Original Article

Surgical Outcomes of Sleeve Resections Performed for Non-Small Cell Lung Cancer; A Single Center Experience

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Abstract

Background: Although bronchial sleeve resections were performed instead of pneumonectomy in patients with insufficient pulmonary function initially, it is currently available as an alternative to pneumonectomy even in patients with adequate pulmonary reserve. **Aims:** In this study, we aimed to evaluate the sleeve resections performed for lung cancer in terms of technical, postoperative complication mortality, survival rates and survival factors, complication and to compare them with the literature. **Methods:** Patients who underwent sleeve lung resection with diagnosis of non-small cell lung cancer at our department between January 2012 and December 2017 were included in the study. Patients' data were analyzed according to tumor size, tumor histopathology, hilar/mediastinal lymph nodes invasion status, postoperative complications, operative mortality, resection type, overall survival and diseases-free survival, tumor location, and length of stay in intensive care unit. **Results:** A total of 71 patients included the study. Right upper sleeve lobectomy was applied to 40 (56.3%) patients and left upper sleeve lobectomy was performed to 19 (26.8%) patients. The most common histopathological diagnosis was squamous cell carcinoma. The mean tumor diameter was 3.39 (SD: 2.25) cm. There was no nodal invasion in 41 (57.7%) patients and N1 nodal positivity was detected in 18 (25.4%) patients and N2 positivity in 12 (16.9%) patients. Median survival time was 43.6 months (35.4-51.8 months), the 3- and 5-year overall survival were 65.7% and 40.6%, respectively. There was a statistically significant correlation relationship between nodal invasion and recurrence, but this relation was not found in overall survival. **Conclusion:** In our study, no significant correlation was found between mediastinal lymph node invasion and overall survival. Supporting this result with multi-centered and prospective studies may encourage surgeons for sleeve resection in indicated patients had lung cancer with nodal invasion.

Keywords: *Lobectomy, lung cancer, sleeve resection*

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Introduction

The main goal of surgical resection performed for lung cancer is complete resection of tumor (R0) and systematic lymph node dissection. Pneumonectomy may be required for centrally located tumor to provide the R0 resection. Insufficient pulmonary function and high morbidity and mortality of pneumonectomy have led surgeons to consider parenchyma protective techniques.[1] Although bronchial sleeve resections were performed instead of pneumonectomy in patients with insufficient pulmonary function formerly, it is currently available as an alternative to pneumonectomy even in patients with adequate pulmonary reserve.[2,3] For this reason, initially acceptable sleeve resection/standard

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pulmonary resection rate is 5–8%, but now it increased to 13%.[4]

Studies have shown that the sleeve lobectomy performed for appropriate patients has similar oncologic outcomes with pneumonectomy and it is superior to pneumonectomy in terms of quality of life, morbidity, and functional performance.[5] Sleeve resection should be considered when malignant N1 lymph nodes or masses infiltrating the lobar bronchus and/or the pulmonary artery branch and it is often performed for upper lobe, but rarely are applied for left lower lobe or right bilobectomy.[6,7] In this study, we aimed to evaluate the sleeve resections performed for lung cancer in terms of technical, postoperative complications, mortality, survival rates, and survival factors and compared them with the literature.

Subjects and Methods

Patient selection

After the approval of the local ethics committee of Gazi University the records of the patients who underwent sleeve resection surgery for non-small cell lung cancer in our department between January 2012 and December 2017 were reviewed retrospectively. Standard preoperative preparation, examinations, pulmonary function tests, anesthesia consultation, and fiberoptic bronchoscopic evaluation were performed on all the patients. Patients who do not receive adjuvant/neoadjuvant treatment according to the stage of cancer despite the indication and those whose follow-up records could not be obtained were not included in the study. Data of patients were analyzed according to tumor diameter, tumor stage, histopathology, hilar/mediastinal lymph node invasion status, postoperative complications, operative mortality (in 30 days after the operation), resection type, tumor location, duration of intensive care unit, overall survival (OS), and disease-free survival (DFS). Also correlation between 5-year OS and DFS and lymph node metastasis and tumor diameter was investigated.

