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INTEGRATED PROGNOSTIC MODELING OF TUMOR STAGE, MULTIMODAL THERAPY, AND FUNCTIONAL STATUS IN LUNG CANCER SURVIVAL: A REAL-WORLD COHORT STUDY

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ABSTRACT

Lung cancer is a leading cause of cancer mortality, and prognosis is heavily dependent on the stage of the disease, treatment choice, comorbidity and functional status. The present study evaluated the integrated effects of tumor stage, multimodal treatment strategies, and comorbidity burden on mortality and survival outcomes among patients with lung cancer using publicly available multi-hospital clinical data. A retrospective observational analysis was conducted using a cohort of 1,782 lung cancer patients. Descriptive statistics were used to summarize baseline characteristics, while chi-square testing and multivariable logistic regression were applied to assess predictors of mortality. Comorbidity burden was calculated from available clinical conditions. Kaplan–Meier survival analysis and Cox proportional hazards regression were additionally performed to evaluate long-term survival patterns and prognostic factors. Mortality increased progressively with advancing cancer stage, from 16.3% in Stage I to 79.2% in Stage IV disease. In adjusted analysis, cancer stage emerged as the strongest predictor of mortality (OR = 2.71, 95% CI: 2.42–3.02, $p < 0.001$). Surgery demonstrated lower mortality compared with chemotherapy (OR = 0.67, 95% CI: 0.49–0.91, $p = 0.011$), while comorbidity burden was not independently associated with mortality. Survival analysis demonstrated declining survival probability over time, with female sex and ECOG performance status independently associated with survival outcomes. Treatment modality and functional status offered further prognostic information, with the stage of tumor being the single most important determinant of mortality. The results underscore the need for comprehensive clinical assessment to enhance lung cancer risk stratification and survival prediction.

KEYWORDS: lung cancer, tumor stage, treatment strategy, comorbidity burden, survival analysis

1. INTRODUCTION

Lung cancer is an important and major public health problem in the world, given its high incidence rate, rapid disease progression and large mortality rate. Although there have been significant advancements in diagnostic and therapeutic technologies, lung cancer remains a substantial cause of mortality globally (Schabath & Cote, 2019). In 2022, there were an estimated 2.5 million new cases of lung cancer and 1.8 million deaths due to lung cancer worldwide (World Health Organization, 2026). The disease is often diagnosed at late stages, which means that treatment choices are reduced, and the prognosis will significantly decrease. With the increasing clinical and epidemiological impact of lung cancer, more tools are needed for accurate prognosis, early diagnosis, and the best possible treatment planning strategies.

While smoking exposure, environmental factors, old age and genetic susceptibility are all important for lung cancer development, the epidemiology of lung cancer shows a wide variation between populations (Thandra et al., 2021). Tobacco smoking is by far the most important preventable risk factor, and occupational hazards and air pollution are also contributing to the high burden of disease. Change in diagnosis management and treatment has led to better patient management over the last few decades, but long-term survival remains poor for many patients, especially those who present with metastatic or late-stage disease (Lu et al., 2019). Therefore, the interactions between disease severity, treatment choice, and patient clinical characteristics have become increasingly relevant in today's cancer research.

Early diagnosis is a key to better survival rates in lung cancer. Late diagnosis often leads to late presentation, which means that there are fewer curative treatment options and a higher risk of death (Ning et al., 2021). Advances in imaging technology, molecular diagnostics and screening strategies have enhanced diagnostic accuracy and clinical decision making, but access, the variability in disease manifestation and response to treatment remain issues that impact patient outcomes (Nooreldeen & Bach, 2021). It has been due to this that clinical studies are more and more focused on the need for an integrated framework of prognosis that includes multiple determinants of disease progression and survival.

In the management of lung cancer, tumor stage is among the most significant factors of prognosis and treatment. The TNM staging system gives a standard method of assessing the extent of disease, whether it has spread or not and the clinical severity, which can then be used to inform treatment decisions and estimate survival (Rami-Porta et al., 2024). Surgical intervention and potentially curative treatment are more likely to benefit the patient with early-stage disease; advanced-stage disease may be treated systemically or with multimodal therapies, with less favorable outcomes. Reliable stage-based risk stratification is thus still essential for clinical management and for short- and long-term prognosis.

