICD-0-3 codes for typical carcinoid (8240) or atypical carcinoid (8249) histology with an ICD-10 primary code of bronchus or lung.

- Poorly-differentiated histologies (small or large cell neuroendocrine carcinomas) were excluded.

Covariates:

1. sex; 2. race/ethnicity; 3. county of residence, classified as rural, suburban, or urban; 4. neighborhood sociodemographic status (nSES); 5. marital status; 6. year of diagnosis; 7. first course of treatment within 12 months of diagnosis; 8. insurance payer (for cases diagnosed after 1995).

Primary Outcomes: All-cause mortality. CCR follows patients until death or last follow-up.

Statistical analyses:

- Patient characteristics were compared by stage at diagnosis using Kruskal-Wallis test for continuous variables or chi-square test for categorical variables.

- We used time-to-event survival analysis by Kaplan-Meier method and compared univariate survival among demographic and disease factors by the log-rank test.

- Sequential multivariable survival analyses were performed using Cox proportional hazard models. Models were adjusted sequentially for possible confounders, including previously published predictors and our sociodemographic variables of interest.

- Because the assumption of proportional hazards was violated for age, Cox models were age-stratified to allow baseline hazards to vary.

Results

Table 1. Demographic and Clinical Characteristics of Lung NET Population in California from 1992-2017 by Stage at Diagnosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Unresectable Disease (n=3,443)</th>
<th>Resectable Disease (n=5,684)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>Median</td>
<td>66 (IQR: 52, 76)</td>
<td>66 (IQR: 52, 76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>1,719 (80.9%)</td>
<td>1,391 (70.4%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diagnosis decade</td>
<td>1992-2000</td>
<td>1,107 (90.9%)</td>
<td>480 (70.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Histology</td>
<td>Typical carcinoid</td>
<td>2,068 (86.4%)</td>
<td>334 (86.4%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>NH White</td>
<td>3,269 (88.8%)</td>
<td>141 (91.7%)</td>
<td>0.005</td>
</tr>
<tr>
<td>nSES</td>
<td>Quartile 1</td>
<td>792 (84.1%)</td>
<td>172 (83.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Insurancea,b</td>
<td>Medicare only</td>
<td>2,116 (89.0%)</td>
<td>408 (89.0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
<td>1,738 (87.8%)</td>
<td>252 (87.8%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Cause Mortality</td>
<td>Cancer</td>
<td>3,269 (88.8%)</td>
<td>141 (91.7%)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Abnormal findings: HR, hazard ratio; CI, confidence interval.

Figure 1. Kaplan-Meier OS Curves by Disease Characteristics

Figure 2. Kaplan-Meier OS Curves by Sociodemographic Variables

Conclusions

- There were sociodemographic differences by stage at diagnosis. Compared with patients with locoregional disease, patients with metastatic disease were older, more likely to be diagnosed in most recent decades, more likely to have atypical carcinoid histology, less likely to be NH White, more likely to come from lowest nSES quartile, and more likely to have insurance.

- Beyond disease-related factors, sociodemographic factors are independently associated with overall survival in lung NETs. Sex, nSES, marital status, age, health insurance, stage, and receipt of surgery, radiation, chemotherapy, and immune treatments were all independently associated with survival. Race/ethnicity was associated with survival in univariate models, but not in multivariable models.

- These results can guide future research into the pathogenesis of lung NETs and help identify opportunities for interventions to reduce survival disparities.