

Familial Lung Cancer: A Comparative Study on Epidemiological

and Clinical Characteristics





Introduction

Incidence Rates and Disparities Lung cancer (LC) remains the leading cause of cancer-related

- mortality globally It is estimated that 226,650 people (110,680 men and 115,970
- women) will be diagnosed and 124,730 will die with lung cancer in 2025 (Siegel et al., 2024; CA Cancer J. Clin. 2025)
- Genome-Wide Association Studies (GWAS) have highlighted ancestral differences in non-small cell lung cancer (NSCLC) risk and survival outcomes exclusive of family history of LC
- African American (AA) men experience higher rates of LC incidence and mortality compared to Caucasian men, whereas AA women experience lower rates compared to Caucasian women
- LC incidence and mortality has significantly declined across all demographic groups in recent decades, though disparities persist

Risk Factors

Family History and Genetic Predisposition

• While smoking is the primary driver for LC, accounting for approximately 85% of LC deaths, family history and inherited risk alleles are independent risk factors

Body Mass Index (BMI)

- Obesity is associated with higher risk and reduced survival probability for certain types of cancer
- However, some studies have shown higher BMI to be favorably associated with increased survival in patients with LC

Histology

- NSCLC constitutes 85% of LC cases, with adenocarcinoma (50%) and squamous cell carcinoma (30%) as the primary subtypes
- Adenocarcinoma is the predominant histology in neversmoker LC cases (50–60%) and in familial LC, and it is often associated with better survival, especially in early stages

Objective and Significance

The goal of the present study is to compare the epidemiological and clinical data of African American and Caucasian patients with family history of lung cancer, and to assess the effects on survival.

Methods

Study participants were recruited from southern Louisiana and Detroit. Patients having at least two family members affected with primary lung cancer were eligible for the study.

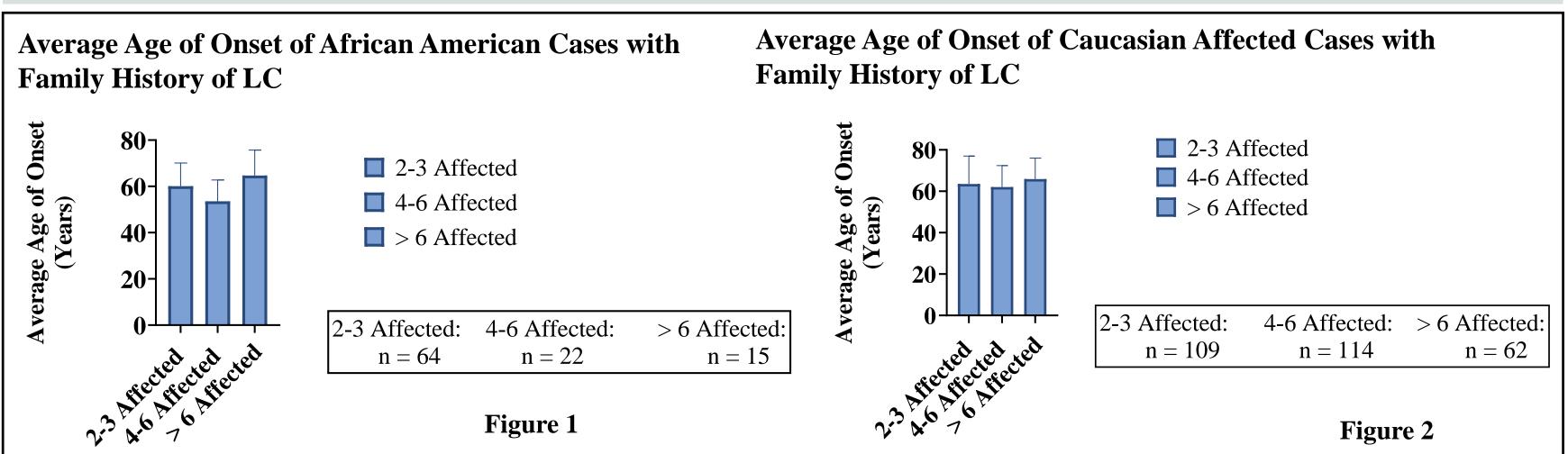
Medical records and pathology reports were used to confirm diagnosis, age of onset, histology, ancestry, sex, smoking history, and BMI. Patient questionnaires were also used.

Data gathered from the medical records, pathology reports, and information supplied by the families were entered into spreadsheets.

A total of 821 familial LC cases (171 AA and 650 Caucasians) were identified and assessed. Among those 821, age of onset was available for 385 individuals; histologic subtype was available for 350 individuals; BMI was available for 102 individuals; and sex at birth was available for 781 individuals.