Therapy for lung cancer generally includes surgery, chemotherapy, radiation or a combination of all three treatments, depending on the stage of the tumor and the patient's health. Surgical therapy is a key therapeutic modality for patients with operable disease and is beneficial in appropriately selected cases (Hoy et al., 2019). Treatment options for locally advanced disease are often multimodal (combination of systemic therapy, surgery and radiotherapy), to achieve better disease control and long-term outcomes (Huber et al., 2019). Chemotherapy is still being used in the adjuvant and advanced disease settings; however, its efficacy depends on patient characteristics and disease severity (Harada et al., 2021). In a similar way, radiotherapy is also a useful tool for the management of lung cancer, especially in the case of locally advanced or inoperable disease (Vinod & Hau, 2020).

Clinical factors related to the patient (apart from tumor stage and the choice of treatment) may also significantly affect prognosis and survival. Cancer patients may have other illness conditions that can impact the tolerability, functional status and overall risk of mortality. A previous study has shown that the burden of comorbidity could negatively affect the survival experience of lung cancer patients, especially those older than 65 years and people with multiple chronic conditions (Morishima et al., 2019). Functional performance status has also become a significant prognostic factor, as minimal functional reserve might restrict eligibility for treatment and make patients susceptible to progression of disease.

In recent years, the research and development of lung cancer has provided more understanding of molecular pathways, disease mechanisms, and treatment responsiveness, which has led to more individualized management of patients (Salehi-Rad et al., 2020). However, numerous studies still exist that look at variables for prognosis independently, without considering their synergistic effects on prognosis and survival outcomes in the context of tumor stage, treatment strategy, comorbidity burden, and survival outcomes in a single analysis. In addition, there is also very little evidence available from multi-centre clinical cohorts from real-world patient populations in developing health care settings.

This paper aims to fill this gap by conducting an integrated analysis of the state of the tumor, multimodal treatment strategies, burden of comorbidities, mortality, and survival patterns for lung cancer patients. The study employs regression-based mortality modelling and survival analysis methods to determine independent predictors of adverse outcomes and looks at trends in long-term survival using a multi-hospital clinical cohort. The results could help to better understand clinically relevant prognostic factors and facilitate the development of more holistic methods of outcome assessment for lung cancer.

2. METHODOLOGY

2.1 Research Design

A retrospective observational cohort study design was used to explore how these factors are associated with tumor stage, treatment strategy, comorbidity burden, mortality and survival outcomes for patients with lung cancer. The statistical modeling and survival analysis methods were used to assess the risk of mortality and survival trends in the study population.

2.2 Data Source

The primary analysis was performed with a public dataset of multi-hospital lung cancer data reported by Paul and Khan (2026). The data consisted of anonymized clinical and demographic data of 1,782 patients with lung cancer from tertiary healthcare institutions in Dhaka, Bangladesh. Data collected included patient characteristics, cancer stage, treatment, comorbidities, and survival.

A secondary survival-analysis data set was also used for the Kaplan–Meier analyses and Cox proportional hazards models to provide additional evaluation of long-term survival outcomes. This supplemental data set contained variables that were pertinent to survival (ECOG performance status, weight loss, and follow-up time) that could be evaluated in detail to assess prognostic survival factors (Therneau, 2026).

2.3 Study Population and Variables

The study had 1,782 patients diagnosed with lung cancer. The variables analyzed were age, sex, cancer stage, treatment type, smoking status, BMI, cholesterol level and comorbidities (hypertension, asthma, cirrhosis and previous cancer history). Mortality status (1=deceased, 0=alive) was considered as the primary outcome and the basis for regression-based mortality analysis.

Other factors, such as ECOG performance status, weight loss and survival duration, were also considered in the survival analysis to evaluate their relationship with long-term survival outcomes. Cancer stage was classified as Stage I, Stage II, Stage III and Stage IV disease. Treatment modalities included surgical, chemotherapy, radiation, and any combination of these treatments.

2.4 Data Preprocessing

In order to be consistent with the statistical analysis, the data were preprocessed. All date variables were converted to datetime and categorical variables to numerical, where this was necessary for regression models. For mortality analysis, dead patients were classified as events and living patients as non-events, which were binary outcome variables. A cumulative comorbidity score based on hypertension, asthma, cirrhosis, and a history of cancer was used to quantify the burden of comorbidity. Records were not included in multivariable survival modeling if they were missing some information relating to survival.

