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RESEARCH ARTICLE

Evaluation of Surgical Procedures with Technological Limitations for Diagnosis and Staging of Lung Cancers

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ABSTRACT

Objectives: Early diagnosis of lung cancer increases survival. However, advanced technological capabilities for diagnosis and staging may not be available in every hospital. This study evaluated the use of surgical procedures with technological limitations to provide relevant information to similar institutions worldwide.

Methods: Sixty patients, 49 males (84.2%) and 11 females (15.8%), who underwent diagnostic and curative surgery for lung cancer between January 2011 and January 2021were enrolled and analyzed retrospectively. Diagnostic surgery and curative surgery were performed in 23 (38.3%) and 37 (61.7%) patients, respectively. Age, sex, smoking, diagnostic methods, tumor cell type, staging, radiological localization of the lesion, treatment received, and survival were recorded.

Results: The predicted survival for patients >65 years old was 35 (range: 22.6–49.2) months, significantly lower than the 69.4 (range: 51.5–87.4) months for patients ≤65 years ($p>0.05$). Predicted survival was significantly lower for diagnostic surgery than for curative surgery group (19.5 vs. 76.4 months; $p<0.05$) and for small-cell lung cancer (n=5, 8.3%) than for non-small-cell lung cancer (9.9, range: 5.6–14.3 months vs. 60, range: 46.6–73.4 months; $p<0.05$). SCLC was significantly associated with mortality ($p<0.05$) but did not differ among patients with adenocarcinoma or squamous cell or sarcomatoid carcinoma.

Conclusion: Early diagnosis found to significantly improve survival. The most appropriate treatment was radical resection with early diagnosis, which can increase survival in treatable patients with early-stage lung cancer in any center with a thoracic surgeon.

Keywords: Lung cancers, lung resections, staging, survival

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Introduction

Lung cancer is one of the leading causes of cancer-related death in men and women worldwide.[1] survival depends at the stage of illness; therefore only 20% of patients recover. It was diagnosed as Stage I and Stage II.[2] Since lung cancer is asymptomatic in the early period, it is typically diagnosed in the advanced stages.[3] However, early diagnosis enhances survival significantly.[4]

There are noninvasive and invasive (interventional) methods for diagnosing lung cancers. Noninvasive diagnostic methods include radiological examinations, sputum cytology, tumor markers, and nuclear and genetic studies.[5,6] Invasive diagnostic methods include bronchoscopy, endobronchial ultrasonography, transthoracic fine needle aspiration (TTFNA), mediastinoscopy, mediastinotomy, pleural fluid aspiration, video-assisted thoracoscopic biopsy (VATS), and thoracostomy procedures.[5]

Lung cancers are classified as small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC).[7] A combination of chemotherapy and radiotherapy (RT) is used to treat NSCLC. On the other hand, surgery can be performed to treat very early-stage SCLC,[8] and most patients without metastatic disease might be cured by surgery.[7]

Despite progress in targeted therapies, immunotherapy,

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and innovative variations of RT, surgical resection during early-stage disease remains the only realistic hope for patients with lung cancer.[9] The 5-year recurrence-free survival rate following lung cancer surgery is >80% in patients with stage I disease.[10,11] Surgical resection still provides the longest survival in advanced stages.[12]

Within the scope of this research, we aimed to contribute to the literature on surgical procedures with technological limitations and provide information that may be useful to other similar institutions worldwide.

Methods

In this study, 60 patients who underwent diagnostic and curative surgery for lung cancer between January 2011 and January 2021 were analyzed retrospectively. All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was granted from our institution in 2022 with protocol number 2022/19–01. As this was retrospective research, No informed consent was obtained from the participants because of the retrospective nature of the study.

The patients were evaluated according to age, sex, smoking history, diagnostic methods, tumor cell type, staging, radiological localization of the lesion, treatment received, and survival. The TNM staging system, recommended by the American Joint Committee on Cancer, was used in this study. The patients' data were obtained through our institution's electronic database and the e-pulse system. Follow-up was conducted from the electronic database of our hospital of the patients who came to the hospital regularly as members of the control, and via the e-pulse system or by phone for the other patients.

