

Outcome of Concurrent Chemoradiotherapy versus Sequential Chemotherapy Followed by Radiotherapy for Limited Stage Small Cell Lung Cancer Treatment

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Abstract

Background: Limited-stage small cell lung cancer (LS-SCLC) is a highly aggressive malignancy with poor prognosis. Concurrent chemo-radiotherapy (CCRT) is recommended by guidelines, but sequential chemotherapy followed by radiotherapy (SCRT) is often used in settings with resource limitations and afraid of intolerability. This study compares CCRT with SCRT in terms of clinical and radiological response, and treatment-related toxicities.

Methods: This quasi-experimental prospective study included 60 histologically proven LS-SCLC patients at the National Institute of Cancer Research & Hospital, Dhaka, from July 2020 to June 2021. Patients were divided equally into two arms: Arm A received CCRT (60 Gy in 30 fractions via 3DCRT with concurrent EP chemotherapy), while Arm B received SCRT (4 cycles of EP followed by 60 Gy in 30 fractions via 3DCRT). Response evaluation was done after 12 weeks post-treatment by clinical and radiology using RECIST 1.1 criteria and RTOG toxicity grading.

Results: Complete clinical response was higher in Arm A (86.7%) vs Arm B (80.0%). Radiological response was similar (86.7% vs 83.3%). Improvement in symptoms such as dyspnea (100% vs 100%), weight loss (63.3% vs 31.8%, $p=0.039$), and chest pain (61.5% vs 23.0%, $p=0.016$) was significantly better in Arm A. Toxicities were manageable; esophagitis (70.0% vs 63.3%) and radiation pneumonitis (43.3% vs 36.7%) were higher in Arm A but not statistically significant.

Conclusion: In this series CCRT demonstrates noninferior clinical outcomes compared to SCRT in LS-SCLC, with comparable response rates and manageable toxicity. It remains a feasible treatment option for limited stage small cell lung cancer treatment.

Keywords: LS-SCLC, concurrent chemoradiotherapy, sequential chemotherapy, RECIST, RTOG, treatment response

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Introduction

Small cell lung cancer (SCLC) represents approximately 15% of all lung cancers and is characterized by rapid growth and early metastasis. The limited-stage subset (LS-SCLC) is confined to one hemi thorax and regional lymph nodes, making it potentially curable with aggressive therapy. According to the National Comprehensive Cancer Network (NCCN) guidelines¹, concurrent chemo-radiotherapy (CCRT) is the standard of care. However, due to logistical constraints and patient

comorbidities, sequential chemotherapy followed by radiotherapy (SCRT) is still commonly practiced in many centers.

Previous studies have shown mixed results regarding the superiority of concurrent over sequential treatment. Meta-analyses and phase III trials^{2,3} support early, concurrent thoracic radiotherapy for improved survival. Nevertheless, the benefit must be balanced against increased toxicity and practical feasibility.

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This study aimed to compare the clinical and radiological response and toxicities between CCRT and SCRT in patients with LS-SCLC treated in a resource-limited setting.

Materials and methods

A prospective, quasi-experimental study was conducted at the Department of Radiation Oncology, National Institute of Cancer Research & Hospital, Dhaka, from July 2020 to June 2021. Sixty patients with histologically confirmed LS-SCLC (Stage I-III) were enrolled and randomized into two arms (n=30 each).

- **Arm A (CCRT):** 60 Gy in 30 fractions (via 3DCRT 2 Gy/fraction, 5 fraction per week) over 6 weeks with concurrent EP chemotherapy (Etoposide 100 mg/m², Cisplatin 75 mg/m² every 3 weeks for 4 cycles).
- **Arm B (SCRT):** 4 cycles of the same EP regimen followed by radiotherapy (60 Gy in 30 fractions via 3DCRT 2 Gy/fraction, 5 fraction per week).

Pre-treatment evaluation included clinical history, blood tests, chest CT, abdominal ultrasound, and MRI brain (if indicated). Treatment response was assessed clinically and radiologically CT scan 12 weeks post-therapy using RECIST 1.1 criteria. Toxicities were graded using RTOG criteria.