2.5 Statistical Analysis

Baseline demographic and clinical data for the study sample were summarized using descriptive statistics. The continuous variables were presented as mean ± SD, while the categorical variables were expressed as frequencies and percentages. Chi-square tests were used to determine the association between mortality outcomes and categorical clinical variables. A multivariable logistic regression analysis was then conducted to determine independent factors associated with mortality. All the covariates used in the regression model were adjusted to calculate adjusted odds ratios (ORs), 95% confidence intervals (CIs), and p-values. Predicted mortality probabilities were also calculated by treating cancer stage and treatment modality as interaction effects to assess the interaction patterns between cancer stage and treatment modality. The preprocessing and statistical analysis, regression modeling, and plotting of figures were carried out using Python.

2.6 Survival Analysis

Overall survival probability was determined by Kaplan–Meier survival analysis. Survival curves were generated for the supplementary survival-analysis cohort overall and stratified by sex and ECOG performance status. Multivariate Cox proportional hazards regression analysis was conducted to see which variables were independently associated with survival. Demographic and clinical variables were included in the survival model, and hazard ratios (HRs) with corresponding 95% confidence intervals were calculated. Schoenfeld residual-based diagnostics were used to evaluate the proportional hazards assumptions.

3. RESULTS

3.1 Clinical and Demographic Characteristics of the Study Population

There were 1,782 patients with lung cancer in total who were included in the analysis. The mean age of the cohort was 56.5 ± 18.9 years. Male and female patients were almost equally distributed, with males accounting for 50.2% and females accounting for 49.8% of the study population. The most common stage of disease was Stage II (30.2%), followed by Stage I (25.8%), Stage III (24.0%) and Stage IV (20.0%). Treatment by radiation therapy was most common (26.5%), followed by surgery, chemotherapy, and combined treatment strategies, with relatively similar distributions across the cohort. There was also moderate variation in the body mass index and cholesterol in the cohort, indicating that there was some intracohort variability in baseline metabolic parameters among patients. Basic demographic and clinical data are presented in Table 1.

Table 1: Baseline Clinical and Demographic Characteristics of Patients Included in the Multi-Hospital Lung Cancer Cohort

Variable	Value
Age (mean ± SD)	56.5 ± 18.9
BMI (mean ± SD)	25.5 ± 5.4
Cholesterol (mean ± SD)	228.2 ± 52.9
Male (%)	50.2
Female (%)	49.8
Stage I (%)	25.8
Stage II (%)	30.2
Stage III (%)	24.0
Stage IV (%)	20.0
Surgery (%)	24.1
Chemotherapy (%)	24.2
Radiation (%)	26.5
Combined Treatment (%)	25.1

3.2 Mortality Distribution Across Lung Cancer Stages

As the cancer stage increased, mortality rates increased. The lowest mortality was observed in patients with Stage I disease (16.3%), while a significantly higher mortality was observed in patients with Stage IV disease (79.2%). Stage II (32.5%) and Stage III (55.6%) illness categories were found with intermediate mortality rates. The progressive mortality rates across stages reflect a strong association between the severity of the disease and clinical outcomes. The fairly small confidence intervals also indicate good estimates of the stages within the study population. The mortality rates by cancer stage are shown in Figure 1.

