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All Author's Names given below
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Clinicopathological profile and treatment outcomes of lung cancer: An ambispective study from south India

Dr. Divya Bharathi S, Divya Bharathi S, Kannan J, Raja G, Pandidurai M, Arun Ramanan V, Karthikeyan S, Satheesh Kumar D, Kiranmayee N and Vasanth Rooban Narasimman

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Abstract

Introduction: Global Cancer Observatory 2020 reported that worldwide, lung cancer accounts for 11.40 percent of all cancer diagnoses and 18 percent of all cancer-related deaths. Reviewing the histological classification, the epidemiology of lung cancer in India has undergone significant changes over time. In India, information with respect to site wise conveyance of disease can be accumulated from populace based malignant growth libraries. The histological subtypes, on the other hand, are not reported by these data.

Methodology: This record based Ambispective (bidirectional) study was conducted among 394 lung cancer patients registered in a nodal centre located in Chennai, Tamil Nadu. The data pertaining to symptoms, co-morbidities, TNM staging, metastatic sites (if any), Superior vena cava obstruction, performance of PET CT, bronchoscopy, Histopathological class, Chemotherapy, radiotherapy & survival time were collected.

Results: More than half of the candidates (57%) were classified in stage IV A, according to American Joint Committee on Cancer (AJCC) staging manual 8th edition (Table 1). As per TNM staging, Metastasis was seen in 71% of the participants. Epidermal Growth Factor Receptor (EGFR) mutation was seen in 42% of candidates. On Histopathological examination majority of the candidates (60%) were found to have Adenocarcinoma.

Conclusion: Even though differences exist in the survival between lung cancer patients with chemo and without chemo, lung cancer patients with EGFR mutation and without the same and lung cancer patients with metastasis and without metastasis, the difference was not statistically significant.

Keywords: Adenocarcinoma, EGFR, lung cancer, survival

Introduction

Cancer remains a significant global health challenge, casting a profound shadow across the world's health landscape. As of 2020, the staggering statistic of 18.1 million individuals diagnosed with cancer worldwide sends ripples of concern through the global health community. The quartet of breast cancer, lung cancer, bowel cancer, and prostate cancer stands as the most prevalent malignancies, collectively representing over 40% of all cancer incidents. Dauntingly, projections indicate that by 2040, we could see a staggering surge to 28 million new cancer cases annually ^[1].

In the year 2020, the Global Cancer Observatory laid bare the grim truth: lung cancer accounted for 11.40 percent of all cancer diagnoses globally and contributed to a formidable 18 percent of all cancer-related fatalities ^[2]. Drilling down to India, we observe that the specter of lung cancer looms ominously with an estimated prevalence of 7.8 per 100,000 males and 3 per 100,000 females. In this subcontinent, lung cancer, now the second most prevalent cancer, poses a formidable challenge to the medical fraternity and public health ^[3]. While it's no secret that smoking remains a primary trigger for lung cancer, emerging findings hint at additional contributors. Occupational exposure to carcinogens, indoor air pollution, and dietary habits have come under scrutiny for their potential roles in lung cancer development. A diet rich in vegetables and fruits is acknowledged as a protective shield against lung cancer, while the consumption of animal products and dairy items seems to tilt the scales toward susceptibility ^[3].

Corresponding Author:
Dr. Divya Bharathi S
Senior Resident, Department
of Medical Oncology,
Government Royapettah
Hospital affiliated to
Government Kilpauk Medical
College, Tamil Nadu Dr. MGR
University, Chennai, Tamil
Nadu, India

India's high tuberculosis burden further complicates matters, leading to cases where lung cancer patients may initially receive tuberculosis treatment. Nonetheless, certain factors such as age, smoking history, superior vena cava obstruction, and mediastinal signs like voice hoarseness and dysphagia steer the diagnosis toward lung cancer. Clinical examinations may uncover symptoms such as lung collapse, mass, nailbed clubbing, and various lung cancer-related complications, both metastatic and non-metastatic. Radiologically, lung cancer typically manifests as a mass, sometimes accompanied by collapse [4]. The prevalence of tuberculosis in India may also contribute to delayed patient presentations at oncology outpatient departments, often spanning 4 to 6 months [5].

In the arena of histological classification, the epidemiology of lung cancer in India has undergone noteworthy metamorphosis. Historically, squamous and small cell types, closely tied to tobacco consumption, held sway. However, recent years have witnessed a seismic shift, with adenocarcinoma emerging as a prominent histological variant. Today, it stands as the predominant type in India's lung cancer landscape [6]. In the contemporary era of precision oncology, molecular epidemiology has ascended to new prominence. Over the past decade, the tally of identifiable oncogenic drivers in non-small cell lung cancer (NSCLC) has surged, encompassing a minimum of four mutations: EGFR, BRAF, MET, and ERBB2 (HER2) [7].