Statistical analysis was performed using SPSS v25. Descriptive statistics were used for demographic data. Chi-square or Fisher's exact test was applied where appropriate, with significance set at $p < 0.05$.

Results

Patient Characteristics:

The median age was 58 years in both arms, with a male predominance (93.3%). Majority were urban residents and belonged to poor or middle-income groups. Most patients were illiterate or had education below SSC.

Table I
Baseline Demographic Characteristics of the Patients (n=60)

Parameter	Arm A (n=30)	Arm B (n=30)
Age (years), Mean $\pm$ SD	58.3 $\pm$ 11.5	57.7 $\pm$ 6.2
Age Range (years)	37–68	38–68
Male, n (%)	28 (93.3%)	28 (93.3%)
Female, n (%)	2 (6.7%)	2 (6.7%)
Urban Residence, n (%)	19 (63.3%)	17 (56.7%)
Rural Residence, n (%)	11 (36.7%)	13 (43.3%)
Poor Socioeconomic E21Class(%)	42.0%	42.0%
Middle Class (%)	38.0%	38.0%
Upper Class (%)	20.0%	20.0%
Illiterate, n (%)	19 (63.3%)	18 (60.0%)
Below SSC, n (%)	10 (33.3%)	9 (30.0%)
SSC and above, n (%)	1 (3.3%)	3 (10.0%)

Clinical Stage and Performance Status:

Stage III was more common (56.6% in Arm A vs 63.3% in Arm B), followed by Stage II. Most patients had a Karnofsky Performance Score of 70 or above.

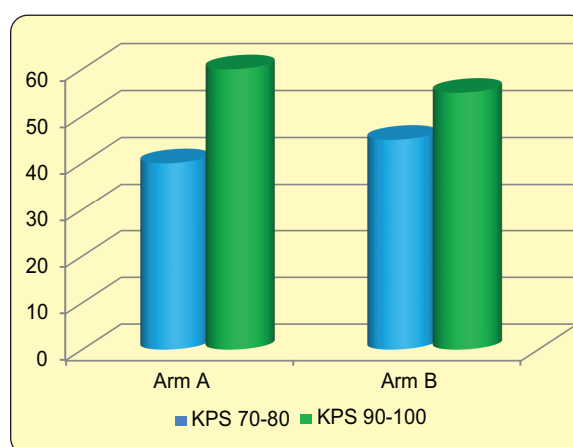
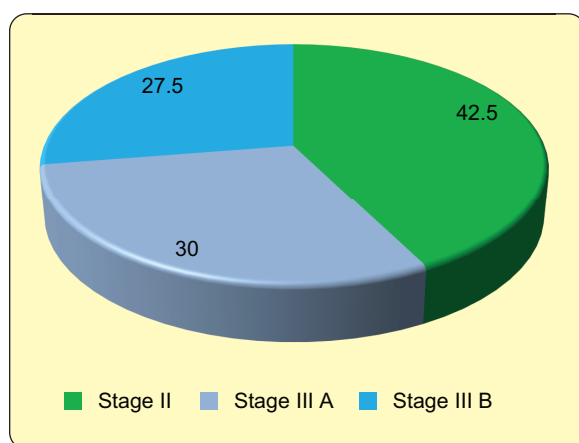


Figure 1: Clinical Stage & KPS Score Distribution

Response Evaluation (12 weeks post-treatment):**Table II**

<i>Response Evaluation by Clinical and Imaging Findings</i>					
Response Type	Clinical – Arm A (n=30)	Clinical – Arm B (n=30)	Imaging – Arm A (n=30)	Imaging – Arm B (n=30)	p-value
Complete Response (CR)	26 (86.7%)	24 (80.0%)	26 (86.7%)	25 (83.3%)	0.723*
Partial Response (PR)	4 (13.3%)	6 (20.0%)	4 (13.3%)	5 (16.7%)	0.723*
Cough Improved	19 (63.3%)	17 (56.7%)			0.855*
Hemoptysis Improved	18 (72.0%)	23 (82.1%)			0.678*
Dyspnea Improved	14 (100.0%)	11 (100.0%)			0.722*
Chest Pain Improved	8 (61.5%)	3 (23.0%)			0.016*
Weight Loss Improved	12 (63.3%)	7 (31.8%)			0.039

Arm A showed better symptom improvement in chest pain ($p=0.016$) and weight loss ($p=0.039$). Radiological responses were similar but numerically better in Arm A.

