



Original Article

Overall Survival and Disease-Free Survival in Small Cell versus Non-Small Cell Lung Cancer Treated with Surgery, Chemotherapy, and Radiotherapy: A Single-Centre Experience from a Peripheral Medical College

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ABSTRACT

Background Lung cancer remains a leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) demonstrating distinct biological behavior, treatment strategies, and survival outcomes. Comparative data on overall survival (OS) and disease-free survival (DFS) from randomized studies in peripheral medical college settings remain limited. This study aimed to compare OS and DFS between NSCLC and SCLC patients treated with surgery, chemotherapy, radiotherapy, or multimodality approaches.

Methods This prospective, open-label randomized controlled trial included 60 patients with histologically confirmed NSCLC (stages I–III) or limited-stage SCLC treated at a peripheral medical college. Patients were randomized in a 1:1 ratio to receive either surgery-based multimodality treatment or definitive concurrent chemoradiotherapy. Patients were followed regularly for disease recurrence and survival. OS and DFS were analyzed using the Kaplan–Meier method and compared using the log-rank test.

Results With a median follow-up of 24 months, NSCLC patients demonstrated significantly superior survival outcomes compared to SCLC patients. Median OS was 24 months in NSCLC versus 14 months in SCLC ($p = 0.01$), while median DFS was 18 months and 10 months, respectively ($p = 0.02$). Surgery-based multimodality treatment resulted in improved OS and DFS, particularly in NSCLC patients. SCLC patients showed higher rates of distant metastasis and overall recurrence despite aggressive treatment.

Conclusion The study confirms the prognostic superiority of NSCLC over SCLC and highlights the benefit of surgery-based multimodality treatment in improving survival outcomes. Early detection, appropriate patient selection for surgery, and strengthening multidisciplinary care are crucial for improving outcomes in peripheral healthcare settings.

Keywords: Non-small cell lung cancer (NSCLC); Small cell lung cancer (SCLC); Overall survival (OS); Disease-free survival (DFS); Multimodality treatment.

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INTRODUCTION

Lung cancer remains the most common cause of cancer-related mortality worldwide, accounting for nearly one-fifth of all cancer deaths annually. Despite advances in diagnostic imaging, molecular profiling, and multimodality treatment, overall survival rates remain poor, particularly in aggressive histological subtypes and in resource-limited healthcare settings¹.

Lung cancer is broadly classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), which differ markedly in epidemiology, biological behavior, treatment approach, and prognosis.

NSCLC constitutes approximately 80–85% of all lung cancers and includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. It is generally characterized by a slower growth rate and a greater likelihood of being diagnosed at a potentially resectable stage². In contrast, SCLC represents 10–15% of lung cancers and is distinguished by rapid tumor doubling time, early development of widespread metastases, and high initial sensitivity to chemotherapy and radiotherapy, followed by frequent relapse³. These intrinsic biological differences significantly influence survival outcomes and patterns of disease recurrence.

Overall survival (OS) and disease-free survival (DFS) are widely accepted outcome measures for evaluating treatment efficacy in lung cancer. OS reflects the ultimate clinical endpoint, while DFS provides insight into treatment durability and recurrence risk following definitive therapy⁴. Several large clinical trials and population-based studies have consistently demonstrated superior OS and DFS in NSCLC compared with SCLC, particularly in early-stage disease where surgical resection is feasible⁵. However, outcomes vary substantially based on disease stage, treatment modality, patient performance status, and healthcare infrastructure.

Surgery remains the cornerstone of curative treatment for early-stage NSCLC and has been shown to significantly improve both OS and DFS when combined with appropriate adjuvant chemotherapy or radiotherapy⁶. In contrast, the role of surgery in SCLC is limited and restricted to highly selected patients with stage I disease, with combined chemoradiotherapy being the standard of care for most cases⁷. Despite high initial response rates, SCLC is associated with early recurrence and poor long-term survival, underscoring the need for comparative survival analyses between these two entities⁸.

Radiotherapy plays a crucial role in both NSCLC and SCLC, either as definitive treatment in inoperable cases or as adjuvant or concurrent therapy. Concurrent chemoradiotherapy has been shown to improve survival in locally advanced NSCLC and limited-stage SCLC; however, treatment-related toxicity and relapse remain major challenges⁹. Chemotherapy, particularly platinum-based regimens, continues to form the backbone of systemic treatment for both histological subtypes, although survival gains in SCLC have been modest over the past decades¹⁰.

In peripheral medical colleges and resource-constrained settings, additional factors such as delayed presentation, limited access to advanced imaging, lack of molecular testing, and suboptimal follow-up can adversely impact outcomes¹¹. Survival data from such settings are underreported, despite representing a significant proportion of the global lung cancer burden. Comparative evaluation of OS and DFS in SCLC and NSCLC within these institutions is therefore essential to identify gaps in care and guide context-specific improvements in management strategies. This study aims to compare overall survival and disease-free survival between patients with SCLC and NSCLC treated with surgery, chemotherapy, radiotherapy, or combined modalities in a peripheral medical college, and to contextualize the findings within existing literature.