Surgery remains the primary recourse for treating early-stage lung cancer; however, the proportion of eligible and treated patients hovers in the narrow range of 1% to 5%. In tertiary care settings, the utilization of curative treatments remains dishearteningly low, with only 31% of patients diagnosed at stages I to III A receiving treatment with curative intent [8]. Radiation therapy plays an indispensable role in lung cancer treatment across various stages.

Yet, a glaring urban-rural divide exists in terms of access to radiotherapy facilities and the ability to afford the associated costs. India grapples with insufficient data on the utilization of stereotactic body radiotherapy (SBRT) for lung cancer treatment, mainly due to late-stage diagnoses in many regions and a dearth of infrastructure to support such advanced treatment modalities [9].

In India, population-based cancer registries provide valuable insights into the geographic distribution of cancer. However, these databases typically do not include histological subtypes, necessitating an examination of hospital-based archives for a comprehensive understanding [10]. Thus, this study was conceived with the aim of scrutinizing the clinicopathological profile, treatment outcomes, and survival prospects of lung cancer patients within a pivotal medical center.

Methodology

Conducting a meticulous Ambispective (bidirectional) examination, this study delved into the experiences of 394 lung cancer patients enrolled in a pivotal center nestled within the heart of Chennai, Tamil Nadu.

Embarking on this investigative journey in 2020, we harnessed the vast reservoir of data encompassing lung cancer patients registered from 2017 to 2020, unraveling the retrospective tapestry through the sophisticated threads of our electronic medical record system.

Simultaneously, we cast our gaze forward, encapsulating the narratives of patients gracing the outpatient department of

the nodal center up until 2022, brandishing the banner of prospective insight. Thus, the expansive dataset of our study paints a comprehensive picture of patients registered at the nodal center between 2017 and 2022.

Prior to commencing this study, we diligently sought the imprimatur of the institutional ethical committee, ensuring the sanctity of our research. In the retrospective phase, our data mining expedition was nothing short of exhaustive, drawing from meticulous registers, and any elusive data were meticulously extracted through direct telecommunication with patients.

In the prospective phase, our approach was judiciously purposive. We meticulously examined a total of 394 patient records, comprising 238 retrospective and 156 prospective profiles. It is noteworthy that each of these 394 registries was incontrovertibly confirmed as histologically established cases of lung carcinoma.

Our meticulous data curation encompassed an array of vital parameters, including symptoms, co-morbidities, TNM staging, metastatic sites (if any), Superior vena cava obstruction, utilization of PET CT, bronchoscopy, histopathological classification, chemotherapy, radiotherapy, and crucially, the thread of survival time.

For the discerning eye of statistical scrutiny, we harnessed the formidable Statistical Package for Social Sciences version 24. In our analytical journey, univariate data found expression in proportions and, when quantitative in nature, as means and standard deviations. Bivariate data, on the other hand, underwent a rigorous examination through the Mantel Cox log-rank test.

As a compass guiding our exploration of survival dynamics, we invoked the venerable Kaplan-Meier analysis. Throughout our analytical odyssey, a P value threshold of < 0.05 stood as the lodestar of statistical significance, permeating every facet of our analysis, anchoring our quest for insights and discoveries.

Results

The mean age of the study participants was 58.46 ± 10.51 . Majority of the study participants were Males (71%). More than half of them (53%) were smokers. According to the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, nearly half 47% were ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.

On taking a note on the symptoms; half the candidates (51%) had cough with expectorations, 32% had haemoptysis, 49% had dyspnoea, 29% had chest pain, 10% had head ache, 2% had fever, 5% had hoarseness of voice. Co-morbidities like Hypertension (18%) and Diabetes (19%) was seen in nearly equal proportion of participants.

More than half of the candidates (57%) were classified in stage IV A, according to American Joint Committee on Cancer (AJCC) staging manual 8th edition (Table 1). As per TNM staging, Metastasis was seen in 71% of the participants, of which 14% had Mets in contralateral Lung, 6% in pleura, 34% in bones, 12% in brain, 11% in brain, 8% in adrenal gland, 4.8% in non-regional lymph nodes, 1% in kidneys and 12% presented with PE-pleural effusion. 9% of the candidates had superior vena cava obstruction.

