Turk Thorac J 2020; 21(5): 308-13 DOI: 10.5152/TurkThoracJ.2019.19064

Original Article

The Role of Sublobar Resection in T1 N0 Non-Small-Cell Pulmonary Carcinoma

Demet Yaldız[1], Funda Cansun Yakut[2], Şeyda Örs Kaya[2], Soner Gürsoy[1], Mehmet Sadık Yaldız[1]

[1]Department of Thoracic Surgery, Manisa Celal Bayar University, Hafsa Sultan Hospital, Manisa, Turkey
[2]Department of Thoracic Surgery, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, İzmir, Turkey

Cite this article as: Yaldız D, Yakut FC, Örs Kaya Ş, et al. The role of sublobar resection in T1 N0 non-small-cell pulmonary carcinoma. Turk Thorac J 2020; 21(5): 308-13.

Abstract

OBJECTIVES: In this study, we aimed to investigate the effect of resection type on survival in patients with stage IA non-small-cell lung cancer (NSCLC) and other factors affecting the prognosis.

MATERIALS AND METHODS: Between January 2005 and December 2016, we retrospectively screened 269 patients who were resected and were having T1N0M0 non-small-cell pulmonary carcinoma. The survival time after surgery was obtained from the National Population Registration System (MERNIS) system. Patients were classified according to the extent of resection. Additionally, age, sex, smoking, concomitant disease, histological type, pathological stage (T1a-T1b-T1c), and the presence of postoperative complications were evaluated to determine whether they are prognostic factors or not.

RESULTS: A lobectomy was performed in 257 cases (95.5%), and a sublobar resection was performed in 12 patients (4.5%). The 5-year survival was 62.5% for lobectomies and 73.3% for sublobar resections. Although 5-year survival was better in patients with a limited resection, it was not statistically significant (p=0.301). Histopathological evaluation revealed that 130 patients (48.3%) had adenocarcinoma, 113 (42.0%) had squamous cell carcinoma, and 26 (9.7%) had the other types. The 5-year survival rate was 69.9% in patients with adenocarcinoma and 53.2% in squamous cell carcinoma, and this was statistically significant (p=0.036). The overall 5- and 10-year survival rates in all patients were 65.0% and 47.2%, respectively.

CONCLUSION: Although lobectomy is the standard type of resection in the early stage of lung cancer cases in the Thoracic Surgery Department of Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital patients who underwent sublobar resection were found to be having partially better survival, but it was not statistically significant. Owing to the small number of cases, we think that sublobar resections should be prospectively investigated with more extensive series in patients with T1 NSCLC.

KEYWORDS: Wedge resection, segmentectomy, early stage lung cancer

Received: *16.05.2019* ***Accepted:*** *4.09.2019*

INTRODUCTION

Owing to both high incidence and poor prognosis, lung cancer is ranked first among cancer-related deaths. Non-small-cell lung cancer (NSCLC) accounts for approximately 80% of all lung cancers [1]. For the staging of lung cancer, an international TNM (Tumor-Node-Metastases) staging system is used. The T factor is determined by the size of the primary tumor measured on the long axis, the degree of invasion of the tumor, the endobronchial location, and the presence or absence of a satellite nodule.

Although lobectomy and mediastinal lymph node dissection were the standard surgical procedures for NSCLC, there is increasing evidence that sublobar resection may achieve similar survival rates when compared with lobectomy in early stage NSCLC [2-4]. However, there is still no consensus on this subject. In this study, we aimed to compare lobectomy with sublobar resection in stage IA NSCLC if sublobar resection is equivalent to lobectomy in survival.