Patients who did not undergo surgery and patients with metastatic tumors, sarcomas, carcinoid tumors, malignant epithelial tumors, and malignant mesothelioma were excluded from the study. The participants had opaque lesions on thorax computerized tomography (CT), and the radiological findings were consistent with malignancies. In addition, the lesion was required to be of primary lung origin and to have shown metabolic activity on positron-emission tomography-CT (PET-CT) performed at a different facility. Patients who met these conditions, were diagnosed with primary lung cancer histopathologically, and had undergone diagnostic or therapeutic surgery at all stages were included in the study.

For histopathologically-diagnosed lung cancers, mediastinoscopy, classical flexible bronchoscopy, and open lung biopsy methods were performed until 2019. In addition to these methods, staging was accomplished by radiological imaging and PET-CT. In previous years tumor resections were performed via posterolateral thoracotomy incision.

We performed resection in patients with stage 1 and 2 lung cancer who were medically suitable for surgery. Chemotherapy and RT were administered to patients who were medically unsuitable for surgery or in advanced stages.

The importance of this study lies in the fact that the centers had limited technological capabilities, such as endobronchial ultrasonography (EBUS) and PET-CT. In addition, video thoracoscopic surgery (VATS), transthoracic fine needle aspiration biopsy (TTFNA), and frozen section have been initiated for the last 3 years in our institution.

Statistical Analysis

SPSS 28.0 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY) software was used to perform all statistical analyses of study data. The descriptive statistics of the data included the mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was measured by performing the Kolmogorov–Smirnov test. An independent sample t-test was performed to analyze independent quantitative data. Statistical significance was accepted for values of $p<0.05$. The chi-square test was performed to analyze independent qualitative data, and the Fischer test was performed when the chi-square test conditions were not met. The effect level was investigated by performing univariate and multivariate logistic regression. Cox regression (univariate and multivariate) and the Kaplan–Meier estimator were performed for survival analysis.

Results

Sixty patients, 49 males (84.2%) and 11 females (15.8%), with a mean age of 61.05±12.1 years were included in the study. The baseline demographics of the study population, type of surgery, additional treatments, stage, survival, follow-up period, tumor type, and mortality are presented in Table 1. All male participants and eight (72.7%) females had a smoking history. Diagnosis was achieved by bronchoscopy in 24 (40%) patients, wedge resection in 14 (23.4%), TTFNA in 13 (21.7%), mediastinoscopy in 6 (10%), pleural biopsy in 2 (3.3%), chest wall biopsy in 1 (1.6%), and frozen section during the operation in 3 (5%).

Surgical methods were preferred for patients with advanced-stage lung cancer that could not be diagnosed with minimally invasive methods, such as bronchoscopy and TTFNA. Therefore, the surgical procedure performed in 24 (40%) patients did not go beyond diagnostic proce-

Table 1. Types of surgery, additional treatments, stage, survival, follow-up times, tumor type