Toxicity Profile:**Table III**

<i>Combined Toxicity Summary Table</i>			
Toxicity Type	Arm A (n=30)	Arm B (n=30)	p-value
Skin Reaction ($\geq$ Grade 1)	24 (80.0%)	23 (76.7%)	0.821
Esophagitis ($\geq$ Grade 1)	21 (70.0%)	19 (63.3%)	0.092*
Nausea/Vomiting ($\geq$ Grade 1)	25 (83.3%)	21 (70.0%)	0.507*
Fatigue ($\geq$ Grade 1)	18 (60.0%)	17 (56.7%)	0.842
Radiation Pneumonitis ($\geq$ Grade 1)	13 (43.3%)	11 (36.7%)	0.289*
Anemia ($\geq$ Grade 1)	26 (86.7%)	23 (76.7%)	0.795*
Neutropenia ($\geq$ Grade 1)	17 (56.7%)	14 (46.7%)	0.662*
Thrombocytopenia ($\geq$ Grade 1)	11 (36.7%)	7 (23.3%)	0.278*
Neuropathy ($\geq$ Grade 1)	4 (13.3%)	1 (3.3%)	0.202*

Overall toxicity was higher in Arm A but was manageable with conservative treatment. No grade 3 or higher toxicities were reported.

Discussion

Our study demonstrated that concurrent chemoradiotherapy resulted in superior short-term clinical outcomes compared to sequential therapy in patients with LS-SCLC. Complete and partial responses were higher in Arm A, with significantly greater symptom relief in terms of weight loss and chest pain.

These findings are consistent with those of the Japan Clinical Oncology Group Study 9104², which reported a

median overall survival (OS) of 27.2 months in the concurrent group compared to 19.7 months in the sequential group. While our study did not evaluate long-term survival, the significantly better symptomatic improvement and response rates in the concurrent arm support the early initiation of thoracic radiotherapy

Zhao et al.³ reported that CCRT following 3–4 cycles of induction chemotherapy resulted in higher progression-free survival (PFS) and OS in patients with bulky LS-SCLC. Our study population included advanced stage

II and III cases, and Arm A achieved complete response in 86.7% despite disease burden.

De Ruyscher et al.⁴ emphasized that thoracic radiotherapy initiated within 30 days of chemotherapy initiation yields the best survival. In our study, radiotherapy was started with the second chemotherapy cycle in Arm A, reflecting early initiation and likely contributing to better symptom control.

While we used conventional 2 Gy per fraction schedules due to resource limitations, studies using hyperfractionation such as Murray et al.⁵ achieved similar or better outcomes. Our pragmatic approach still demonstrated high efficacy in a low-resource setting.

Gridelli et al.⁶ documented higher toxicity with CCRT, particularly in elderly patients. Our toxicity rates were comparable, with no Grade ≥ 3 events and slightly increased but tolerable esophagitis and hematological effects in Arm A.

Sun et al.⁷ demonstrated non-inferiority of delayed CCRT initiation (3rd cycle), offering flexibility in practice. Our design, starting from the 2nd cycle, sits between early and delayed start and supports flexible yet effective implementation.

Collectively, these findings align with global evidence while highlighting feasibility and clinical benefit of CCRT in real-world, low-resource environments such as Bangladesh.

Conclusion

Concurrent chemo-radiotherapy offers superior short-term clinical benefit in LS-SCLC compared to sequential therapy, with manageable toxicity. It should be prioritized in eligible patients.

Conflict of interest:

Nothing to declare

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