MATERIALS AND METHODS

This study was performed retrospectively by analyzing the data of T1N0M0 patients who underwent resection with the diagnosis of NSCLC in our clinic between January 1, 2005, and December 31, 2016. All patients were evaluated with chest computed tomography (CT), and after 2010, additionally, with positron emission tomography CT (PET-CT). Patients without enlarged lymph nodes in PET-CT underwent directly to the surgery. Patients with enlarged lymph nodes on CT underwent EBUS-TBNA and/or mediastinoscopy. Neoadjuvant therapy, an incomplete resection (<1 cm between the

Address for Correspondence: Demet Yaldız, Department of Thoracic Surgery, Manisa Celal Bayar University, Hafsa Sultan Hospital, Manisa, Turkey
E-mail: demetyaldiz@gmail.com

tumor and surgical margin), metastatic disease, or different nodules during surgery were determined as exclusion criteria. A total of 269 patients were included in the study. Using the eighth TNM staging system, demographic, clinical, and pathological features of all patients were classified according to age, sex, smoking, comorbidity, type of resection, and histological type of tumor.

Most of the operations were performed by using a posterolateral thoracotomy, and after 2010, 25% of the patients were operated with video-assisted thoracoscopic surgery. All patients received mediastinal lymph node dissection in addition to the pulmonary resection. Approximately 10 mediastinal nodes from at least three mediastinal stations including the seventh station were removed.

Any death occurring within 30 days after surgery has been defined as operative mortality. Follow-up was performed every 3 months for the first 2 years, and every 6 months thereafter. The last follow-up date was January 1, 2017. All records of the patients were obtained from the Cancer Registry and Monitoring System, which is special software created in the hospital information operating system and which can automatically capture the survival information from the National Population Registration System (MERNIS).

Statistical Analysis

The Statistical Package for Social Sciences 21.0 (IBM SPSS Corp., Armonk, NY, USA) was used for statistical analysis. Kaplan-Meier was used for survival analysis, and Cox regression test was used for multivariate analysis of independent variables. Categorized data were compared using chi-square test. $p<0.05$ was considered significant in all analyses.

RESULTS

The study included 269 patients who were operated as pathological T1N0M0 according to the eighth TNM staging system. Of these patients, only 12 (4.5%) had a sublobar resection, all of which consisted of peripheral nodules. Three of these patients underwent sublobar resection because of impaired pulmonary function. In the remaining nine patients, the frozen study was unable to distinguish between metastatic or primary disease. After pathological follow-up, complementary lobectomy could not be performed due to the absence of patients in follow-up or refusal.

A total of 39 (14.5%) patients were women, and 230 (85.5%) patients were men, and there was a significant difference in the 5-year survival between the two genders (men: 58.2%; women: 93.0%; $p<0.001$). The mean age was 59.8±9.9 years (range: 22-82), and at least one comorbidity was present in 50.2% (n=135), most of which were chronic obstructive lung disease, diabetes mellitus, coronary artery disease, or hypertension. Smoking history was 53.8% in women and 80.0% in men (chi-square test, $p<0.001$). There was no significant difference in survival between smoking and non-smoking patients for both genders ($p>0.05$). In all patients, the rate of smoking was 76.2%, and the 5-year survival was similar to nonsmokers (61.5% vs 69.0%; p=0.718). The tumors were located on the left hemithorax in 52.8% of the cases and were slightly more dominant than the right. Only 4.5% of all patients (three segmentectomies and nine wedge resections) underwent sublobar resection (n=12), while the majority underwent lobectomy (95.5%; n=257). The 5-year survival rate for the two groups was 73.3% and 62.5%, respectively (p=0.301) (Figure 1).

The mean diameter of the tumor was 2.2±0.8 cm (range: 0.2–3.0). A total of 33 patients (12.3%) were T1a, 96 (35.7%) were T1b, and 140 (52.0%) were T1c. There was no significant difference in 5-year survival among these three groups ($p>0.05$). Two patients had carcinoma in situ and five had T1mi (minimally invasive adenocarcinoma). Only nine nodules (3.4%) were subsolid in type.