	Mortality (-)				Mortality (+)				p	
	n	%	Mean±SD	Median	n	%	Mean±SD	Median		
Age (year)			57.1±9.4	56.5			63.3±13.2	64.5	0.049	t
Age (year)										
<65	17	77.3			1	50.0			0.038	X^2
≥65	5	22.7			19	50.0				
Gender										
Female	5	22.7			6	15.8			0.503	X^2
Male	17	77.3			32	84.2				
Follow-up months)			54.5±33.3	59.8			32.1±26.7	27.3	0.006	t
Side										
Righ	11	50.0			19	50.0			1.000	X^2
Left	11	50.0			19	50.0				
Lobe										
Lower	12	54.5			20	52.6			0.886	X^2
Middle	1	4.5			2	5.3				
Upper	9	40.9			16	42.1				
Incision										
PLT	13	59.1			19	50.0			0.535	X^2
VATS	8	36.4			14	36.8				
Mediastinoscopy	1	4.5			5	13.2				
Surgery technique										
Lobectomy	14	63.6			16	42.1			0.108	X^2
Wedge resection	5	22.7			12	31.6			0.463	X^2
Lymph node biopsy	1	4.5			5	13.2			0.284	X^2
Pneumonectomy	2	9.1			2	5.3			0.619	X^2
Pleural biopsy	0	0.0			2	5.3			0.528	X^2
Chest wall biopsy	0	0.0			1	2.6			1.000	X^2
Surgical purpose										
Curative	19	86.4			18	47.4			0.003	X^2
Diagnostic	3	13.6			20	52.6				
Exchange rate	18	81.8			18	47.4			0.009	X^2
Neoadjuvant chemotherapy	1	4.5			5	13.2			0.270	X^2
Neoadjuvant RT	0	0.0			4	10.5			0.286	X^2
Adenocarcinoma	8	36.4			19	50.0			0.306	X^2
Small Cell carcinoma	0	0.0			5	13.2			0.148	X^2
Squamous cell carcinoma	13	59.1			13	34.2			0.061	X^2
Sarcomatid carcinoma	1	4.5			1	2.6			1.000	X^2
Adjuvant CT	13	59.1			37	97.4			0.000	X^2
Adjuvant RT	10	45.5			31	81.6			0.004	X^2
Stage										
I	9	40.9			1	2.6			0.000	X^2
II	8	36.4			9	23.7				
III	4	18.2			12	31.6				
IV	1	4.5			16	42.1				

t: Independent sample t-test; X^2: Chi-square test(Fischer test). SD: Standard deviation; PLT: Posterolaretal thoracotomy; VATS: Video-assisted thoracoscopic surgery; RT: Radiotherapy; CT: Computerized tomography.

dures. Curative surgery was performed in 36 (60%) operable patients. VATS was applied in 8 (13.3%) of 36 patients who underwent curative surgery.

The predicted life expectancy in patients >65 years old was 35 (range: 22.6–49.2) months. Hence, the predicted life expectancy was significantly higher at 69.4 (range: 51.5–87.4)

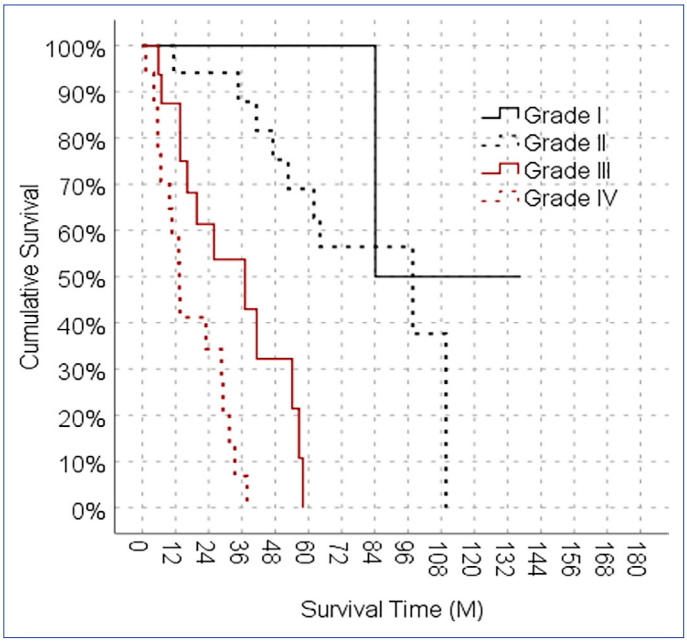

Figure 1. Cumulative survival graph according to stages.

months (p>0.05) in individuals <65 years old. The median time to follow-up was 40.3±31 (range: 1.2–136.8) months. On the other hand, no significant relationship was observed between mortality and sex.

