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## Correlation between therapy modalities and survival of lung cancer patients in Surabaya, Indonesia

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### Abstract

Lung cancer is one of the leading causes of death worldwide. Lung cancer treatment are including surgery, chemotherapy, targeted therapy and radiotherapy. Despite therapy modalities mentioned above, lung cancer survival is remained poor. In this research we want to find out the correlation between the current treatment modalities used and the survival of lung cancer patients. Data source is secondary data collected from electronic medical records in oncology polyclinic of Dr. Soetomo General Academic Hospital. Data will be analyzed regarding the correlation between the therapy given and survival of the patients also the correlation between histologic types of lung cancer and therapy given using contingency coefficient. Coefficient we found weak correlation between cancer type and therapy modalities given ( $p < 0.01$  and  $C = 0.301$ ) where targeted therapy is related with adenocarcinoma. Moderate correlation between therapy given and survival of the patients ( $p < 0.01$ ,  $C = 0.533$ ). Targeted therapy related with better survival outcome compared to chemotherapy and patient that get only supportive care. Targeted therapy is related with better prognosis compared to chemotherapy and supportive care. Targeted therapy drugs that used in Adenocarcinoma found in this research is mainly targeting EGFR mutation. Squamous cell carcinoma and small-cell carcinoma mainly treated using platinum-based chemotherapy.

**Keywords:** Lung cancer; Chemotherapy; Targeted therapy; Survival

### 1. Introduction

Lung cancer is malignancies in lung that originates from lung parenchyma or bronchial epithelium [1]. In worldwide lung cancer accounting for 12.4% of new cases and accounting for 17.6% of mortalities caused by malignancies [2]. According to the histological aspect, lung cancer is divided into 2 types, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Non-small cell lung cancer further divided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma [3].

Lung cancer treatment are including surgery, chemotherapy, targeted therapy and radiotherapy. Surgery are used as first treatment in early stage non-small cell lung cancer [4]. Chemotherapy can be used as combination after surgery or together with radiotherapy to increase efficacy. Chemotherapy also used to relieve the symptoms and to slow down the cancer spread when a cure is not possible [5]. Recent development in lung cancer treatment is targeted therapy where the treatment is based on histology and gene mutation typing that present in the lung cancer [6], for example targeted therapy such as tyrosine kinase inhibitor used in lung cancer with EGFR mutation [7].

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Despite therapy modalities mentioned above, lung cancer survival is remained poor, especially for late stage lung cancer. 5-year survival rate when diagnosed in late stage is only around 1% [8]. In this research we want to find out the correlation between the current treatment modalities used and the survival of lung cancer patients.

## 2. Material and methods

Design of this research is analytical observational retrospective study. Sample in this research is lung cancer patients that visit Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in year 2017 until 2019. Data source is secondary data collected from electronic medical records in oncology polyclinic of Dr. Soetomo General Academic Hospital. Variables we used in this research are demographic data including age, sex and smoking history, lung cancer types, stages when diagnosed, therapy modality given to the patients and survival of the patients.

Data that already collected will be processed such as editing, coding, entry and cleaning, after that the data presented with frequency table and pie chart. Data will be checked regarding the correlation between the therapy given and survival of the patients also the correlation between histologic types of lung cancer and therapy given. Both will be analyzed using contingency coefficient to determine the relation and quality of the relation. Statistical analysis will be conducted using IBM SPSS software.

## 3. Results

Total data collected from electronic medical records in oncology polyclinic of General Academic Hospital Dr Soetomo was 1301 data with 962 patients with complete medical record.

**Table 1** Demographic data of lung cancer patients

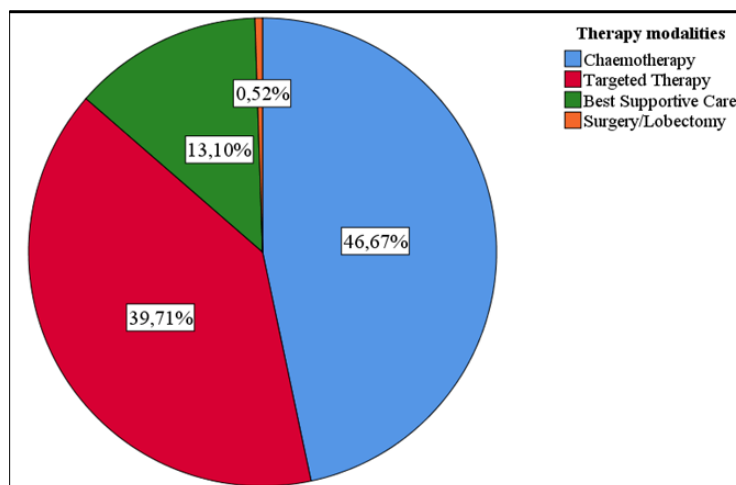
Variable		Number of patients (%)
Age (years)	≤30	13 (1.4%)
	31-40	60 (6.2%)
	41-50	166 (17.3%)
	51-60	340 (35.3%)
	61-70	273 (28.4%)
	71-80	94 (9.8%)
	>80	16 (1.6%)
Sex	Male	592 (61.5%)
	Female	370 (38.5%)
Smoking History	Smoker	520 (64.4%)
	Non-smoker	288 (35.6%)