A total of 130 (48.3%) tumors were diagnosed as adenocarcinoma, 113 (42.0%) as squamous cell carcinoma, and 26 (9.7%) as other types. The 5-year survival rate of these histologic types was 69.9%, 53.2%, and 69.6%, respectively. A significant difference was found only between adenocarcinoma and squamous cell carcinoma in 5-year survival (p=0.036). Nine (75.0%) patients with sublobar resection were classified as having adenocarcinoma, two with squamous cell (16.7%), and one (8.3%) as the other type, while those rates for patients with lobectomy were 117 (45.5%) for adenocarcinoma, 114 (44.4%) for squamous cell, and 26 (10.1%) for other types. Adenocarcinoma was significantly higher in patients who underwent sublobar resection (chi square test, p=0.043).

Smoking history was associated with 75.4% of adenocarcinoma, 82.3% of squamous cell carcinoma, and 53.8% of

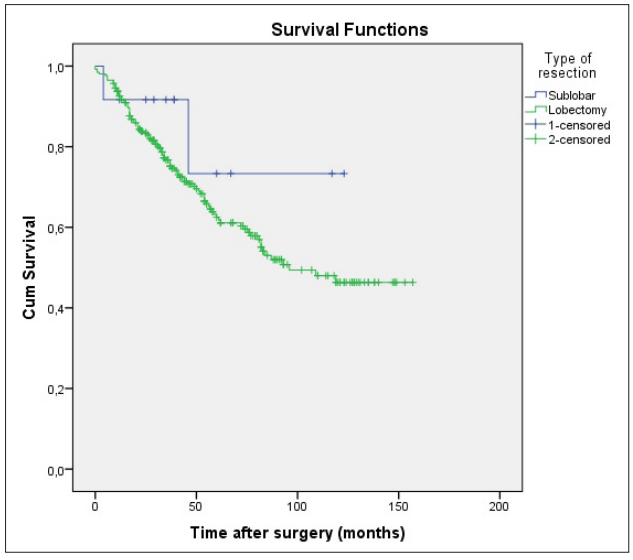

Figure 1. Survival in sublobar resection and lobectomy

MAIN POINTS

- Extend of resection is significant in the surgical treatment of NSCLC.
- There is increasing evidence that sublobar resection may achieve similar survival rates when compared with lobectomy in early stage NSCLC.
- The survival results of sublobar resections due to various reasons were similar to lobectomies in T1N0 NSCLC.

other types. Adenocarcinoma and squamous cell carcinomas had a significant association with smoking (chi square test, p=0.009).

The last follow-up date was January 1, 2017, and the mean follow-up period was 53.9 months. Overall, the mean survival time was 99.0±4.4 months (range: 90.4-107.6), the 5-year survival rate was 63.0%, and the 10-year survival rate was 47.2%. All clinical and pathological features and 5-year survival rates are shown in Table 1, clinical features of patients with lobectomy and sublobar resection are shown in Table 2, and clinical features and survival for both genders are shown in Table 3.

DISCUSSION

Surgical treatment is the primary treatment option for patients with stage I and II lung cancer. For stage I patients, 5-year survival is reported as 60%-90% [5-7]. In our study, 5-year survival was 65.0%, and 10-year survival was 47.2%. The subsolid nodule ratio was 3.4%. Kocaman et al. [6] reported 81.5% for 5-year survival in stage I patients. In their study, a subsolid ratio was reported to be 32.5%. We think that the reason for the relatively low survival rate in our study was attributed to the low rate of the subsolid nodule (3.4%).

The 5-year survival rate was 58.2% for men and 93.0% for women in our study, and it was significantly better in women (p<0.001). Although smoking history was significantly higher in men (p<0.001), the survival of women was significantly better in men with and without a smoking history (p=0.009 vs p=0.014). Some studies have indicated that in early stage lung cancer, adenocarcinoma histology had been confined as a positive prognostic effect in women [8, 9]. In addition, in our study, there was no difference in squamous histologic type (p=0.072), and there was a significant difference in adenocarcinoma between the two genders (p=0.033) (Table 3).

