ORIGINAL RESEARCH

43. Survival Factors in Lung Cancer Patients with Mutations in the PROS1, SERPINC1, F2, and F5 Genes

Raniya Ahmad[1], Ryan Brownlee[1], Aditya Birla[1], Dongyu Zhang[1], Hung Bui[1], Mashoor Al Ahammed[1], Girindra Raval[1]

[1] Medical College of Georgia, USA

https://www.youtube.com/watch?v=4rJ3DHWeKRs&list=PLhqNq3xJClbafO0Y5bvBcgMmXpgzJxd44&index=6&t=15122s

Background: Lung cancer remains a leading cause of cancer mortality globally, with poor 5-year survival rates largely due to late-stage detection. Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are distinguished by distinct growth patterns, metastatic potential, and genetic profiles. Genetic markers in coagulation pathways, including F2, F5, PROS1, and SERPINC1, are implicated in tumor progression, metastasis, and hypercoagulable states. This study investigates the association of these gene mutations with clinical outcomes, tumor location, stage, and demographic factors in lung cancer patients.

Aim: The objective of this study was to characterize the prognostic significance of F2, F5, PROS1, and SERPINC1 mutations in lung cancer by analyzing clinical outcomes and survival patterns. Using TCGA-LUAD and TCGA-LUSC cohorts, we assessed how these mutations interact with patient age, race, tumor laterality, anatomic site, stage, and treatment strategies. The overarching aim was to determine whether thrombophilia mutations represent independent factors influencing survival and to explore their potential role in guiding personalized therapy.

Methods: Primary lung cancer patients with mutations in F2, F5, PROS1, or SERPINC1 were identified from TCGA-LUAD and TCGA-LUSC datasets. STAR RNA gene expression quantification was obtained for each gene. Patients were divided into mutation (n = 569) and comparison (n = 850) groups. Univariate and multivariate Cox proportional hazards analyses were conducted to evaluate associations between overall survival and patient age, race, AJCC pathologic stage, tumor primary site, laterality, and treatment type (chemotherapy, ancillary, immunotherapy, pleurodesis, radiation, targeted therapy). Hazard ratios (HR) with 95% confidence intervals (CI) were calculated.

Results: Across all mutations, higher pathologic stage and right-sided tumor location were consistently associated with worse survival. F5 mutations were significantly associated with improved outcomes in middle lobe (HR = 1.49, 95% CI [1.04–2.13], p = 0.028), pleura (HR = 1.33, 95% CI [1.08–1.64], p = 0.006), and upper lobe tumors (HR = 1.20, 95% CI [1.02–1.41], p = 0.025). PROS1 and SERPINC1 mutations conferred survival benefit in upper lobe tumors. In upper lobe cancers, African American patients harboring F5 mutations exhibited significantly worse survival (age at diagnosis HR = 1.01, 95% CI [1.00–1.02], p = 0.015; race HR = 1.33, 95% CI [1.04–1.71], p = 0.024). Gene counts were significant in the comparison group but not in mutation groups, potentially reflecting the averaging of gain- and loss-of-function mutations.

Conclusion: Thrombophilia-associated mutations in F2, F5, PROS1, and SERPINC1 influence lung cancer survival outcomes in a site- and demography-specific manner. Higher pathologic stage consistently predicts worse outcomes. F5 mutations confer protective effects in middle lobe, pleura, and upper lobe tumors, while PROS1 and SERPINC1 mutations are protective in upper lobe tumors. Notably, African American patients with F5 mutations experience reduced survival, and right-sided tumors harboring F2, F5, PROS1, or SERPINC1 mutations are associated with worse outcomes. These findings underscore the importance of considering thrombophilia gene status in prognostication and support the development of targeted therapies aimed at optimizing survival in lung cancer patients

Table 1. Univariate Cox Proportional Hazards Analysis of mutation group

Characteristic	Hazards Ratio (HR)	95% CI	p-value
PROS1	0.99	[0.94,1.05]	0.7
SERPINC1	0.97	[0.88,1.06]	0.5
F2	1.06	[1.00,1.13]	0.053
F5	1.05	[1.02,1.09]	0.003

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