**Table 2** Type and stage distribution of lung cancer patients

Variable			Number of patients (%)
Lung cancer type		Adenocarcinoma	836 (86.9%)
		Squamous cell carcinoma	98 (10.2%)
		SCLC	28 (2.9%)
Stage	NSCLC	1	3 (0.3%)
		2	11 (1.2%)
		3	110 (11.8%)
		4	810 (86.7%)
	SCLC	Limited	0 (0%)
		Extensive	28 (100%)

Most lung cancer diagnosed in 51-60 years old (35.3%) with the average age of 57.4 years old and median age of 58 years old. Majority of patients is male and smoker is more common compared to non-smoker patients (table 1).

Most common type of lung cancer we found is Adenocarcinoma, and the least common is small-cell lung cancer. Most of NSCLC patients diagnosed at late stage and all of small-cell lung cancer patients diagnosed at extensive stage (table 2).



**Figure 1** Therapy modalities distribution

**Table 3** Correlation between lung cancer type and therapy modalities given

Type	Therapy modalities given (%)				p value	C value
	Surgery	Chemotherapy	Targeted Therapy	Best Supportive Care		
Adenocarcinoma	5 (0.6%)	344 (41.1%)	382 (45.7%)	105 (12.6%)	0.000*	0.301
Squamous cell carcinoma	0 (0%)	79 (80.6%)	0	19 (19.4%)		
Small cell carcinoma	0	26 (92.9%)	0	2 (7.1%)		

\*Significant if  $p < 0.01$

**Table 4** Correlation between therapy modalities given and survival of the lung cancer patients

Survival (months)	Therapy modalities given (%)				p value	C value
	Surgery/Lobectomy	Chemotherapy	Targeted Therapy	Best Supportive Care		
0-6	1 (20%)	233 (51.9%)	147 (38.5%)	125 (99.2%)	0.000*	0.533
7-12	0 (0%)	96 (21.4%)	87 (22.8%)	1 (0.8%)		
13-18	0 (0%)	48 (10.7%)	53 (13.9%)	0 (0%)		
19-24	1 (20%)	33 (7.3%)	34 (8.9%)	0 (0%)		
25-30	0 (0%)	17 (3.8%)	25 (6.6%)	0 (0%)		
31-36	1 (20%)	8 (1.8%)	16 (4.2%)	0 (0%)		
37-42	0 (0%)	5 (1.1%)	10 (2.6%)	0 (0%)		
43-48	1 (20%)	3 (0.7%)	3 (0.8%)	0 (0%)		
49-54	0 (0%)	2 (0.4%)	5 (1.3%)	0 (0%)		
55-60	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)		
61-66	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
67-72	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)		

73-78	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
79-84	1 (20%)	0 (0%)	0 (0%)	0 (0%)		
85-90	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
91-96	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
97-102	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
103-108	0 (0%)	1 (0.2%)	1 (0.3%)	0 (0%)		

\*Significant if  $p < 0.01$ 

Figure 1 above shown the distribution of therapy modalities given to the patients. Only 5 patients get surgery or lobectomy. Most of the patients get chemotherapy with 499 patients and followed by targeted therapy with 382 patients. Chemotherapy agents that given to the patients are platinum-based therapy combined with either Pemetrexed, Paclitaxel, Gemcitabine, Vinorelbine or Etoposide as first line therapy. Docetaxel is used as second line chemotherapy. Targeted therapy drugs that given to the patients is either Gefitinib, Afatinib or Erlotinib as first line, and Osimertinib as second line. The rest of the patients (13.1%) get best supportive care or palliative treatment.

From table 3, only adenocarcinoma patients get surgery or targeted therapy. Majority of patients with squamous cell carcinoma or small-cell carcinoma is given chemotherapy as treatment. From statistical analysis using contingency coefficient we found weak correlation between cancer type and therapy modalities given ( $p < 0.01$  and  $C = 0.301$ ) where targeted therapy is related with adenocarcinoma.

From table 4 there were no patient who survive more than 1 year when only given with best supportive care. The best result in general is found in patients who given targeted therapy with 38.6% of them manage to survive more than 1 year compared with 26.6% of patients who get chemotherapy. From statistical analysis using contingency coefficient, we found moderate correlation between therapy given and survival of the patients ( $p < 0.01$ ,  $C = 0.533$ ). Targeted therapy related with better survival outcome compared to chemotherapy and patient that get only supportive care related to worse survival.