Positron Emission Tomography and Computed Tomography (PET-CT) was done in 40% of the candidates, 14% of the candidates had underwent bronchoscopy. On Histopathological examination majority of the candidates

(60%) were found to have Adenocarcinoma (Table 2). 66% of the candidates have been treated with Chemotherapy, 17% with Radiotherapy to the primary site and 30% with radiotherapy to the metastatic site. Cisplatin + etoposide was the most commonly used regimen and was given to nearly a quarter (23%) of the study candidates. A total of 145 cycles of chemotherapy was given among which many people had 6 cycles of chemo (13%). Epidermal Growth Factor Receptor (EGFR) mutation was seen in 42% of candidates and 16% of candidates mutation status was unknown.

At the end of the study, there were almost equal proportions of alive (40%) and dead (46%) candidates and 14% of them were loss to follow up.

Figure 1 shows that the overall lung cancer patients with chemotherapy has survived longer than the lung cancer patients without chemotherapy. The mean survival time period for a lung cancer patient without chemotherapy was found to be 15.07 months (13.01-17.13) and with chemotherapy was found to be 16.36 (12.12-20.59). The log rank (Mantel Cox) comparison for time to event has not found any statistically significant difference ($p = 0.460$).

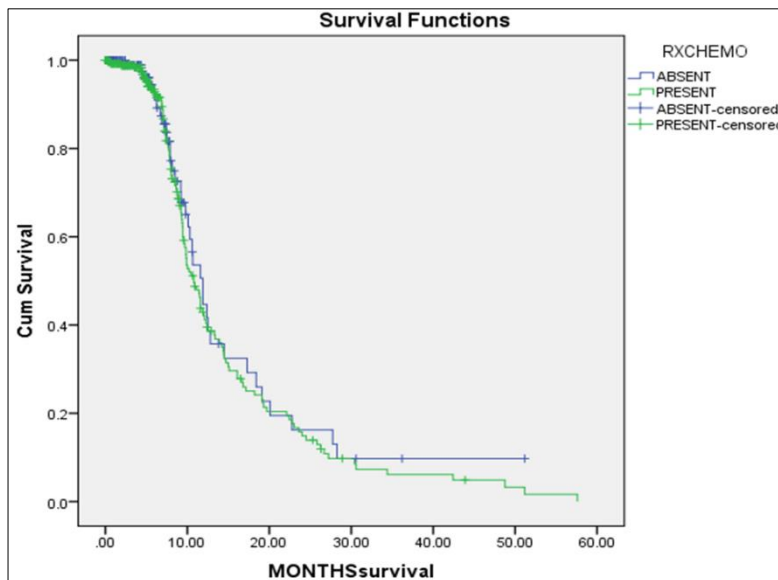


Fig 1: Comparison of survival of Lung cancer patients with and without Chemotherapy

Figure 2 shows that over all patients with metastasis has a lesser survival rate when compared to those without metastasis. The mean survival time of lung cancer patients with metastasis is 21.02 months (17.25-24.79) as that of

patients without metastasis is 23.99 (17.00-30.99). The log rank (Mantel Cox) comparison for time to event has not found any statistically significant difference ($p = 0.332$).

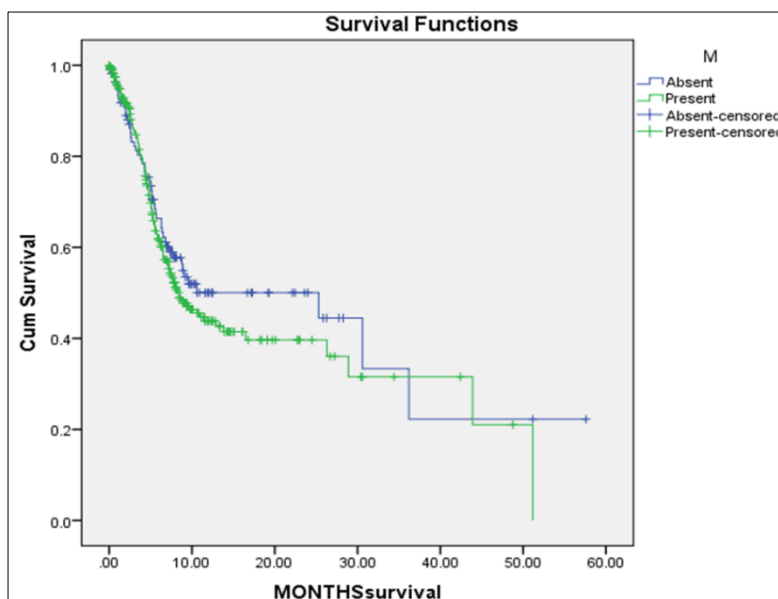


Fig 2: Comparison of survival of Lung cancer patients with and without Metastasis

Figure 3 shows that overall lung cancer patients with EGFR mutation has a greater survival rate than lung cancer patients without EGFR mutation. The mean survival time of patients with EGFR mutation is 22.74 months (17.15-28.33) as that

of patients without EGFR mutation is 20.92 months (16.58-25.26). The log rank (Mantel Cox) comparison for time to event has not found any statistically significant difference ($p = 0.956$).

