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CHARACTERISTICS, TREATMENT PATTERNS AND OUTCOMES OF PATIENTS WITH SMALL CELL LUNG CANCER - A RETROSPECTIVE ANALYSIS

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Abbreviations:

SCLC-small cell lung cancer,

LD-limited disease,

ED-extensive disease,

CR-complete response,

PR-partial response,

CT-chemotherapy,

RT-radiotherapy,

TRT-thoracic radiotherapy,

PCI-prophylactic cranial irradiation

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ABSTRACT

PURPOSE: The aim of this retrospective study is to present data of patient characteristics, treatment patterns, and treatment results in an unselected patient population with small cell lung cancer (SCLC) in limited disease (LD) and extensive disease stage (ED).

MATERIAL AND METHODS: All patients of carcinoma lung from April 2007 to December 2009 were analyzed for present study, conducted in department of radiotherapy, PGIMS Rohtak, Haryana. Total diagnosed lung cancer patients found were 531, out of which 41 patients were having small cell lung cancer (SCLC). These patients have been analyzed with respect to patient characteristics, chemotherapy, radiotherapy, and treatment outcome.

RESULTS: Twelve (29.27%) of all patients had LD SCLC. Mean age of patient was 58.9 years. Two (5.55%) patient had complete response (CR). Rest 32 (77.77%) patients had partial response. Seven (16.66%) patients did not turn up after treatment. Consecutive thoracic palliative radiotherapy was given in 22 (53.65%) patients. Additional prophylactic cranial irradiation (PCI) was administered to two patients. Sixteen patients (39.02%) received CT with Carboplatin and Etoposide and three (7.32%) patients received oral Etoposide. Mean survival was 3.53 months. ED SCLC was diagnosed in rest 29 (70.73%) of cases. Main metastatic sites were liver 11 (26.82%), bone 6 (14.63%), paraaortic lymph nodes 1 (2.43%) and adrenal in 1 (2.43%) patient. For bone metastasis three patients received palliative RT. Stable disease and progressive disease were the result of first line chemotherapy in both groups. Maximum follow up of patients was up to 15 months.

CONCLUSION: Combined modality treatment with chemotherapy and thoracic radiation therapy is the standard treatment for patients with small cell lung cancer. This is a comprehensive retrospective analysis of SCLC patient population with respect to their demographic characteristics, chemotherapy, radiotherapy, treatment outcome, and survival. Age and gender reached no statistical significance.

INTRODUCTION: Lung cancer is the most common (13%) and deadliest form of cancer out of which, SCLC represents approximately 15%-25% of lung cancer [1]. This is characterized by high growth fraction, rapid doubling time, and early propensity for metastases and equally sensitive to both for radiotherapy (RT) and chemotherapy (CT) [2]. Relapse is frequent within months and overall survival remains poor [3]. It has worst 5-year survival of all histological types [3, 6]. SCLC is strongly associated with smoking, and rarely seen in non smokers [2]. Exposure to ionizing radiation, Uranium, Radon, Methylated ethers are well known cause of this disease [2].

Most common clinical presentation include cough, dyspnoea, chest pain, hemoptysis due to large hilar mass with bulky medaiastinal adenopathy, and symptoms due to metastatic disease i.e. weight loss, debility, bone pain etc [4]. Common site of metastasis are liver [6-8], adrenal, bone marrow [8], bone [9] and brain [7, 8]. Prognosis is related to number of metastatic sites involved [6, 9]. SCLC may also present as endocrine or neurological paraneoplastic syndromes [10, 15].

Staging of SCLC - Two stage classification schemes was used [8].

1. Limited stage disease - limited to ipsilateral hemithorax.
2. Extensive stage disease - spreading beyond the ipsilateral hemithorax including both contra lateral hilar or supraclavicular adenopathy and malignant pleural or pericardial effusion.

Early stage SCLC is diagnosed in less than 5% of SCLC patients. For these patients complete resection with a lobectomy with mediastinal nodal dissection should be considered. For patients with positive nodal involvement, after resection post operative chemotherapy and radiotherapy should be given [11, 13, 14].

Most patients with SCLC extensive disease present with bulky & extensive lymph node involvement. Management of this group of SCLC is more effective combination chemotherapy [11]. Loco regional therapy alone either surgery or radiotherapy improved survival only slightly.

The aim of this retrospective study is to present data of patient characteristics, treatment patterns, and treatment results in an unselected patient population with small cell lung cancer (SCLC) in limited disease (LD) and extensive disease stage (ED).