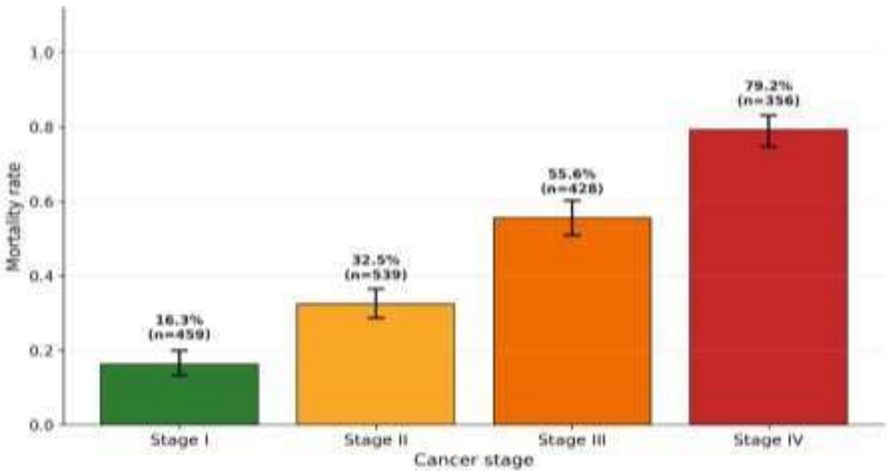

Figure 1: Observed Mortality Rates Across Lung Cancer Stages

3.3 Adjusted Predictors of Mortality

Independent predictors of mortality were analyzed after adjusting for demographic and clinical covariates through multivariable logistic regression analysis. The odds ratio and 95% confidence intervals for the adjusted effects of clinical variables on mortality are shown in Figure 2. Cancer stage was the most significant predictor of mortality (OR = 2.71, 95% CI: 2.42-3.02, p < 0.001), meaning that each additional step in cancer progression increased the odds of death significantly. Of the treatment modalities, surgery showed a significant protective association with respect to chemotherapy (OR = 0.67, 95% CI: 0.49–0.91, p = 0.011). No statistically significant associations were observed for radiation therapy or for a combination of treatments after adjustment. Likewise, age, sex and burden of comorbidities were not independently correlated with mortality in the adjusted model.

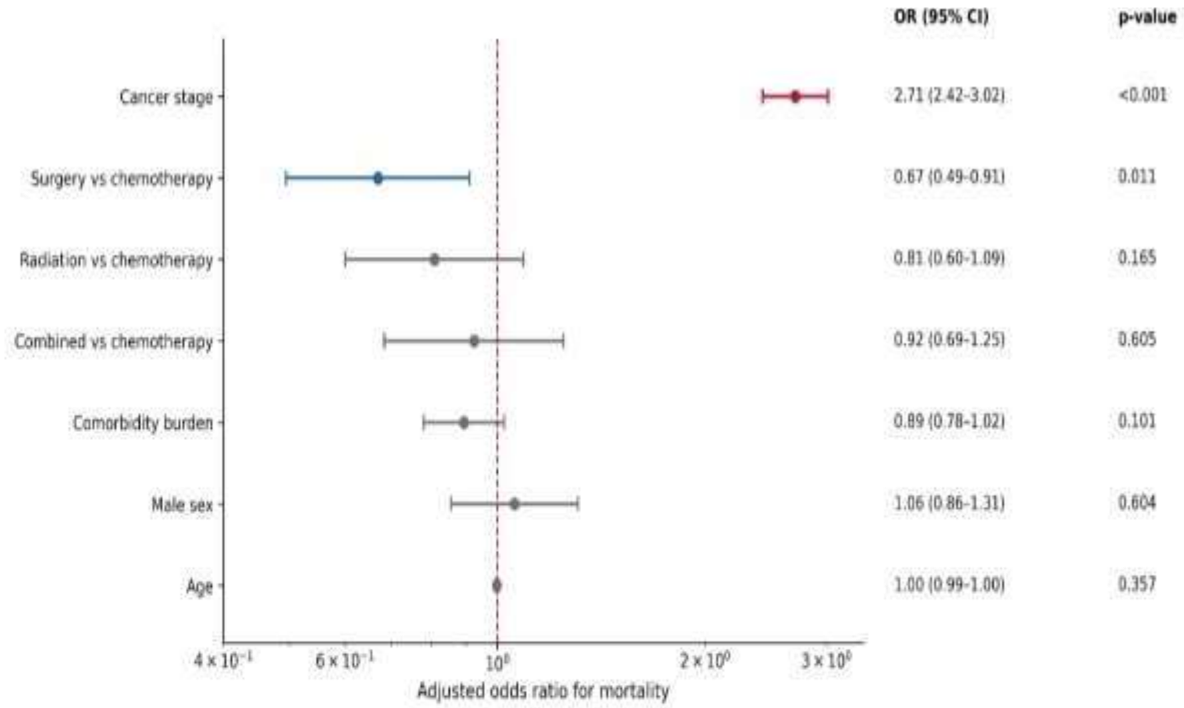

Figure 2: Adjusted Predictors of Mortality in Lung Cancer Patients

The variables on the right-hand side of the null reference line (OR = 1) represent a higher risk of death, while those on the left-hand side represent a lower risk of death. The greatest effect size with confidence intervals that were well outside the null line was for cancer stage, where there was a strong independent association with mortality. Surgery was protective compared to chemotherapy, and other treatment modalities and demographic factors had confidence intervals that crossed the null value (no association) after multivariable adjustment. In general, these results suggest that disease stage is the most important factor for mortality, and surgery might provide relatively good clinical results for certain patients.

