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"Familial Lung Cancer: A Comparative Study on Epidemiological and Clinical Characteristics"

Lung cancer (LC) remains a leading cause of cancer-related mortality globally, with an estimated 226,650 new cases and 124,730 deaths projected for 2025. While smoking is the primary driver (accounting for approximately 85% of LC deaths), family history and genetic predisposition are recognized independent risk factors. Non-small cell lung cancer (NSCLC) constitutes 85% of LC cases, with adenocarcinoma (50%) and squamous cell carcinoma (30%) as primary subtypes. Adenocarcinoma is the predominant histology among never-smokers (50−60%) and in familial LC and is often associated with better survival, especially in early stages. Genome-Wide Association Studies (GWAS) have highlighted ancestral differences in NSCLC risk and survival outcomes. However, the specific epidemiological patterns and clinical characteristics of familial LC, particularly concerning disparities between African Americans (AAs) and Caucasians, remain underexplored. Existing research indicates differential LC incidence and mortality by sex and ancestry: higher rates for AA men than Caucasian men, but lower rates for AA women compared to Caucasian women due to historically lower smoking prevalence among AA women. While significant declines in LC incidence and mortality have occurred across all demographic groups in recent decades, disparities persist. Notably, localized-stage LC diagnosis is less frequent in AAs (24%) than in Caucasians (28%). The role of body mass index (BMI) in LC survival also shows complex ancestry-specific patterns. The goal of the current project is to compare the epidemiological and clinical data of AA and Caucasian patients with a family history of LC, and to evaluate how these factors impact survival.

This retrospective cohort study investigated the distinct epidemiological features, clinical characteristics, and survival outcomes of familial LC patients. A total of 821 familial LC cases (171 AA, 650 Caucasian) recruited from Southern Louisiana and Detroit were assessed. Data on ancestry, sex, smoking history, histology, BMI, and age of onset were collected from medical and pathology reports, as well as patient questionnaires. Statistical analyses, including chi-square tests, were conducted. Our findings revealed that AA familial LC patients had a significantly lower age of onset compared to Caucasians ($p \leq 0.0014$). Further analysis revealed no statistical significance between the two primary subtypes of NSCLC with regard to ancestry; however, significance was observed upon the inclusion of less frequent histological subtypes ($p \leq 0.0122$). Furthermore, while patients with adenocarcinoma exhibited a greater survival rate than patients with squamous cell carcinoma for both ancestral groups, Caucasians with adenocarcinoma showed a noticeably higher survival rate than AAs. Regarding BMI and survival, we found that overweight or obese Caucasian and AA patients faced a lower probability of survival compared to patients with a healthy weight. These results underscore significant disparities in the presentation and prognosis of familial LC patients across the two ancestries. Acknowledging these differences is crucial for developing more targeted screening strategies, improving early detection, and tailoring personalized treatment and surveillance approaches to reduce health inequities in lung cancer care. This research highlights the need for continued analysis, particularly concerning ancestry, histological subtypes, and BMI, given the limited data currently available for African Americans with a family history of lung cancer.