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Pulmonary artery reconstruction methods and long-term results in patients with lung cancer

Akciğer kanserli hastalarda pulmoner arter rekonstrüksiyon yöntemleri ve uzun dönem sonuçlar

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ABSTRACT

Background: This study aims to evaluate the long-term results of patients with non-small cell lung cancer who underwent pulmonary artery resection and reconstruction.

Methods: Between January 2010 and January 2023, a total of 50 patients (47 males, 3 females; mean age: 60.5±8 years; range, 43 to 83 years) who underwent lobectomy and pulmonary artery resection and reconstruction due to invasion of the pulmonary artery were retrospectively analyzed. Partial resection was performed in 45 patients. Circular pulmonary artery resection was performed in the remaining five patients. Demographic data of the patients, histopathology, lymph node metastasis, tumor size, T status, stage, comorbidity, neoadjuvant treatment and adjuvant treatment were recorded. Survival analysis was performed.

Results: All patients were operated via thoracotomy. Except for those who underwent tangential resection with a stapler, the proximal and distal parts of the artery were resected by placing a Satinsky clamp. In 35 (70%) patients, pulmonary artery invasion originated from the tumor itself, while in 15 (30%) patients, it originated from the lymph node. The five-year survival rate was 46%, with an operative mortality rate of 6% and a morbidity rate of 24%. Cox regression analysis identified neoadjuvant treatment and N2 disease as statistically significant factors influencing survival. The median disease-free survival time for all patients was 27.9 (range, 4.5 to 51.2) months. Operated side, neoadjuvant treatment, N status, reason for pulmonary artery resection, sleeve resection and type of pulmonary artery resection showed statistically significant differences in the Kaplan-Meier analysis.

Conclusion: Our study results suggest that pulmonary artery resections and reconstructions are feasible with acceptable morbidity and mortality rates. Neoadjuvant treatment, N2 disease, and the reason and type of pulmonary artery resection are potential factors influencing long-term survival. Pulmonary artery reconstruction is safe in experienced clinics with promising long-term survival outcomes.

Keywords: Morbidity, mortality, non-small cell lung cancer, pulmonary artery reconstruction, survival.

ÖZ

Amaç: Bu çalışmada küçük hücreli dışı akciğer kanseri olan pulmoner arter rezeksiyonu ve rekonstrüksiyonu yapılan hastaların uzun dönem sonuçları değerlendirildi.

Çalışma planı: Ocak 2010 - Ocak 2023 tarihleri arasında pulmoner arter invazyonu nedeniyle lobektomi ve pulmoner arter rezeksiyonu ve rekonstrüksiyonu yapılan toplam 50 hasta (47 erkek, 3 kadın; ort. yaş: 60.5±8 yıl; dağılım, 43-83 yıl) retrospektif olarak incelendi. Kırk beş hastaya kısmi rezeksiyon yapıldı. Geri kalan beş hastaya dairesel pulmoner arter rezeksiyonu yapıldı. Hastaların demografik verileri, histopatolojisi, lenf nodu metastazı, tümör boyutu, T durumu, evresi, eşlik eden hastalıkları, neoadjuvan tedavi ve adjuvan tedavileri kaydedildi. Sağkalım analizi yapıldı.

Bulgular: Tüm hastalar torakotomi ile ameliyat edildi. Stapler ile tanjansiyel rezeksiyon yapılanlar hariç, arterin proksimal ve distal kısımları Satinsky klempi yerleştirilerek rezeke edildi. Pulmoner arter invazyonu 35 (%70) hastada tümörün kendisinden kaynaklanırken, 15 (%30) hastada lenf nodundan kaynaklandı. Beş yıllık sağkalım oranı %46, operatif mortalite oranı %6 ve morbidite oranı %24 idi. Cox regresyon analizinde neoadjuvan tedavi ve N2 hastalık sağkalımı etkileyen istatistiksel olarak anlamlı faktörler olarak bulundu. Tüm hastalar için medyan hastalıksız sağkalım süresi 27.9 (dağılım, 4.5-51.2) ay idi. Ameliyat edilen taraf, neoadjuvan tedavi, N durumu, pulmoner arter rezeksiyonu nedeni, sleeve rezeksiyonu ve pulmoner arter rezeksiyon tipi Kaplan-Meier analizinde istatistiksel olarak anlamlı farklılıklar gösterdi.