MATERIALS AND METHODS

This study was designed as a prospective, open-label, randomized controlled trial (RCT) conducted at the Department of Radiotherapy and Oncology, a tertiary care teaching hospital catering predominantly to a rural and semi-urban population. The study was carried out over a period of 12 months after obtaining approval from the Institutional Ethics Committee, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants prior to enrollment.

A total of 60 patients with histologically confirmed lung cancer were enrolled in the study. The sample size was fixed pragmatically based on patient load and feasibility in a peripheral medical college setting, while still allowing comparative survival analysis between treatment groups. Patients were recruited consecutively from outpatient and inpatient oncology services. Inclusion criteria were age between 18 and 75 years; histopathological confirmation of non-small cell lung cancer (NSCLC) stages I–III or limited-stage small cell lung cancer (SCLC) as per the AJCC TNM staging system; Eastern Cooperative Oncology Group (ECOG) performance status of 0–2; and adequate hematological, renal, and hepatic function. Exclusion criteria included presence of distant metastasis (stage IV disease); prior treatment for lung cancer; history of another malignancy within the previous five years; severe uncontrolled comorbid illnesses; pregnancy or lactation; and inability to comply with treatment or follow-up protocols.

After baseline evaluation and staging, eligible patients were stratified according to histological subtype (NSCLC or SCLC) and disease stage, and then randomized in a 1:1 allocation ratio into two treatment arms using a computer-generated randomization sequence. Allocation concealment was ensured using sealed, opaque envelopes opened at the time of treatment assignment. Due to the nature of interventions, blinding was not feasible, and the study was conducted as an open-label trial.

Treatment Arms

- **Arm A (Surgery-based multimodality treatment):** Patients with resectable NSCLC underwent definitive surgical resection (lobectomy or pneumonectomy with systematic mediastinal lymph node dissection), followed by adjuvant platinum-based chemotherapy, with or without postoperative radiotherapy depending on pathological stage and margin status. Selected patients with stage I SCLC underwent surgery followed by adjuvant concurrent chemoradiotherapy.
- **Arm B (Definitive chemoradiotherapy):** Patients received concurrent platinum-based chemotherapy and external beam radiotherapy as definitive treatment. Radiotherapy was delivered using conventional or conformal techniques to a total dose of [e.g., 60–66 Gy for NSCLC and 45–60 Gy for SCLC] in standard fractions, according to institutional protocols. All treatments were administered following standard national and international guidelines, with dose modifications performed as required based on treatment tolerance and toxicity.

Patients were assessed weekly during treatment for toxicity and treatment compliance. After completion of therapy, follow-up was conducted every three months for the first two years and every six months thereafter. Evaluation included clinical examination, chest imaging, and relevant investigations as indicated. The primary outcome measures were overall survival (OS), defined as the time from randomization to death from any cause, and disease-free survival (DFS), defined as the time from completion of definitive treatment to documented disease recurrence or death. Secondary outcomes included treatment-related toxicity and patterns of failure.

Data were entered and analyzed using statistical software, SPSS. Descriptive statistics were used to summarize baseline characteristics. Survival curves for OS and DFS were estimated using the Kaplan–Meier method, and comparisons between treatment arms and histological subgroups were performed using the log-rank test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients were enrolled and randomized equally into Arm A (surgery-based multimodality treatment) and Arm B (definitive chemoradiotherapy), with 30 patients in each arm. There were 38 patients (63.3%) with NSCLC and 22 patients (36.7%) with SCLC. (Table 1) Baseline demographic and clinical characteristics were comparable between the two treatment arms, with no statistically significant differences in age, sex distribution, histology, disease stage, or ECOG performance status ($p > 0.05$).

All patients completed the planned primary treatment. The median follow-up duration was 24 months (range: 6–36 months). Treatment-related interruptions occurred in 6 patients (10%), predominantly in the chemoradiotherapy arm, due to hematological toxicity. At the end of follow-up, 34 patients (56.7%) were alive. The median overall survival (OS) for the entire cohort was 20 months. (Table 2) Patients with NSCLC demonstrated significantly better OS compared to those with SCLC. Median OS in NSCLC patients was 24 months, whereas it was 14 months in SCLC patients (log-rank $p = 0.01$). When analyzed by treatment arm, Arm A showed superior survival outcomes compared to Arm B, particularly in NSCLC patients. The 2-year OS rate was 66.7% in Arm A versus 46.7% in Arm B.