Surgical technique and postoperative approach

Posterolateral thoracotomy with single lung ventilation under the double-lumen intubation was performed to patient. Only 1 patient operated with video-assisted thoracic surgery (VATS) technique. Lymph node dissection was performed before pulmonary resection to identify possible lymph node metastasis, to make bronchial anastomosis comfortable, and to prevent it from being damaged. The pulmonary artery/vein was devised with conventional suture technique or vascular stapler. The proximal and distal edges of bronchus planned anastomosis were released, cut, and then bronchial anastomosis was performed by continued suture technique with polydioxanone (PDS 3,0). Frozen section study of surgical margins was performed in all patients. Anastomosis line was covered by pericardial fat tissue after the air-leak control. Patients were extubated in the operating room and they were admitted to intensive care unit and antibiotic prophylaxis and low molecular weight heparin therapy were initiated. Chest tubes were removed according to lung expansion and drainage.

Statistical analyses

The SPSS for Windows version 20.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The OS and DFS were investigated by Kaplan–Meier test. Log rank (Mantel-Cox) and Cox Regression methods were used to analyze the difference in survival between the groups. Statistical analyses were performed in 95% confidence interval, two-sided *P* value was calculated and considered significant when it was less than 0.05.

Results

A total of 71 patients who fulfilled the inclusion criteria were in the included the study. Indication of sleeve lung resection was non-small cell lung cancer in all patients. The percentage of number of patients undergoing sleeve lung resection to standard lung resections (segmentectomy, lobectomy, or pneumonectomy) between January 2012 and December 2017 was 8.1% (71/869) in our department. The clinicopathological characteristics of patient were given in Table 1. Complication rate was 19.7% and most common complication was prolonged air leak. Revision operation was required to 1 patient for hemorrhage and 2 patients for anastomosis separation.

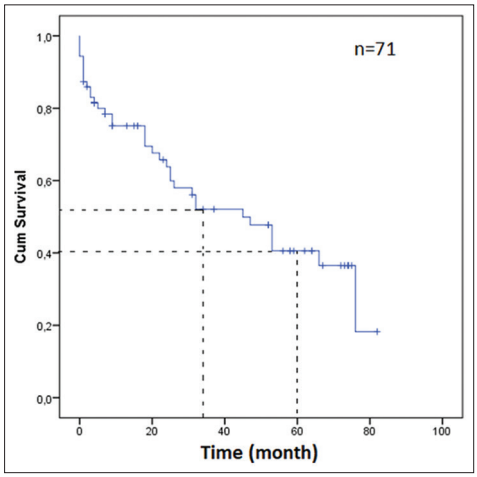

Figure 1: The overall survival curve of patients

Table 1: Clinicopathological characteristics of patients

		Study population *n*=71	Percentage
Gender			
	Male	61	85,9
	Female	10	14,1
Age (mean±SD)	59±1,2		
Age range (years)	25-76		
Histology			
	Squamous Cell Carcinoma	44	62,0
	Adenocarcinoma	13	18,3
	Carcinoid Tumor	7	9,9
	Other	7	9,9
Tumor Stage (IASCL-TNM8)			
	I	30	42,3
	II	30	42,3
	IIIA	10	14,1
	IIIB	1	1,4
Tumor Diameter (mean±SD)	3,39±0,26 cm		
Tumor Diameter Range (cm)	0,2-11		
Duration of ICU (mean±SD)	2±0,3 day		
Duration of ICU Range (day)	1-23		
Tumor Diameter (cm)			
	≤1	18	25,4
	1-≤3	16	22,5
	3-≤5 cm	31	43,7
	5-≤7 cm	3	4,2
	>7 cm	3	4,2
Mediastinal Lymph Node			
	N0	41	57,7
	N1	18	25,4
	N2	12	16,9
Local Recurrence Status			
	No	56	78,9
	Yes	15	21,1
Technique			
	RUL	40	56,3
	LUL	19	26,8
	RLSB	4	5,6
	LLL	4	5,6
	P	4	5,6