3.4 Predicted Mortality and Survival According to Treatment Strategy and Cancer Stage

Adjusted predicted mortality increased progressively with each cancer stage, irrespective of treatment modality, indicating worsening outcome probability with increasing disease severity. Differences in treatment strategies were evident at all stages. The lowest predicted probabilities of death were seen in surgery, and comparatively better predictive survival outcomes were seen in surgery, compared to chemotherapy, which had the highest predicted probability of death, especially in Stage III and Stage IV disease. As the cancer stage increased, the difference between treatment curves became more evident, suggesting that there may be increasing death and survival differences between treatments in advanced lung cancer. Although there was a significant rise in mortality in all treatment groups in stage IV disease, surgery still showed relatively lower predicted mortality probabilities. The results indicate that cancer stage and treatment strategy jointly contribute to mortality risk stratification in patients with lung cancer. Figure 3 shows the relationship between the stage of cancer and treatment approach.

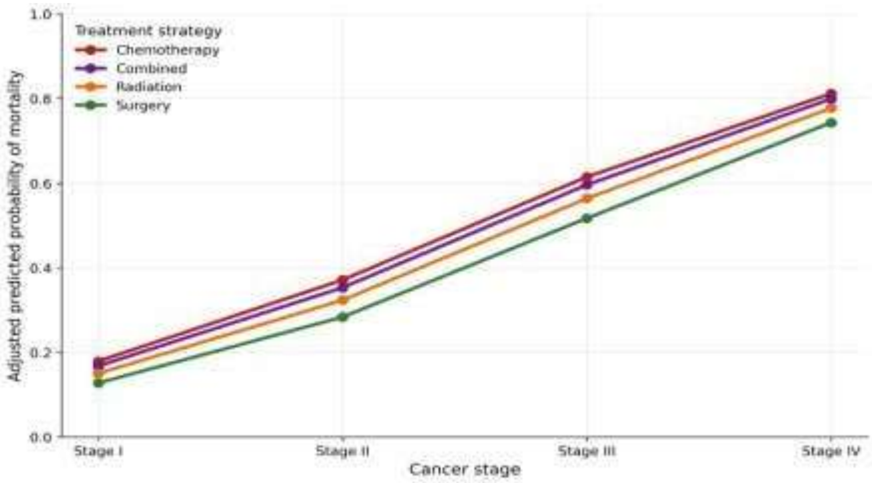

Figure 3: Adjusted Predicted Mortality by Cancer Stage and Treatment Strategy

3.5 Survival Outcomes

To provide additional evaluation of long-term survival patterns, Kaplan–Meier survival analysis was performed using the supplementary survival-analysis cohort. As the overall survival probability showed progressive decline during the follow-up period, the study population had an increasing rate of mortality over time. The overall survivorship curve is shown in Figure 4A. Females had relatively better survival probabilities than males in most follow-up intervals, as illustrated by sex-stratified survival analysis, indicating relatively more favourable outcomes of survival in women of the cohort. Survival curves according to sex are shown in Figure 4B. ECOG performance status was also a factor in determining survival outcomes. The patients with a lower ECOG score had significantly higher probabilities of survival, and the patients with an ECOG score of 2 had the fastest declining survival probability with time. This analysis highlights the importance of assessing functional capacity at diagnosis for the prognosis of lung cancer. The ECOG-stratified survival curves are presented in Figure 4C.