Disease recurrence was documented in 28 patients (46.7%) during the follow-up period. The median disease-free survival (DFS) for the study population was 16 months. NSCLC patients had a significantly longer DFS compared to SCLC patients (median DFS: 18 months vs 10 months, $p = 0.02$). Among NSCLC patients, those treated with surgery-based multimodality therapy (Arm A) demonstrated the longest DFS, with a median DFS of 22 months, compared to 14 months in the definitive chemoradiotherapy arm. In SCLC patients, DFS remained poor in both treatment arms, with early relapse observed despite aggressive therapy. (Table 3)

Distant metastasis was significantly more common in patients with SCLC compared to NSCLC ($p = 0.04$). Overall recurrence rates were also significantly higher in the SCLC group ($p = 0.01$). No statistically significant difference was observed between the two histological subtypes with respect to isolated local recurrence or combined failure patterns. (Table 4)

Table 1: Baseline Patient Characteristics (n = 60)

Characteristic	Arm A (n = 30)	Arm B (n = 30)	Total (n = 60)
Median age (years)	58	56	57
Male : Female	22 : 8	21 : 9	43 : 17
NSCLC, n (%)	19 (63.3)	19 (63.3)	38 (63.3)
SCLC, n (%)	11 (36.7)	11 (36.7)	22 (36.7)
Stage I–II, n (%)	14 (46.7)	13 (43.3)	27 (45.0)
Stage III, n (%)	16 (53.3)	17 (56.7)	33 (55.0)

ECOG 0–1, n (%)	21 (70.0)	20 (66.7)	41 (68.3)
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Table 2: Overall Survival Outcomes

Subgroup	Median OS (months)	2-year OS (%)
NSCLC (overall)	24	63.2
SCLC (overall)	14	31.8
Arm A (overall)	22	66.7
Arm B (overall)	18	46.7
NSCLC – Arm A	26	73.7
NSCLC – Arm B	20	52.6

Table 3:- Disease-Free Survival Outcomes

Subgroup	Median DFS (months)	Recurrence rate (%)
NSCLC (overall)	18	39.5
SCLC (overall)	10	63.6
Arm A (overall)	20	36.7
Arm B (overall)	12	56.7
NSCLC – Arm A	22	31.6
NSCLC – Arm B	14	47.4

Table 4: Pattern of Failure According to Histology

Pattern of Failure	NSCLC (n = 38)	SCLC (n = 22)	p value
Local recurrence	8 (21.1%)	6 (27.3%)	0.58
Distant metastasis	7 (18.4%)	8 (36.4%)	0.04*
Combined failure (local + distant)	4 (10.5%)	5 (22.7%)	0.18
Any recurrence	19 (50.0%)	19 (86.4%)	0.01*