Abbreviations: Cm: Centimeter, ICU: Intensive care unit, LLL: Left lower sleeve lobectomy, LUL: Left lower sleeve lobectomy, RLSB: Right lower sleeve bilobectomy, RUL: Right upper sleeve lobectomy, P: Sleeve pneumonectomy

Operative mortality rate (until the postoperative 30th day) was 5.6%. The median duration of intensive care unit was 2 day (range 1-23). Right upper sleeve lobectomy was performed in 40 patients (56.3%) and left upper sleeve lobectomy was performed in 19 patients (26.8%). Squamous cell lung cancer was the most common histopathological diagnosis and it was detected in 44 patients (62%). Adenocarcinoma was detected in 13 patients (18.3%). Mean tumor diameter was detected as 3.39 cm (SD: 25). When patients were classified according to IASLC TNM 8 staging 30 patients (42.3%) were classified as stage I, 30 patients (42.3%) were classified as grade II, 10 patients (14.0%) were classified as grade IIIA, and only 1 patient (1.4%) was belong grade IIIB. Mean number of removed N1 lymph node was 6.76 and N2 was 13.7. There was no mediastinal lymph node metastasis in 41 patients (57.7%), whereas lymph node metastasis was detected in 18 patients (25.4%) at N1 stations and in 12 patients (16.9%) at N2 stations. Median survival of our study was 44 months, 3- and 5-year OS were found as 65.7% and 40.6% respectively [Figure 1]. Patients classified according to tumor diameter, and statistically significant correlation was detected between the groups with tumor diameter ≤ 1 cm and > 1 cm (P = 0.03) in terms of OS. According to mediastinal lymph node invasion median survival was 48, 43 and 22 months in patients with N0, N1 and N2 positive respectively, but that difference was not statistically significant [Figure 2, P = 0.09]. When the patients were analyzed according to their recurrence status, local recurrence was detected in 15 patients (21.1%). There was a statistically significant correlation between DFI and lymph node metastasis [Figure 3, P = 0.001].

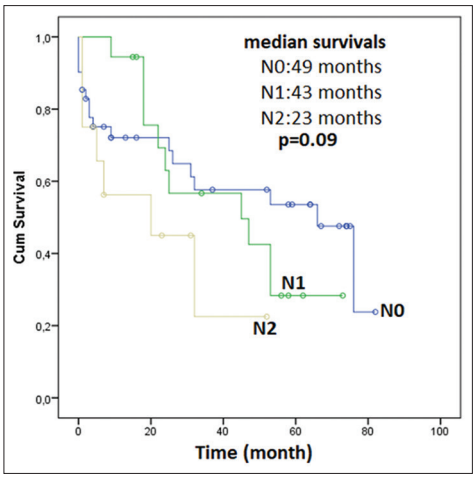

Figure 2: The survival differences according to lymph node invasion (the best OS was detected in patients with N0 and the worst OS was in N2-positive patients, but this correlation was not statistically significant)

Table 2: Outcomes of sleeve resection performed for lung cancer in various studies.