MATERIALS AND METHODS:

Inclusion Criteria: All patients of carcinoma lung from April 2007 to December 2009 were analyzed for present study, conducted in department of radiotherapy, RCC, PGIMS Rohtak, Haryana. Total diagnosed lung cancer patients found were 531, out of which 41(8%) patients were having SCLC.

Pretreatment evaluation included - detail history, general physical examination, chest radiograph (AP & Lateral), standard laboratory test, ultrasound (USG), CT chest, abdomen & brain for proper staging and metastatic evaluation of liver adrenal, lymph nodes, or MRI (Preferred) and also bone scan when required clinically.

TABLE 1: SHOWING PATIENTS CHARACTERISTICS

PATIENTS CHARECTERISTICS		No.		PERCENTAGE
No of patients received T/t		41(8%)	RT - 22	53.65%
			CT+RT -16	39.02%
			ORAL CT -3	7.31%
Age (years)		<65	33	80.48%
		66-75	5	12.19%
		>75	3	7.31%
Irradiation		Thoracic	38	92.68%
		PCI	2	4.87%
		Palliative bone RT	3	7.31%
Thoracic Surgery			0	0
Stage		LD	12	29.26%
		ED	29	70.73%
Lymph nodes	Total cases 17	Supraclavicular	9	21.95%
		Mediastinal	8	19.51%
Sex		Male	39	95.12%
		Female	2	4.87%
SVC syndrome			7	17.07%
Performance status		>60	38	92.68%
		<60	3	7.31%

Symptoms	Dyspnoea	33	80.48%
	Cough	31	75.60%
	Chest pain	26	63.41%
	Hemoptysis	8	19.51%
Personal habits	Smoker	37	90.24%
	Others	4	9.75%
Metastasis	Liver	11	26.28%
	Bone	6	14.63%
	Adrenal	1	2.43%
	Para aortic LN	1	2.43%

Treatment Design: Age and General Condition of the patients was main factor in determining the Treatment plans. Twenty two patients (53.65%) received Thoracic RT (TRT) - 20 Gy/5 Fr/1 week, and 16 (39.02%) patients received CT with Carboplatin 300mg/m^2 IV and Etoposide 200mg IV Day one and then Etoposide 50 mg capsule TDS for Day-2 and Day-3 followed by TRT and 3 patients (7.31%) were treated with single agent CT with Oral Etoposide 50mg daily. RT volumes and prescribed dose for CT was different for different patients.

TABLE 2: SHOWING TREATMENT PATTERNS OF PATIENTS

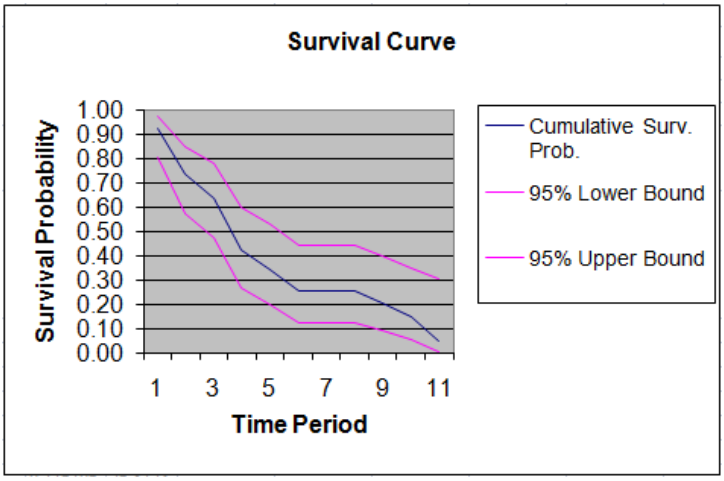
T/t PATTERN	No	PERCENTAGE
TRT	22	53.65%
CT+RT	16	39.02%
ORAL CT	3	7.31%
PCI	2	4.87%
PALLIATIVE RT BONE	3	7.31%

TRT was given by Theratron 780 E or Equinox-80, Co60 machine through AP-PA, parallel opposed field to chest in supine position. Additional prophylactic cranial irradiation (PCI) was administered to two patients. For bone metastasis three patients received palliative RT 800 cGy single session.

TABLE 3: SHOWING RADIATION THERAPY DOSE SCHEDULES

RADIOTHERAPY	DOSE	No
TRT	20Gy/5Fr	22(53.65%)
PCI	30Gy/10Fr	2(4.87%)
PALLIATIVE	8Gy/1Fr	3(7.31%)

RESULTS: Maximum duration of follow up was 15 months, Mean age was 58.69 year, Sex ratio (men: women) was 19:1. Mean overall survival was 3.53 months. Median duration of survival for limited disease was 15 months and for extensive disease 10 months.