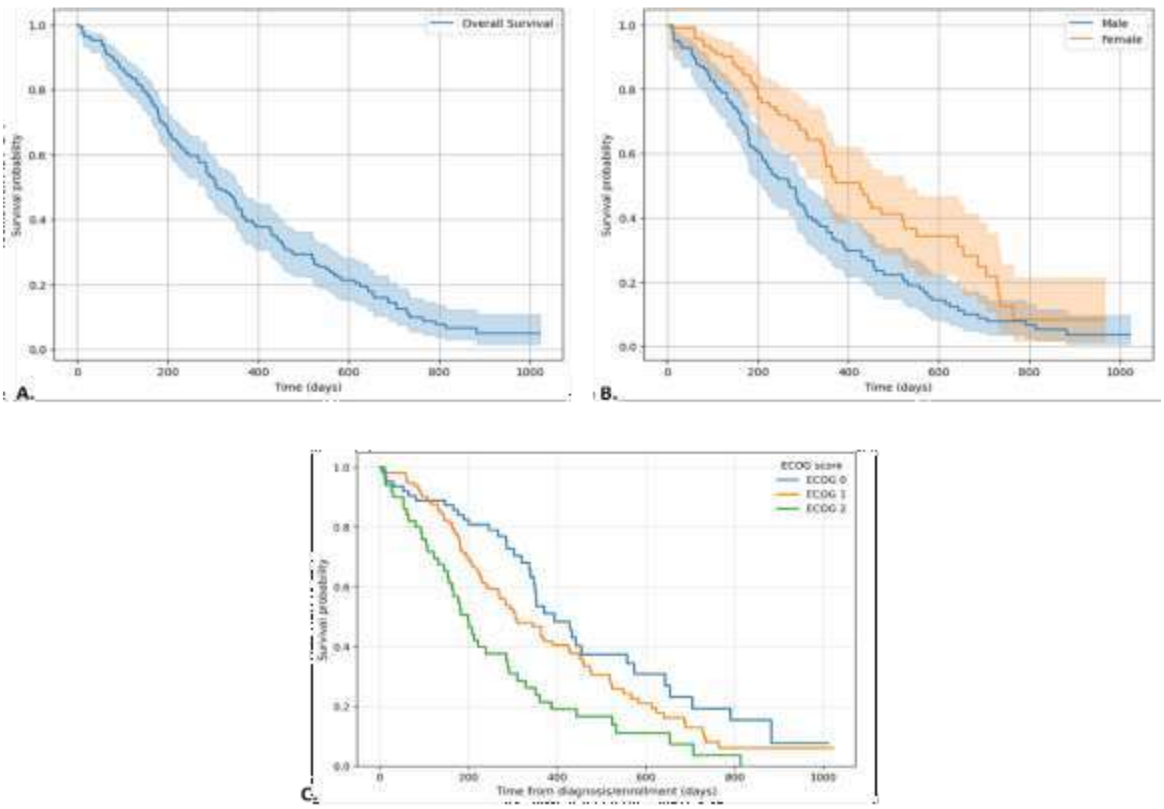

Figure 4: Kaplan–Meier Survival Analysis of Lung Cancer Patients (A) Overall Survival Curve, (B) Survival Stratified by Sex, and (C) Survival Stratified by ECOG Performance Status

The results of multivariate Cox proportional hazards regression analysis showed that the independent prognostic factors for survival were female gender and ECOG performance status; age and weight loss were not statistically significant predictors (Table 2).

Table 2: Multivariable Cox Regression Analysis of Survival Outcomes

Variable	Hazard Ratio (HR)	95% CI	p-value
Age	1.01	0.99 – 1.03	0.17
Sex (Female)	0.61	0.44 – 0.83	<0.005
ECOG Score	1.54	1.23 – 1.93	<0.005
Weight Loss	0.99	0.98 – 1.01	0.29

The findings demonstrate that tumor stage, treatment strategy, and functional status collectively influence mortality and survival outcomes among patients with lung cancer. Advanced-stage disease was consistently associated with poorer outcomes, while surgical management and better ECOG performance status were linked with comparatively favorable prognosis. These results support the importance of integrated clinical assessment for improving prognostic evaluation and treatment planning in lung cancer care.

4. DISCUSSION

In the present study, the most prominent determinant of mortality was advancing tumour stage. Mortality rose progressively from Stage I to Stage IV, and multivariable modelling confirmed cancer stage as the strongest adjusted predictor of death. This pattern suggests that disease extent remains a major prognostic factor even after simultaneous adjustment for treatment strategy, demographic variables and comorbidity burden. The sharp increase in mortality among patients with advanced-stage disease mirrors the clinical reality of higher tumor burden, fewer curative treatment options, and a greater likelihood of systemic disease progression in late-stage lung cancer. The treatment strategy was also a significant contributor to the variance in outcome. Surgery was associated with lower adjusted mortality than chemotherapy, and predicted mortality curves consistently showed more favorable outcomes for patients managed surgically across cancer stages. The finding should be interpreted with caution, since surgical eligibility is influenced by tumor stage, operability, functional status and patient fitness. However, the association observed suggests that patients who are surgical candidates may represent a subgroup with a better clinical prognosis. Comorbidity burden was included as an integrated clinical factor and was not independently associated with mortality after adjustment. This may reflect the limited nature of the comorbidity score, which was based on the available conditions selected and not a weighted clinical index. By contrast, in survival analysis, a strong correlation between ECOG performance status and survival probability was observed, indicating that functional capacity may be a more clinically relevant indicator of frailty and treatment tolerance than simply the number of comorbidities.