#### 4. Discussion

In this research we found that targeted therapy is mainly used in Adenocarcinoma. About 45% of Adenocarcinoma patients receive targeted therapy for EGFR mutation. Asian population known to have highest percentage of positive EGFR mutation (47%) followed by South America (36%) and Europe with smallest percentage (15%) [9]. Similar results also found where mutations in EGFR gene are observed at a frequency of 10-15% in lung adenocarcinoma. Other gene mutation such as ALK, KRAS, BRAF, PIK3CA, HER2 when combined with EGFR, found in 50% of adenocarcinoma patients [10]. In comparison to non-small cell lung cancer, progress in tumor genetics, chemotherapy, and targeted therapy for SCLC has been slow. Chemotherapy regimens have remained mostly unchanged in the last 40 years, and platinum-etoposide remains the standard of SCLC treatment [11].

First generation of tyrosine kinase inhibitor drugs that target EGFR mutation are gefitinib and erlotinib [12]. Iressa Pan-Asia Study shows that Gefitinib has better progression-free survival rate with 24.9% when compared to paclitaxel-carboplatin chemotherapy with only 6.7% of progression-free survival [13]. Erlotinib, which originally used as second- or third-line therapy given to the patients after progression on platinum-based chemotherapy, now also approved as standard treatment for patient with positive EGFR mutation [14]. Our study also finds that targeted therapy is related with better survival of the patients when compared to chemotherapy, with larger proportion of patient that survive more than 2 years when treated with targeted therapy compared to when treated with chemotherapy. The small amount of patient that receive surgery as treatment may be caused by the small amount of lung cancer patients that diagnosed in the early stage, and surgery is recommended only in early stage of NSCLC or as multimodal treatment in locally advanced lung cancer [15].

The reason we found many patients only survive less than 6 months was because some many patients did not return after the first few visits. This may be responsible for the low overall survival rate in our findings.

#### 5. Conclusion

Targeted therapy is related with better prognosis compared to chemotherapy and supportive care, shown with larger proportion of patients that survive more than 2 years when treated with targeted therapy drugs. Targeted therapy drugs

that used in Adenocarcinoma found in this research is mainly targeting EGFR mutation. Squamous cell carcinoma and small-cell carcinoma mainly treated using platinum-based chemotherapy.

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## Compliance with ethical standards

### *Acknowledgments*

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### *Disclosure of conflict of interest*

There is no conflict of interest regarding this research.

### *Statement of ethical approval*

The presence research work does not contain any studies performed in animals or human subjects by any of the author. The research follows proper ethical procedure.

### *Statement of informed consent*

This research does not involve information of any individual.

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## References

- [1] Siddiqui F, Siddiqui AH. Lung Cancer. Cambridge Handb Psychol Heal Med Second Ed. 2021; 605–6.
- [2] Cruz CSD, Tanoue LT, Matthay RA. Lung cancer: epidemiology, etiology, and prevention. Clin Chest Med. 2011; 32: 605–44.
- [3] Zappa C, Mousa SA. Non-small cell lung cancer: current treatment and future advances. Transl Lung Cancer Res. 2016; 5: 288.
- [4] Raman V, Yang CFJ, Deng JZ, D'Amico TA. Surgical treatment for early stage non-small cell lung cancer. J Thorac Dis. 2018; 10: S898–904.
- [5] National Health Service [Internet]. Lung Cancer – Treatment. UK: NHS. 2019.
- [6] Lwin Z, Riess JW, Gandara D. The continuing role of chemotherapy for advanced non-small cell lung cancer in the targeted therapy era. J Thorac Dis. 2013; 5.
- [7] Ohmori T, Yamaoka T, Ando K, Kusumoto S, Kishino Y, Manabe R, et al. Molecular and clinical features of egfr-tki-associated lung injury. Int J Mol Sci. 2021; 22: 1–18.
- [8] Walach H, Schad F, Thronicke A, Steele ML, Merkle A, Matthes B, Grah C, Matthes H: Overall survival of stage IV non-small cell lung cancer patients treated with Viscum album L. in addition to chemotherapy, a real-world observational multicenter analysis. PLoS One 2018;13:e0203058. Complement Med Res. 2018; 25: 372–4.
- [9] Midha A, Dearden S, McCormack R. EGFR mutation incidence in non-Small-cell lung cancer of adenocarcinoma histology: A systematic review and global map by ethnicity (mutMapII). Am J Cancer Res. 2015; 5: 2892–911.
- [10] Mayekar MK, Bivona TG. Current landscape of targeted therapy in lung cancer. Clin Pharmacol Ther. 2017; 102: 757–64.
- [11] Chan BA, Coward JIG. Chemotherapy advances in small-cell lung cancer. J Thorac Dis. 2013; 5.
- [12] Chan BA, Hughes BGM. Targeted therapy for non-small cell lung cancer: Current standards and the promise of the future. Transl Lung Cancer Res. 2015; 4: 36–54.
- [13] Mok TS, Wu Y, Thongprasert S, Yang C, Saijo N, Sunpaweravong P, et al. Gefitinib or carboplatin–paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009; 361: 947–57.
- [14] Aggarwal C. Targeted therapy for lung cancer: present and future. Ann Palliat Med. 2014; 3: 229–22935.
- [15] Lackey A, Donington J. Surgical management of lung cancer. Semin Intervent Radiol. 2013; 30: 133–40.