The mean survival duration in the diagnostic surgery group was 19.5±8.7 (range: 14.3–24.6) months and significantly lower than that in the curative surgery group of 76.4±15.2 (range: 60.4 –92.4) months (p<0.05).

The predicted survival time of 9.9 (range: 5.6–14.3) months for patients with SCLC (n=5, 8.3%) was significantly lower than the 60 (range: 46.6–73.4) months in the patients with NSCLC (p<0.05). SCLC was significantly associated with mortality (p<0.05) but did not differ within adenocarcinoma, squamous cell, or sarcomatoid carcinoma.

The mortality rate was higher in patients who were administered adjuvant chemotherapy and adjuvant RT (p<0.05) (Table 1). In the univariate model, age, curative surgery, and adjuvant chemotherapy were significantly associated with mortality (p<0.05). Advanced age, advanced stage, adjuvant chemotherapy, and RT were significantly associated with mortality, whereas curative surgery, early stage, and younger age were significantly associated with survival (p<0.05) (Table 1). Age, curative surgery, neoadjuvant radiotherapy, adjuvant chemotherapy, adjuvant radiotherapy, and SCLC were found to be significant predictors of survival (p<0.05).

Adjuvant chemotherapy and adjuvant radiotherapy were administered to patients with stage 2b and more advanced stages of cancer. The predicted survival time in the group that received adjuvant chemotherapy was 45.7 (range: 34.9–6.6) months, whereas it was 110.5 (range: 74–147) months in patients who did not receive chemotherapy (p<0.05). The mean predicted survival time in the adjuvant RT group was 40.8 (range: 29.1–52.5) months, whereas it was 83.8 (range: 60.3–107.3) months.

Table 2. Factors affecting survival

	Survival time	95% CI	p
Age			
<65	69.4±10.2	51.4–87.4	**0.005**
≥65	35.9±7.6	22.6–49.2	
Curative surgery			
(–)	23.9	14.4–33.5	**0.000**
(+)	74.7	58.6–90.7	
Neoadjuvant RT			
(–)	59.0	44.5–73.4	**0.015**
(+)	18.4	2.2–34.6	
SCLC			
(–)	60.0	46.6–73.4	**0.000**
(+)	9.9	5.6–14.3	
Adjuvan chemotherapy			
(–)	110.5	74.0–147.0	**0.003**
(+)	45.7	34.9–56.6	
Adjuvant RT			
(–)	83.8	60.3–107.3	**0.002**
(+)	40.8	29.1–52.5	
Stage			
I	110.5	74.0–147.0	**0.000**
II	79.3	62.4–96.3	
III	33.5	23.2–43.7	
IV	17.5	11.7–23.3	
Total	55.7	43.0–68.4	

Kaplan Meier (LogRank). CI: Confidence interval; RT: Radiotherapy; SCLC: Small-cell lung cancer; KT: Chemotherapy.

The mean 5-year progression-free survival was 100% at stage 1, 76.4%. 43.5% at stage 2 and stage 3. None of the individuals achieved 5-year survival. The mean survival of the whole study population was 2.8 months. As the stage increased, the predicted survival time decreased significantly (p<0.05) (Fig. 1). The predicted survival duration in the diagnostic surgery group was 23.9 (range: 14.4–33.5 months) months, whereas it was 74.7 (ranged: 58.6–90.7) months in the curative surgery group (p<0.05) (Table 2).

Discussion

The male-to-female ratio in lung cancer varies between 7.5% and 24.1% in Türkiye (4,5,14). In this study, the male-to-female ratio was 5.3%, and the number of female patients was higher than that in the literature. This finding may be attributed to both the high rate of tobacco use in our region's female population and the females' biomass

inhalation exposure. In a large cohort including 11.849 cases, the mean age in lung cancers was 58.4 years but was 59.4 years in another series.[6,13,14] This study's mean age was 61.05 years, approximately similar to the literature. A minority of the patients (n=3, 5%) had never smoked in their lifetime, consistent with literature findings.[13,15]