Strong associations between advanced-stage disease and poorer outcomes are consistent with population-based evidence that survival from lung cancer remains tightly linked to the extent of disease at diagnosis (Lin et al., 2019). The sex-related survival difference in favor of females in the current study is consistent with recent comparative evidence reporting prognostic differences between men and women with non-small cell lung cancer across treatment modalities (Li et al., 2025). The surgery protective association is consistent with literature highlighting the importance of quality of surgical care and treatment access in lung cancer survival outcomes. The role of hospital volume and aspects of healthcare delivery in affecting the results of treatment after surgery for lung cancer patients is also documented (Thai et al., 2019). The information about the regional difference in surgeries for lung cancer further reinforces this idea by demonstrating the effect of surgery on mortality rates (Kim et al., 2026).

While the present study concentrated on clinical and epidemiologic factors, novel molecular data indicate that the prognosis of lung cancer is influenced by immune and tumor microenvironment biomarkers. Prognosis prediction models based on immunology can be used to estimate risk in lung adenocarcinoma patients (Song et al., 2019). Gene signatures associated with tumor microenvironments further prove the biological intricacies behind the variability in patient survival rates (Ma et al., 2020). Circulating immune cell profiling was also found to correlate with advanced lung cancer prognoses, indicating the relevance of integrating biological and clinical markers in future prediction models (Shaul et al., 2020). The lack of a statistically significant relationship between comorbidity burden and mortality contrasts with other population-based cancer literature demonstrating that comorbidities are prevalent and clinically important among cancer patients (Fowler et al., 2020). Recent advances in lung cancer screening research further stress the need for evaluating the significance of comorbid conditions at baseline and longitudinally for prognostic and clinical interpretation (Romeikat et al., 2025). Other possible contributors to lung cancer incidence and outcomes include lifestyle and nutritional factors, based on evidence from a Mendelian randomization investigation of antioxidant vitamin consumption and lung cancer risks (Zhao & Jin, 2022).

These results stress the significance of early diagnosis and proper staging in managing lung cancer. The dramatic rise in the number of mortalities through all stages clearly indicates that any form of delayed diagnosis would decrease the chances of success. These results would mean that, from a clinical perspective, it would be wise to have a better stage-stratified approach. Regarding the treatment results, it appears important to put any outcome into its proper clinical context. Although the surgery was seen to contribute to reduced mortality, this could be influenced by not only treatment itself but also patient selection as well. Using an approach that combines stage, treatment modality, and functional status might, therefore, result in improved prognostic evaluation. Regarding the survival results, another practical implication would include the usefulness of incorporating ECOG functional status into prognostication. This measure can be used in routine clinical practice as opposed to other demographic and comorbidity indicators.

The study has a few limitations. First, the retrospective nature of the study could lead to variations in documentation and information availability for all participating facilities. Second, comorbidity was calculated through selected comorbidities without any validation through a weighted index. Third, there were no patient-level links created from the survival analysis, as survival modeling was done using a separate survival analysis dataset.

Future studies must replicate the current study using a cohort of patients with a history of documented treatments, along with validated comorbid indices and ECOG status. Further, stage-based evaluation of treatment efficacy, as well as the development of integrated models, must be explored.

5. CONCLUSION

The influence of tumor stage on the outcome remained a significant predictor of mortality among those diagnosed with lung cancer, where a higher mortality rate was seen moving from Stage I to Stage IV. The approach for treatment itself was one of the determinants of outcome, with surgery as treatment having lower adjusted mortality compared to that of chemotherapy. Even though the presence of any comorbidities was not a significant predictor of mortality in the adjusted model, it was established through survival analysis that functional status played an important role in survival, as it was seen that individuals with poor ECOG performance had decreased survival probability. Moreover, being female was also a protective factor against unfavorable outcomes according to survival analysis. In conclusion, it was evident that the use of an integrated approach in clinical practices, where factors such as tumor stage, treatment approach, functional status, and patterns of survival are combined, is a better practice compared to considering all these factors independently.

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