Table 1. Clinical and pathological features of patients and 5-year survival

	n (%)	5-year survival	Univariate analysis p[a]	Multivariate analysis p[b] Odds ratio (95% CI)
Age				
<60	124 (46.1)	61.7	0.858	
≥60	145 (53.9)	64.5		
Gender			***<0.001****	***0.003***
Men	230 (85.5)	58.2		5.72 (1.81–18.12)
Women	39 (14.5)	93.0		
Smoking			0.718	
Smoker	205 (76.2)	61.5		
Non-smoker	64 (23.8)	69.0		
Comorbidity			***0.041***	0.079
Present	135 (50.2)	70.2		1.44 (0.96–2.17)
Absent	134 (49.8)	56.3		
Localization			0.713	
Right	127 (47.2)	64.0		
Left	142 (52.8)	62.1		
T factor				
T1a	33 (12.3)	57.3	T1a-T1b: 0.511	
T1b	96 (35.7)	69.2	T1a-T1c: 0.886	
T1c	140 (52.0)	60.0	T1b-T1c: 0.456	
Histologic type				0.243
Adeno (1)	126 (46.8)	70.8	***1–2: 0.028***	0.787 (0.53–1.18)
Squamous (2)	116 (43.1)	53.3	1–3: 0.923	
Other (3)	27 (10.1)	67.0	2–3: 0.233	
Resection type			0.301	
Sublobar resection	12 (14.5)	73.3		
Lobectomy	257 (85.5)	62.5		

[a]Kaplan-Meier log rank test
[b]Cox proportional odds model
*Statistically significant values were marked in bold and italics

Table 2. Clinical features of patients who underwent lobectomy or sublobar resection

(Pearson Chi-square)	Sublobar resection, 12 (4.5%)	Lobectomy, 257 (95.5%)	p
5-year survival rate	73.3	62.5	
Age			0.781
<60	6 (50.0)	118 (45.9)	
≥60	6 (50.0)	139 (54.1)	
Gender			0.058
Men	8 (66.7)	222 (86.4)	
Women	4 (33.3)	35 (13.2)	
Smoking			0.553
Smoker	10 (83.3)	195 (75.9)	
Non-smoker	2 (16.7)	62 (24.1)	
Comorbidity			0.243
Present	8 (66.7)	127 (49.4)	
Absent	4 (33.3)	130 (50.6)	
Localization			0.694
Right	5 (41.7)	122 (47.5)	
Left	7 (58.3)	135 (52.5)	
T factor	Mean: 1.88 cm	Mean: 2.18 cm	0.414
T1a	2 (16.7)	31 (12.1)	
T1b	6 (50.0)	90 (35.0)	
T1c	4 (33.3)	136 (53.9)	
Histologic type			***0.043****
Adeno	9 (75.0)	117 (45.5)	
Squamous	2 (16.7)	114 (44.4)	
Other	1 (8.3)	26 (10.1)	

* Statistically significant values were marked in bold and italics

Table 3. Clinical features and survival for both genders

	Women (n=39)		Men (n=230)			
	n (%)	5-year survival	n (%)	5-year survival	p[a]	p (Pearson Chi square)
Age						0.722
<60	19 (48.7)	92.3	105 (45.7)	56.5	***0.004****	
≥60	20 (51.3)	95.0	125 (54.3)	59.9	***0.032***	
Smoking						
Smoker	21 (53.9)	92.9	184 (80.0)	58.0	***0.009***	***<0.001***
Non-smoker	18 (46.1)	94.4	46 (20.0)	59.5	***0.014***	
Comorbidity						0.400
Present	22 (56.4)	100.0	113 (49.1)	64.5	***0.011***	
Absent	17 (43.6)	83.7	117 (50.9)	52.5	***0.015***	
T factor						0.290
T1a	5 (12.8)	100.0	28 (12.2)	46.8	0.068	
T1b	18 (46.2)	100.0	78 (33.9)	63.4	***0.024***	
T1c	16 (41.0)	84.4	124 (53.9)	56.9	***0.041***	
Histologic type						***<0.015***
Adeno	25 (64.1)	89.6	101 (43.9)	66.6	***0.033***	
Squamous	5 (12.8)	100.0	111 (48.3)	51.0	0.072	
Other	9 (23.1)	100.0	18 (7.8)	57.9	***0.049***	