The rate of lung cancer diagnosis with bronchoscopic methods varies between 71%–90%.[16–19] TTFNA is one of the methods used in the diagnosis of peripherally-located lesions.[20] TTI was also preferred in patients in whom a peripheral mass was detected; however, only 21.7% of the peripherally-located tumors were diagnosed by TTFNA, and 23.4% were diagnosed by wedge resection. Mediastinoscopy, pleural biopsy, and chest wall biopsy were among our less frequently used diagnostic methods, consistent with the literature.[6] EBUS was not yet within our means, and the patients whom we referred outside the province for diagnosis and staging did not complete their treatment in those cities.

In this study, the diagnostic rate via any surgical method was 23%, higher than previously reported.[13,21] Because minimally invasive diagnostic methods were unavailable in our region, the medical teams faced obstacles in using these diagnostic tools.

A significant relationship between age, survival, and predicted life expectancy was observed in this study. The average life expectancy was 35.5.9±7.6 months in individuals >65 years old but higher at 69.4±10.2 months in individuals ≤65 years old ($p<0.05$). Comorbidity factors increase with age, decrease the tolerability of the treatment, and contribute to a negative relationship between survival and age.[22]

A consensus has not been reached regarding the average survival period in the previous literature. Wide-ranging survival analyses have reported an average survival time between 7.9 and 55.2 months, but different results have been obtained because of the different additional treatment procedures used in different institutions.[23–25] All patients were followed up in our center, with a mean survival time of 40.3±31 (range: 1.2–136.8) months. The follow-up and survival periods showed good results in our cohort.

We performed curative surgery on patients diagnosed in the early stages, but the surgery performed in advanced stages was for diagnostic purposes and not always curative. Mean life expectancy in the diagnostic surgery group was significantly lower than in the curative surgery group (19.5±4.2 months vs. 76.4±11.7 months; $p<0.05$). As stated in the literature, the predicted life expectancy decreased with increasing stage, consistent with the literature findings.[2,4,9,26] The fact that we applied VATS in only 13.3% of the cases revealed our previous technological limitations. Therefore, our rate of VATS was lower than that reported in the literature.[9] In subsequent years, the rate of preferring VATS resections gradually increased in our clinic.

The indications for surgical resection in SCLC are limited. In our study, 8.3% of the patients were diagnosed with SCLC, and only diagnostic surgery was performed. The predicted life expectancy was significantly lower in the SCLC patients than in the NSCLC patients (9.9±2.1 months versus 60.0±12.7 months, respectively; $p<0.05$).

In NSCLC, the administration of RT and chemotherapy is controversial. Previous studies indicated that adjuvant RT reduced local recurrence but did not increase survival. In our study, the predicted life expectancy was lower in the groups that received adjuvant RT and chemotherapy than in the groups that did not. This finding can be explained by the advanced stage of the patients receiving adjuvant radiotherapy and chemotherapy. The results of our study were similar to those in the literature showing that adjuvant chemotherapy and RT did not contribute to survival in advanced lung cancers.[4,27,28] There is a consensus that neoadjuvant chemotherapy and RT increase the chance of radical resection by downstaging the tumor. Similar to the literature findings, our study finding showed that some patients also underwent radical resection with down-staged neoadjuvant RT and chemotherapy, but no significant contribution to survival was achieved.[29]

Conclusion

Early diagnosis was found to significantly enhance survival. Advanced technological capabilities may not be available to diagnose and stage lung cancer patients in every hospital. In any health care facility with a thoracic surgeon, interventions must be performed for lung cancer patients. In addition to imaging methods, surgical methods, such as mediastinoscopy, mediastinotomy, pleural biopsy, and wedge resection, can be used to diagnose and stage lung cancer.

Disclosures

Ethics Committee Approval: The study was approved by The Kahramanmaraş Sütçü İmam University Faculty of Medicine Medical Research Ethics Committee (Date: 07/06/2022, No: 2022/19–01).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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