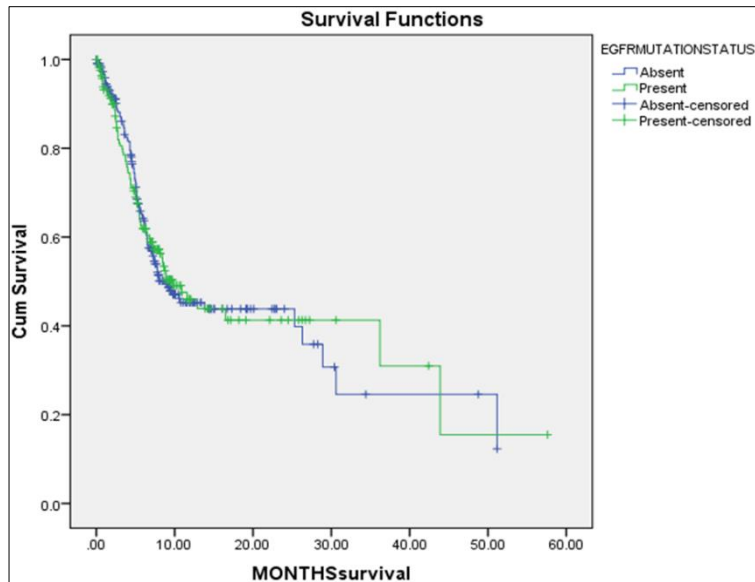


Fig 3: Comparison of survival of Lung cancer patients with and without EGFR mutation

Figure 4 shows that overall lung cancer patients with SVC obstruction has a lesser survival rate when compared to their counterparts. The mean survival time of patients with lung cancer and SVC obstruction was found to be 15.19 months

(13.247-17.137), whereas that of the patients without SVC obstruction was 15.943 months (11.308-20.578). The log rank (Mantel Cox) comparison for time to event has not found any statistically significant difference ($p = 0.360$).

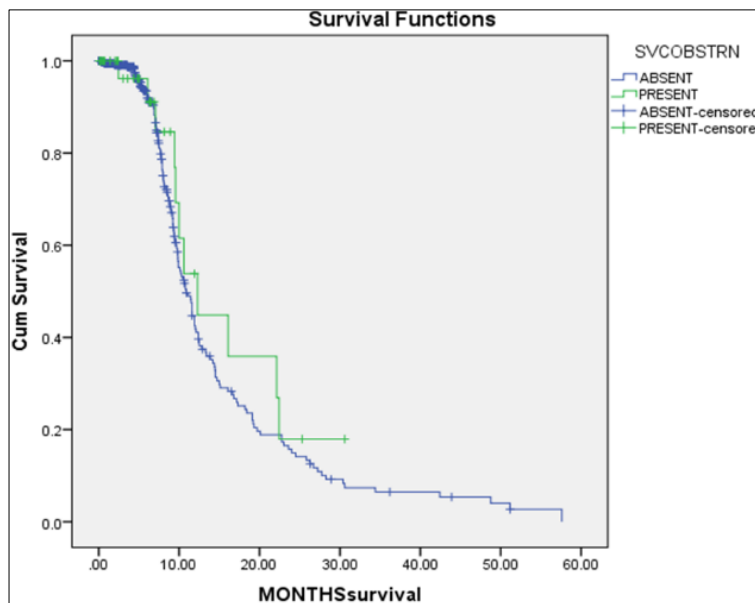


Fig 4: Comparison of survival of Lung cancer patients with and without SVC obstruction

Discussion

In the realm of histological variants, Adenocarcinoma emerged as the reigning monarch, constituting a commanding 60% of all lung carcinoma cases in our study. This resounding prevalence echoes findings from similar investigations. Notably, our results mirror those of Ramani *et al.*, conducted in the southern region of India, where adenocarcinoma held sway as the most prevalent histopathological entity at a staggering 70.4% [4]. In striking contrast, the study by Malik *et al.* at AIIMS revealed Non-small cell lung cancer as the dominant histological variant, commanding an impressive 85.3% share, while Dey *et al.* in eastern India and Jindal *et al.* in Chandigarh unveiled small cell carcinoma as the front-runner at 35.1% and 34.3%, respectively [10, 11, 12].