Associations between ancestry (AA and Caucasian) and risk factors of interest were analyzed using chi-square tests.

Results: Family Data

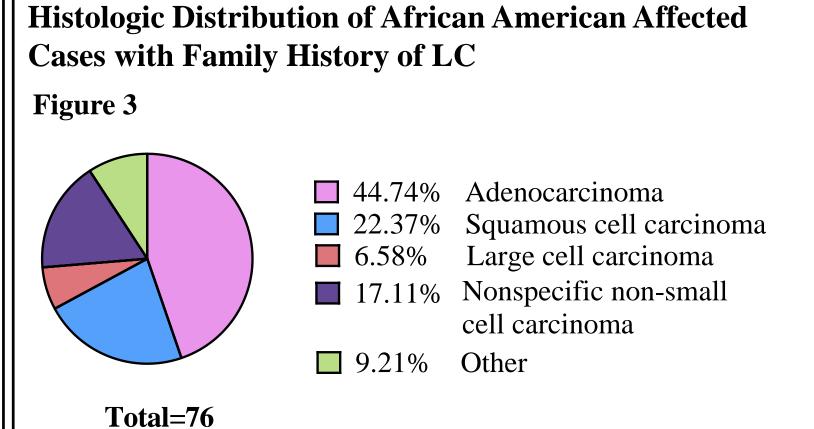


Number of Affected Cases per Family

Number of Affected Cases per Family

Total=274

Figures 1–2. Average age of onset in LC participants of AA and Caucasian ancestry based on number of affected cases in the family The average age for AAs was 60.1, 53.6, and 64.7 years for 2–3, 4–6, >6 affected members per family, respectively. The average age for Caucasians was 63.5, 62.0, and 65.9 years for 2–3, 4–6, and >6 affected members per family, respectively.



Family History of LC Figure 4 49.64% Adenocarcinoma 19.34% Squamous cell carcinoma Large cell carcinoma ■ 6.20% Nonspecific non-small cell carcinoma ■ 19.71% Other

Histologic Distribution of Caucasian Affected Cases with

Figures 3–4. Distribution of histologic subtype based on ancestry for AAs and Caucasians