Two (5.55%) patient had complete response (CR). Thirty two (77.77%) patients had partial response. Seven (16.66%) patients did not turn up after treatment. Main metastatic sites were liver 11 (26.82%), bone 6 (14.63%), paraaortic lymph nodes 1 (2.43%) and adrenal involvement in 1 (2.43%) patient.

TABLE 4: SHOWING RESPONSE AT ONE MONTH AFTER COMPLETION OF T/t

RESPONSE	No	PERCENTAGE
CR	2	4.87%
PR	32	78.04%
LOST TO FOLLOW UP	7	17.07%

DISCUSSION: Among the sixteen published trials comparing CT alone to CT combined with RT for limited small-cell lung cancer, five trials showed that combined therapy had a significant benefit as compared with CT (Bunn *et al*., Birch *et al*., Perry *et al*., and Creech *et al*. and Schütte *et al.*) [12]. The meta-analysis [12] of thirteen largest trials showed that the administration of TRT led to a 14 % reduction in the mortality rate (P = 0.001), and 5 % increase in the 3-year survival rate.

Pignon *et al*., [12] showed a 50% improvement in 3-year survival, from 10% with CT alone to 15% with the

addition of TRT to CT. Major benefit would be, if treatment variables such as the radiation dose, tissue volume, drugs administered, and timing of RT and CT were optimized [13].

The selection of an optimal schedule of CT combined with RT that would lead to a major increase in survival with minimal toxicity is the principal challenge[13]. We hope that the results of future trials will settle this question.

It was found that the benefit from radiotherapy was greatest in patients less than 65 years of age. The smaller effect of treatment in the older patients could be explained by increased toxicity, but it is not possible to examine this hypothesis with the available data.

Although these studies have demonstrated that RT improves local control rates and survival in limited-stage SCLC [12]. Issues such as the optimal integration of TRT with CT (i.e. concurrent vs. sequential vs. alternating) and the appropriate volume and dose/fractionation scheme still remain unresolved.

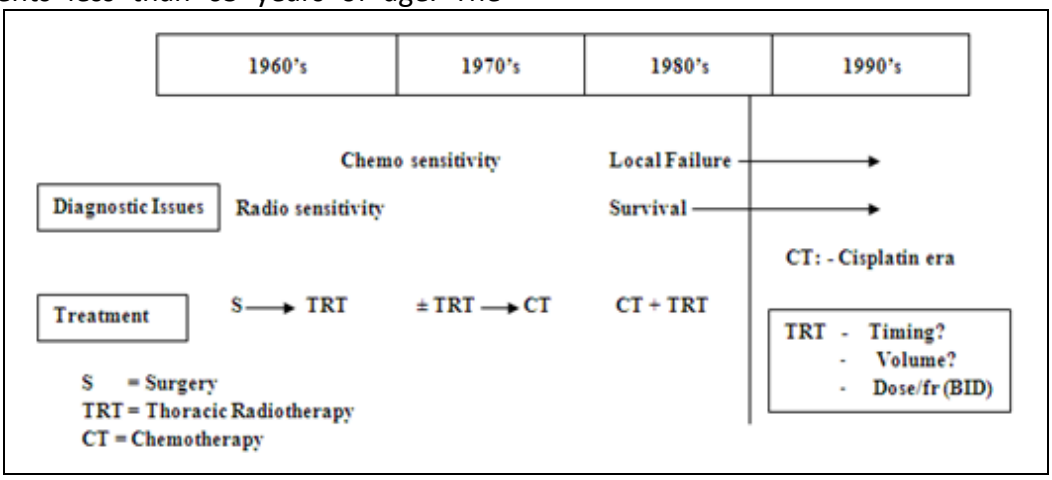


FIG. 1: HISTORIC EVALUATION OF TREATMENT OF SMALL CELL LUNG CANCER

CONCLUSION: Combined modality treatment with CT and TRT is the standard treatment for patients with SCLC. We provide a comprehensive retrospective analysis of SCLC patient population with respect to their demographic characteristics, chemotherapy, radiotherapy, treatment outcome, and survival data. Age and gender reached no statistical significance. The present preferred therapeutic strategy for limited disease is four to six cycles of etoposide-cisplatin (EP) based CT combined with concurrent or alternating RT.

There is no overwhelming evidence that alternating chemotherapeutic regimens are superior to EP-based regimens. TRT moderately improves survival in patients with limited SCLC who are treated with combination CT [15]. CT without RT is the cornerstone of palliative therapy for patients with extensive disease SCLC.

New therapies on the horizon for SCLC include the camptothecin derivatives, mitotic spindle poisons such as taxol, and analogues of the vinca alkaloids.

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