Turning our attention to comorbidities, diabetes made an appearance in 19% of lung cancer patients within our study cohort. This incidence closely aligns with Ramani *et al.*'s findings, where 23.23% of their participants shared this dual burden [4]. Notably, a comprehensive review by Abudawood M in 2019 draws attention to the mounting evidence linking diabetes with cancer [13]. Exploring the intricate landscape of genetic mutations, we observed a nearly equivalent proportion of candidates harboring EGFR mutations in our study, mirroring Ramani *et al.*'s findings at 42% [4]. In contrast, Mural *et al.*'s investigation showcased a higher prevalence, with EGFR mutations detected in a substantial 62% of their study subjects [14]. The mean survival duration for lung cancer patients sans chemotherapy stood at 15.07 months (13.01-17.13), while

those with chemotherapy experienced a slightly extended survival period of 16.36 months (12.12-20.59). Furthermore, patients grappling with metastasis exhibited a mean survival time of 21.02 months (17.25-24.79), whereas their counterparts without metastasis showcased a mean survival duration of 23.99 months (17.00-30.99).

In a parallel narrative, patients carrying EGFR mutations boasted a mean survival time of 22.74 months (17.15-28.33), juxtaposed with patients devoid of EGFR mutations, who recorded a mean survival period of 20.92 months (16.58-25.26). The tale diverges when considering lung cancer patients with SVC obstruction, where the mean survival period was determined to be 15.19 months (13.247 - 17.137), contrasting with patients without SVC obstruction who exhibited a slightly longer mean survival of 15.943 months (11.308-20.578).

Regrettably, none of these differences attained statistical significance. This could be attributed to the relatively marginal distinctions in survival between these cohorts and, to some extent, the limitations inherent in our sample size.

Assessing the clinic demographic profile of lung cancer cases takes on paramount importance in light of the high mortality rate and the relatively uniform survival outcomes across geographic regions. The contemporary diagnostic landscape, enriched with advanced tools capable of detecting both macroscopic and molecular changes in cancerous tissues, coupled with therapeutic advancements, has ushered in a new era of effective interventions.

Table 1: Classification according to American Joint Committee on Cancer (AJCC) staging manual 8th edition

S.NO	Staging	Frequency (n)	Percentage
1	IV A	223	56.6%
2	IV B	51	12.9%
3	III A	34	8.6%
4	III B	56	14.2%
5	III C	11	2.8%
6	II A	7	1%
7	II B	10	2.5%
8	IA 3	2	0.5%
9	Biopsy not taken	3	0.8%
Total		394	100%

Table 2: Histopathological Examination findings

S. no	Type of carcinoma	Frequency (n)	Percentage
1	Small cell carcinoma	20	5.1%
2	Adenocarcinoma	235	59.6%
3	Squamous cell carcinoma	65	16.5%
4	Adenosquamous cell carcinoma	2	0.5%
5	Mucoepidermoid carcinoma	1	0.3%
6	Poorly differentiated carcinoma	18	4.6%
7	Malignancy proven but unknown histology	23	5.8%
8	Non-small cell lung cancer	25	6.3%
9	Carcinoid	2	0.5%
10	Biopsy not taken	3	0.8%
Total		394	100%

Conclusion

In this comprehensive ambispective study, encompassing 394 lung cancer patients, a clear portrait emerged, with adenocarcinoma reigning supreme as the most prevalent histological variant. A notable trend unveiled the majority of patients presenting at an advanced stage, specifically IVA. While our analysis illuminated distinctions in survival

among subsets of lung cancer patients, including those with and without chemotherapy, individuals harboring EGFR mutations compared to their counterparts without, and patients grappling with metastasis versus those without, it's important to note that these disparities, though intriguing, did not attain statistical significance. The intricate web of lung cancer remains a complex challenge, underscoring the need for continued research and more effective interventions to combat this formidable disease.

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All Author's Name

Dr. Divya Bharathi S

Senior Resident, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Kannan J

Professor and Head, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Raja G

Associate Professor, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Pandidurai M

Assistant Professor, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Arun Ramanan V

Assistant Professor, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Karthikeyan S

Senior Resident, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Satheesh Kumar D

Senior Resident, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Kiranmayee N

Senior Resident, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India

Vasanth Rooban Narasimman

Senior Resident, Department of Medical Oncology, Government Royapettah Hospital Affiliated to Government Kilpauk Medical College, Tamil Nadu Dr. MGR University, Chennai, Tamil Nadu, India