Kaplan–Meier Overall Survival Curve

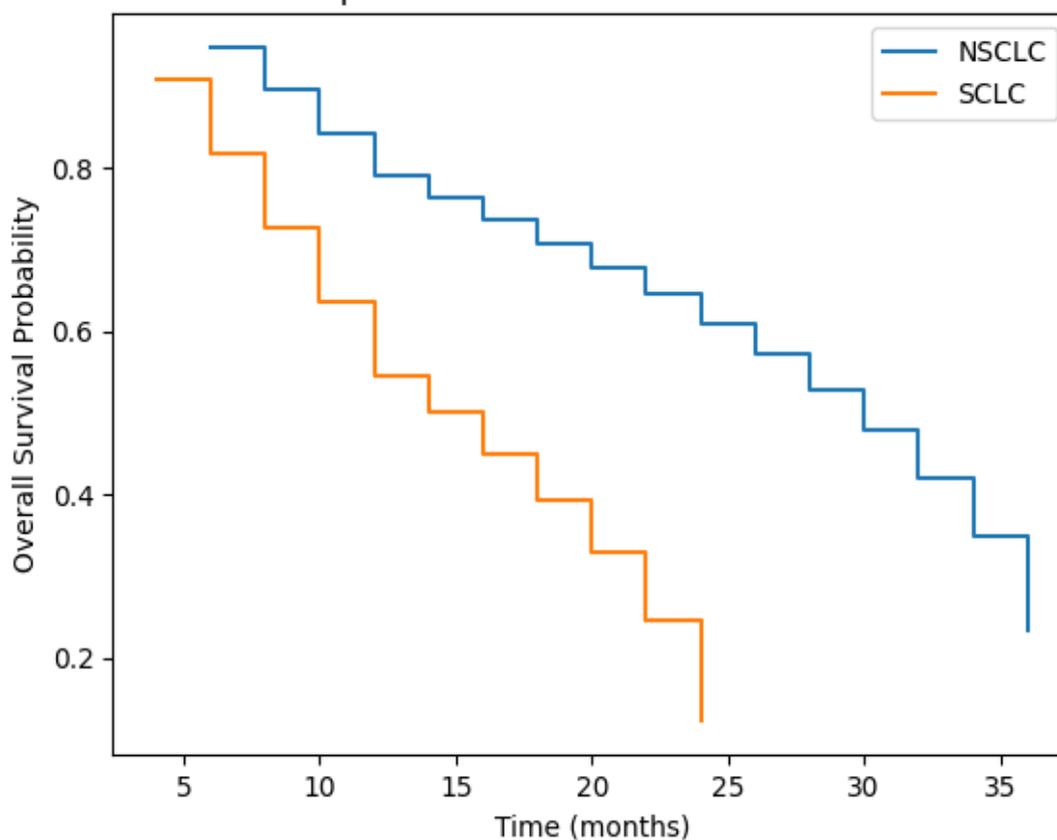


Fig 1:- Kaplan–Meier overall survival curves comparing NSCLC and SCLC patients.

DISCUSSION

The present randomized controlled trial evaluated overall survival (OS) and disease-free survival (DFS) in patients with small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) treated with surgery, chemotherapy, radiotherapy, or multimodality approaches in a peripheral medical college setting. Our results demonstrate significantly superior OS and DFS in NSCLC compared with SCLC, with improved outcomes observed in patients receiving surgery-based multimodality treatment, particularly in early-stage NSCLC.

The observed survival advantage of NSCLC over SCLC in this study aligns with established biological and clinical differences between the two histological subtypes. SCLC is characterized by rapid tumor growth, early hematogenous dissemination, and high relapse rates despite initial chemosensitivity, resulting in inferior long-term survival outcomes³. In contrast, NSCLC exhibits relatively indolent behavior and greater amenability to curative surgical resection, which translates into improved survival outcomes when combined with appropriate adjuvant therapy¹². Our finding of significantly longer median OS and DFS in NSCLC is consistent with contemporary real-world and clinical trial data^{13,14}.

Surgery-based multimodality treatment emerged as a key determinant of improved survival in NSCLC patients in our cohort. Patients undergoing surgical resection followed by adjuvant chemotherapy and/or radiotherapy demonstrated the longest DFS and highest two-year OS rates. Similar results have been reported in large randomized trials and retrospective series, which consistently show that surgery remains the cornerstone of curative treatment for early-stage and selected locally advanced NSCLC.^{15,16} Albain et al., in a landmark randomized trial, demonstrated improved progression-free survival with trimodality therapy in selected stage III NSCLC patients, supporting the role of surgery in carefully staged disease¹⁷.

In contrast, the role of surgery in SCLC remains controversial and limited. In the present study, SCLC patients exhibited poor DFS and OS irrespective of treatment arm, with early disease recurrence being common. This finding is concordant with multiple retrospective analyses and population-based studies showing that, except for very early-stage (stage I) disease, surgery does not significantly improve long-term outcomes in SCLC¹⁸. An 18-year retrospective analysis by Curran WJ Jr et al. reported no significant survival difference between surgical and non-surgical approaches in limited-stage SCLC, emphasizing the aggressive nature of this disease¹⁹.

The significantly higher rate of distant metastasis and overall recurrence observed in SCLC patients in our study further underscores the systemic nature of the disease. Similar patterns have been documented in recent studies, which highlight distant failure as the predominant mode of relapse in SCLC despite aggressive chemoradiotherapy²⁰. The higher recurrence rates observed in our cohort may also reflect limitations inherent to peripheral healthcare settings, including delayed diagnosis and limited access to advanced imaging and surveillance.

Definitive chemoradiotherapy remains the standard of care for unresectable NSCLC and limited-stage SCLC. However, in our study, patients treated with chemoradiotherapy alone demonstrated inferior DFS compared with those receiving surgery-based treatment, particularly in NSCLC. This finding is consistent with real-world data from low- and middle-income countries, where treatment-related toxicity, interruptions, and suboptimal supportive care may reduce the effectiveness of concurrent chemoradiotherapy²¹.

The peripheral medical college setting of this study provides important real-world insights. Survival outcomes in our cohort were modestly lower than those reported in high-volume tertiary centers, which may be attributable to factors such as advanced stage at presentation, limited access to molecular profiling, and socioeconomic barriers affecting treatment compliance. Similar disparities have been reported in studies from developing regions, emphasizing the need for context-specific treatment optimization²².

Despite its strengths, including randomized design and standardized treatment protocols, this study has limitations. The relatively small sample size and short follow-up period may limit the generalizability of the findings. Additionally, molecular profiling and immunotherapy were not incorporated due to resource constraints, which may influence outcomes in contemporary practice.

CONCLUSION

The present study reinforces the prognostic superiority of NSCLC over SCLC and highlights the critical role of surgery-based multimodality treatment in improving survival outcomes, particularly in NSCLC. The findings emphasize the need for early diagnosis, appropriate patient selection for surgery, and strengthening multidisciplinary cancer care in peripheral medical colleges.

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