[a]Kaplan-Meier log rank test
* Statistically significant values were marked in bold and italics

Of the patients undergoing lobectomy and sublobar resection, adenocarcinoma was 45.5% and 75.0% (p=0.043), respectively. As lobectomy was performed as the standard surgical treatment in our clinic, sublobar resection was performed in only three patients for impaired pulmonary function, and in the remaining nine patients, the frozen study was unable to differentiate diagnosis between metastatic or primary disease. After pathological follow-up, complementary lobectomy could not be performed due to the absence of patients from the follow-up or refusal. The significant majority of patients in sublobar resections were adenocarcinoma. This can be explained by the tendency of peripheral settlement and the difficulty to distinguish in the frozen section of adenocarcinoma.

A lobectomy is the standard surgical treatment for operable NSCLC. In 1995, Ginsberg et al. reported a prospective study comparing the results of a lobectomy with a sublobar resection and found high recurrence rates in the sublobar resection group [7]. However, sublobar resections have been the subject of study for protecting pulmonary reserve [10-12]. In recent years, advances in radiological imaging have increased the identification of smaller tumors [3]. On this basis, many studies have reported and showed that patients who underwent a segmentectomy or wedge resection for peripheral T1N0 tumors had survival similar to patients undergoing lobectomy. Therefore, segmentectomy or a wedge resection in order to protec the lung parenchyma was also shown as a feasible method [6, 13, 14].

In one of these studies, in 2003, Koike et al. [15] reported that the results of sublobar resection for peripheral T1N0M0 NSCLC were similar to those for lobectomy. In a later study, 328 clinical stage IA patients underwent segmentectomy or wedge resection, and it was suggested that segmentectomy should be the first surgical procedure for stage IA NSCLC. On the other hand, Okada et al., in a nonrandomized study conducted in 305 patients, found that even in patients tolerating a lobectomy, sublobar resection had results similar to lobectomy in overall survival [16]. This result was supported by the research of Altorki et al. [17].

In our study, the 5-year survival of patients undergoing a lobectomy was 62.5% and was lower than 73.3% of patients undergoing a sublobar resection; however, there was no significant difference similar to the studies mentioned earlier (p= 0.301).

In some other studies comparing sublobar resections consisting of wedge resection and segmentectomy, segmentectomy and systematic lymphadenectomy are recommended instead of a wedge resection [18-20]. In our study, segmentectomy was the preferred procedure in three patients who underwent sublobar resection because of impaired lung function. However, this number is not enough for a statistical study.

In conclusion, in our study, the survival results of sublobar resections due to various reasons were similar to lobectomies. The number of sublobar resections in our study was meager, thus further research on the feasibility of a sublobar resection for selected patients is needed.

Ethics Committee Approval: Ethics Committee approval for the study was obtained from the Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital (E.1089/29/01/2018).