Author	*n*	Op Mort (%)	5-Year OS %	R (%)	Lymph Node Status	Time (Year)
Berry[3]	35	5,7	65,2*	26	N1:100%	2
Yildizeli[9]	218	4,1	57,1	14,4	N0:39% N1:43% N2:18%	25
Park[13]	105	1	58,4	14,3	?	9
Kim[14]	49	6,1	59,5	32,6	N0:37% N1:37% N2:26%	9
Tedder[15]	1915	7,5	40	12,5	?	12
Mehran[16]	142	2,1	46	23	N0:51,4% N1:38,7% N2:9.9%	20
Okada[17]	151	2	48	8	N0:23%, N1:27%, N2:50%	14
Ludwig[18]	116	4,3	39	10,3	N0: 39,6%, N1:28,4%, N2:31,8%	10
Our study	71	5.6	40.6	21.1	N0:57.1, N1:25.4%, N2:16.9%	5

N: number of patient included in study, Op Mort: Operative mortality, OS: Overall Survival. *: 3 year survival rate, R: Recurrence

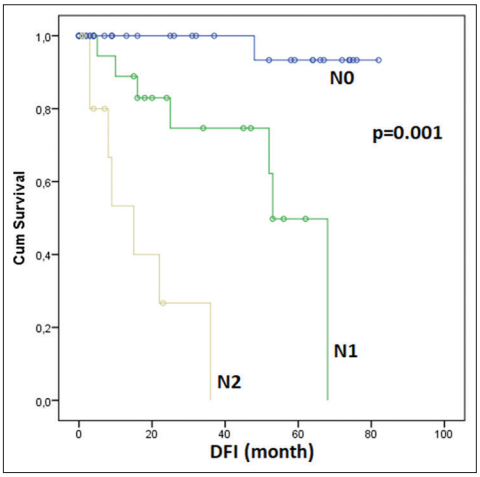

Figure 3: There was statistically significant correlation in terms of the disease-free survival according to lymph node invasion status, P = 0.001)

Discussion

Some authors believe that pneumonectomy is a disorder by itself that should be avoided and they suggest parenchymal protective surgical techniques in appropriate patients.[8] Lung sleeve resections recommended for patients with limited respiratory reserve initially, it is increasingly becoming an alternative to pneumonectomy for indicated situation even if respiratory reserve is adequate.[2,3] It is reported that the sleeve resections are 3-19% of conventional resections such as segmentectomy, lobectomy. or pneumonectomy in literature.[2-9] In our study, that ratio was 8.1% (71/869) and it was consistent with the literature. Studies have reported that although technically more difficult than standard resections, sleeve lobectomy is superior to standard pneumonectomy in terms of increased survival, reduced operative mortality, reduced complication rates, and increased quality of life. Lung sleeve resections can also be performed as arterial sleeve resection in situation when the tumor invades the pulmonary artery.[3,4] The preservation of the bronchial artery supporting the anastomosis line with a well-vascularized tissue and making anastomosis with proper tension are recommended during the sleeve resection.[10] Yildizeli *et al*. reported that in their series the most frequent resection type was right upper sleeve lobectomy (45%) followed by left upper lobe sleeve lobectomy (28%).[9] Yamamoto *et al*. reported that in their study included 173 bronchial sleeve resections, right upper sleeve lobectomy rate was 40% and the upper left sleeve resection rate was 28.3%.[4] The most frequent resection type in our series was right upper lobe sleeve lobectomy as 56.3% followed by left upper lobectomy as 26.8 and this result consistent with literature. Yildizeli *et al*. reported the operative mortality rate was 4.1% in their study and they stated preoperative findings of half of the dead patients were contraindicated for pneumonectomy.[9] Pages *et al*. reported that the operative mortality rate of sleeve resection was about 5% in their meta-analysis and they reported pneumonectomy similar to the mortality rate and they stated that this ratio is similar to pneumonectomy.[11] Yamamato *et al*. reported the operative mortality rate was 1.4%, while Toker said it was 2.59%.[2,4] Various studies have reported that operative mortality of sleeve lobectomies was significantly lower than in pneumonectomies.[11-13] On the contrary Berry and Kim reported that the perioperative mortality was 5.7% and 6.1%, respectively, and they were higher than the pneumonectomy group.[3,14] Tedder *et al*. found that operative mortality was 5.5% in sleeve lobectomy and 20.9% in sleeve pneumonectomy in their study.[15] The operative mortality rate was 5.6% in our study and it was consistent with the literature.