Results: Survival Analysis

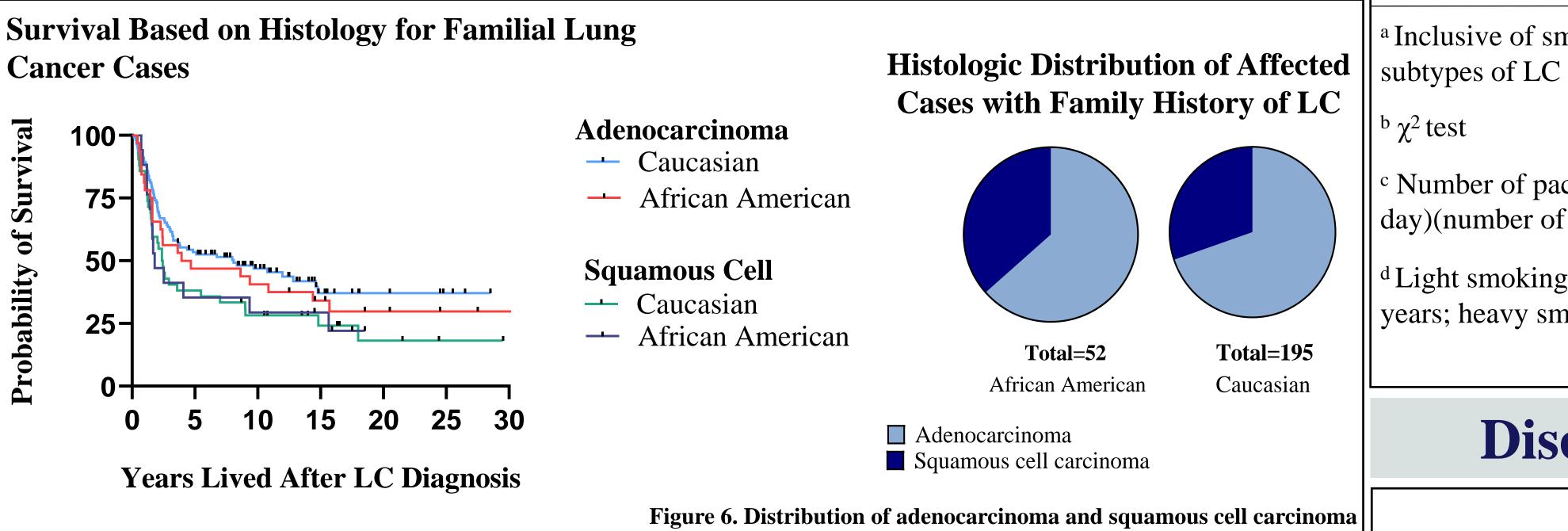


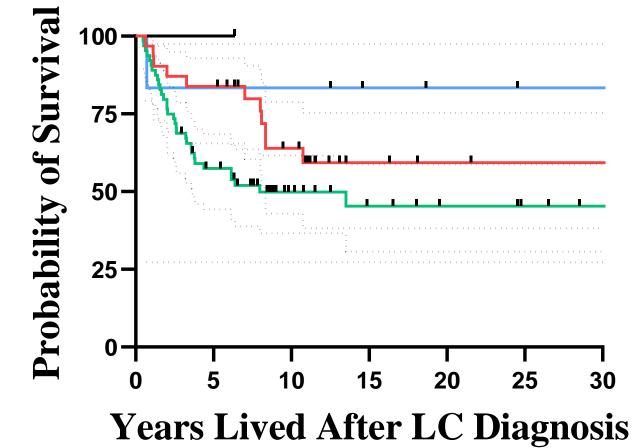
Figure 5. Survival outcomes based on histology for participants of AA and Caucasian ancestry

histologies for participants of AA and Caucasian ancestry For AA participants, 63.46% had adenocarcinoma and 36.54% had squamous cell carcinoma, whereas for Caucasian participants, 69.74% had adenocarcinoma and 30.26% had squamous cell carcinoma.

BMI Distribution of Affected Cases

with Family History of LC

Survival Based on Body Mass Index (BMI) for Familial **Lung Cancer Cases**



Caucasian Overweight and Obese African American Caucasian

Healthy

African American Total=7 Total=95 African American Caucasian Healthy Overweight or Obese **BMI** Ranges *Healthy:* 18.5-24.9 *Overweight:* 25.0-29.9

Figure 7. Survival outcomes based on BMI for participants of AA and Caucasian ancestry

Obese: 30.0 or above Figure 8. Survival outcomes based on BMI for participants of AA and Caucasian ancestry

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Results: Categorical Analysis

Table 1.	Characteristics	of the lung can	cer natients i	n this study

	Ancestry			
	African			
Characteristic	American	Caucasian	P-Value ¹	
Sex				
Male	91 (53.85%)	316 (51.63%)		
Female	78 (46.37%)	296 (48.37%)		
Age of Onset (Years)				
N	101	285		
Mean ± SD	59.4 ± 10.5	63.4 ± 11.7		
Range	39–86	21–91		
< 60	52 (51.49%)	95 (33.45%)	0.00135	
≥ 60	49 (48.51%)	189 (66.55%)		
Smoking Status ^{c,d}			0.064076	
Light	5 (8.77%)	17 (12.23%)		
Moderate	23 (40.35%)	33 (23.74%)		
Heavy	29 (50.88%)	89 (64.03%)		
Histology			0.012226	
Adenocarcinoma	34 (44.74%)	136 (49.64%)		
Squamous cell	17 (22.37%)	53 (19.34%)		
Large cell	5 (6.58%)	14 (5.11%)		
Nonspecific non-small cell	13 (17.11%)	17 (6.20%)		
Othera	7 (9.21%)	54 (19.71%)		

a Inclusive of small cell, oat cell, and other less frequent histological

b χ^2 test

Number of pack years = [(number of cigarettes smoked per day)(number of years smoked)] ÷ 20

Light smoking: < 20 pack years; moderate smoking: 20 to < 40 pack years; heavy smoking: > 40 pack years

Discussion and Conclusion

- African American (AA) familial LC patients had a significantly lower age of onset compared to Caucasians
- Patients with adenocarcinoma exhibited a greater survival rate than patients with squamous cell carcinoma for both ancestral groups
- Caucasian patients with adenocarcinoma showed a noticeably higher survival rate than AAs
- Both overweight—obese AA and Caucasian patients faced a lower probability of survival compared to patients with healthy weight
- Overall, our findings underscore significant racial disparities in the presentation and prognosis of familial LC
- Acknowledging these differences is crucial for developing more targeted screening strategies, improving early detection, and tailoring personalized treatment and surveillance approaches to reduce health disparities in lung cancer care
- The number of AA research participants is limited, and the recruitment of AA LC cases with family history is much needed

Future Directions:

This research highlights the need for continued recruitment of study participants and analysis, particularly concerning ancestry, histological subtypes, and BMI, given the limited data currently available for African Americans with family history of lung cancer