Informed Consent: Written informed consent was obtained from patients participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.Y., ; Design - D.Y, M.S.Y.; Supervision - D.Y., S.G., Ş.Ö.K.; Resources - D.Y., F.C.Y.; Materials - D.Y., S.G., Ş.Ö.K.; Data Collection and/or Processing - D.Y., F.C.Y.; Analysis and/or Interpretation - D.Y., M.S.Y., Ş.Ö.K.; Literature Search - D.Y., F.C.Y.; Writing Manuscript - D.Y., M.S.Y., F.C.Y.; Critical Review - D.Y., S.G., M.S.Y.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Crino L, Weder W, Meerbeeck JV, Felip E. Early stage and locally advanced (non-metastatic) non-small-cell lung cancer: ESMO Clinical practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 Suppl 5:v103-15. [Crossref]
2. Nakamura H, Taniguchi Y, Miwa K, et al. Comparison of the surgical outcomes of thoracoscopic lobectomy, segmentectomy, and wedge resection for clinical stage I non-small cell lung cancer. Thorac Cardiovasc Surg 2011;59:137-41. [Crossref]
3. Sakurai H, Asamura H. Sublobar resection for early-stage lung cancer. Transl Lung Cancer Res 2014;3:164-72.
4. Naidoo R, Windor MN, Goldstraw P. Surgery in 2013 and beyond. J Thorac Dis 2013;5:593-606.
5. Detterbeck FC, Boffa DJ, Kim AW, et al. The eighth edition lung cancer stage classification. Chest 2017;151:193-203 [Crossref]
6. Kocaman G, Yenigün MB, Elhan AH, et al. Prognostic factors for stage I lung adenocarcinoma and surgical management of subsolid nodules. Turk Gogus Kalp Damar Cerrahisi Derg 2018;26:614-20. [Crossref]
7. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 1995;60:615-23. [Crossref]
8. Wheatley-Price P, Blackhall F, Lee SM, et al. The influence of sex and histology on outcomes in non-small-cell lung cancer: a pooled analysis of five randomized trials. Ann Oncol 2010;21:2023-28. [Crossref]
9. Rodriguez RB, Fuentes JM. Lung cancer in women. Lung Cancer 2012;3:79-89. [Crossref]
10. Jensik RJ, Faber LP, Milloy FJ, Monson DO. Segmental resection for lung cancer. A fifteen-year experience. J Thorac Cardiovasc Surg 1973;66:563-72. [Crossref]
11. Read RC, Yoder G, Schaeffer RC. Survival after conser- vative resection for T1 N0 M0 non-small cell lung cancer. Ann Thorac Surg 1990;49:391-98. [Crossref]
12. Kodama K, Doi O, Higashiyama M, Yokouchi H. Inten- tional limited resection for selected patients with T1 N0 M0 non-small-cell lung cancer: a single-institution study. J Thorac Cardiovasc Surg 1997;114:347-53. [Crossref]
13. Ichiki Y, Hanagiri Y, Baba T, et al. Limited pulmonary resection for peripheral small-sized adenocarcinoma of the lung. Int J Surg 2011;9:155-9. [Crossref]
14. Keenan RJ, Landreneau RJ, Maley RH, et al. Segmental resection spares pulmonary function in patients with stage I lung cancer. Ann Thorac Surg 2004;78:228-33. [Crossref]

15. Koike T, Yoshiya K, Tsuchida M, et al. Risk factor analysis of locoregional recurrence after sublobar resection in patients with clinical stage IA non-small cell lung cancer. J Thorac Cardiovasc Surg 2013;146:372-8. [Crossref]
16. Okada M, Koike T, Higashiyama M, et al. Radical sublobar resection for small-sized non-small cell lung cancer: a multicenter study. J Thorac Cardiovasc Surg 2006;132:769-75. [Crossref]
17. Altorki NK, Kamel MK, Narula N, et al. Anatomical segmentectomy and wedge resections are associated with comparable outcomes for patients with small cT1N0 non-small cell lung cancer. J Thorac Oncol 2016;11:1984-92. [Crossref]
18. Smith CB, Swanson SJ, Mhango G, et al. Survival after segmentectomy and wedge resection in stage I non-small-cell lung cancer. J Thorac Oncol 2013;8:73-8. [Crossref]
19. Sienel W, Dango S, Kirschbaum A, et al. Sublobar resections in stage IA non-small cell lung cancer: segmentectomies result in significantly better cancer-related survival than wedge resections. Eur J Cardiothorac Surg 2008;33:728-34. [Crossref]
20. Nakamura H, Taniguchi Y, Miwa K, et al. Comparison of the surgical outcomes of thoracoscopic lobectomy, segmentectomy, and wedge resection for clinical stage I non-small cell lung cancer. Thorac Cardiovasc Surg 2011;59:137-41. [Crossref]