Yamamoto *et al*. reported the complication rate was 39% in the sleeve lobectomy series and they stated that the most frequent complication was long-term air leakage in 7 days. They found anastomosis complication in 7 patients including fistula 4 (1.9%) patients and stenosis 3 (1.4%) patients.[2] Yildizeli *et al*. found that morbidity rates were 22.9% in their series included 218 cases and they indicated the most common complication was pneumonia.[9] Toker *et al*. declared complication rate of their study group was 20.7 and they specified that most frequent complication was prolonged air leak.[4]

In our study, complication rate was 22.5% and the most frequent complication was prolonged air leak (>7 days). Reoperation was required in 2 patients (2.8%) due to anastomosis separation and 1 patient (1.04%) for bleeding.

The most common concern in bronchoplastic resections is increased risk of locoregional recurrence. In various studies, locoregional recurrence rate in N1 station positive patients was found to be higher than pneumonectomy.[3,14] Tedder *et al*. local recurrence rates were reported as 12.5% for sleeve lobectomy and 4.2% for sleeve pneumonectomy.[15] Mehran *et al*. compared the local recurrence rate with nodal positivity and they found local recurrence rate in patients without nodal involvement was 16.6% and 57.1% in N2-positive patients.[16] Kim *et al*. reported the local recurrence rate was 32.5% in their sleeve resection series and they attributed high recurrence rate to R1 resection.[14] In our study, local recurrence was detected in 15 patients (21.1%). There was a statistically significant correlation between the presence of metastases in N1 and N2 lymph node stations and recurrence.

The 5-year OS of sleeve resections performed for the non-small cell lung cancer in various studies has been reported between 39% and 59.5%, it was summarized in Table 2.[3,9,13-18] It has been reported by many authors that the presence of N2 station invasion adversely affects the surveillance.[3,9] Tedder *et al*. reported the 5-year OS was 40% and they emphasized that it was reached to 60% in patients without nodal invasion.[15] It was declared in another study including 151 cases, the most important prognostic factor was N2 nodal invasion for 5-year OS.[17] Similarly, Fadel *et al*. indicated that 5-year OS was similar for N0 and N1 positive patients and significantly worse for N2-positive patient.[19] It is possible to find different findings in the literature. Deslaures *et al*. claimed that there was no statistically significant correlation between N2 station invasion and 5-year OS in patients undergoing sleeve resection for non-small cell lung cancer.[20] Mehran *et al*. also found there was no significant difference in 5-year OS compared to N0 in N1-positive patient underwent sleeve lung resection series.[16] Furthermore, Okada *et al*. specified that T-factor (Tumor diameter) is an independent prognostic factor in non-small cell lung cancer surgery.[21]

The 5-year OS was 40.6 in our study. When patients were classified according to tumor diameter, we have detected that there was statistically significant difference for OS in patients who had smaller than 1 cm tumor diameter compared to other group ($P = 0.03$). We found that the OS of patients worsened from N0 to N2 by mediastinal lymph node invasion but that difference was not statistically significant. These results are consistent with some studies in the literature.[16,20,21] Although that situation may be attributed to number of patients is different between in-groups, it is suggested that the T factor may be a more important prognostic factor than the N factor in the patients planned sleeve resection for lung cancer. Nevertheless, there is a need for studies which involved more cases and multicentralized to support this suggestion.

The limitations of our study are it is a retrospective and single-centered study, it has limited number of patients and there is no homogeneous distribution among the groups.

As a conclusion, there was no significant correlation between the presence of mediastinal nodal invasion and OS in patients undergoing sleeve resection for lung cancer and it was found that studies with similar results were obtained in the literature. If this suggestion is supported by multi-centered and prospective studies involved more patients it would encourage the surgeons for sleeve resection in indicated patients for lung cancer.

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Conflicts of interest

There are no conflicts of interest.

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