Sonuç: Çalışma sonuçlarımız pulmoner arter rezeksiyonları ve rekonstrüksiyonlarının kabul edilebilir morbidite ve mortalite oranları ile uygulanabilir olduğunu göstermektedir. Neoadjuvan tedavi, N2 hastalık ve pulmonar arter rezeksiyonunun nedeni ve tipi uzun dönem sağkalımı etkileyen olası faktörlerdir. Pulmoner arter rekonstrüksiyonu, ümit verici uzun dönem sonuçlar ile deneyimli kliniklerde güvenlidir.

Anahtar sözcükler: Morbidite, mortalite, küçük hücreli dışı akciğer kanseri, pulmoner arter rekonstrüksiyonu, sağkalım.

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Lung cancer is the most prevalent type of cancer globally and ranks first in cancer-related mortality,[1] Surgery remains the gold standard in the treatment of curative non-small cell lung cancer (NSCLC) with lobectomy being the most commonly preferred surgical method. Pneumonectomy is the preferred surgical method in cases with main bronchus, main or interlobar pulmonary artery (PA) or both pulmonary veins involvement.[2] However, high morbidity and mortality rates following pneumonectomy, particularly on the right side, and the associated poor quality of life have underscored the importance of alternative surgical techniques.

Over the past two decades, numerous studies have investigated the importance and efficacy of sleeve lobectomy and PA reconstruction.[3] Research has established bronchial sleeve resection as an oncological alternative to pneumonectomy, preserving lung function and reducing morbidity and mortality.[4] Pulmonary artery resections and reconstructions have not gained the same popularity as bronchial sleeve resections due to high complication rates, scarcity of experienced clinics, fewer studies with large patient series with long-term follow-up and discouraging postoperative outcomes.[5] In general, PA resection and reconstruction is indicated for tumors and lymph nodes invading the PA and hindering complete resection by lobectomy. While the PA may be partially or completely invaded by the tumor, endovascular growth of the tumor is rare. The absence of endovascular growth allows end-to-end anastomosis, repair with primary suture, tangential resection with stapler, or patch repair with prosthetic graft placement. While the most appropriate reconstruction technique is planned with preoperative imaging techniques, the choice of technique is usually based on the extent of vascular involvement during surgery. The diversity in PA reconstruction techniques, the difficulties in techniques, the presence of fatal complications and the small number of patients with long-term follow-up have limited the studies on PA.

In the present study, we aimed to evaluate the long-term results of patients who underwent PA resection and reconstruction in our clinic and our 13-year experience.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at University of Health Sciences, Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, Department of Thoracic Surgery between January 2010 and January 2023. Surgeries were performed in 675 patients with NSCLC. Of these patients, 50 (47 males, 3 females; mean age: 60.5±8 years; range, 43 to 83 years) who underwent lobectomy and pulmonary artery resection and reconstruction due to invasion of the pulmonary artery were included. Data including age, histopathology, lymph node metastasis, tumor size, T status, stage, comorbidity, neoadjuvant treatment and adjuvant treatment were obtained from hospital records, operation reports, patient charts and national survival database. Comorbidities such as chronic lung disease, heart disease, diabetes mellitus, and essential hypertension were recorded. All patients were grouped according to the reconstruction technique applied. A written informed consent was obtained each patient. The study protocol was approved by the Health Sciences University, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital Clinical Research Ethics Committee (date: 20.09.2023, no: 2023-CREC-50-52). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Preoperative assessment

Preoperative evaluation included posteroanterior (PA) chest radiography, thoracic computed tomography (CT), fiberoptic bronchoscopy (FOB), positron emission tomography (PET), cranial magnetic resonance imaging (MRI), pulmonary function tests (PFTs), standard blood gas analysis, and electrocardiography (ECG). Eligible patients underwent transthoracic fine needle aspiration biopsy (TFNAB) for diagnosis and endobronchial ultrasonography (EBUS) and/or mediastinoscopy for staging. Patients with N2 lymph nodes were excluded from the study and referred to neoadjuvant treatment.

Surgical technique

During the operation, posterolateral thoracotomy was performed in all patients after double lumen intubation, arterial and central venous pressure monitoring and epidural analgesia were carried out by anesthetists as standard procedure.

Except for those who underwent tangential resection, a Satinsky clamp was placed on the proximal and distal ends of the artery and resection was performed 0.5 cm away from the tumor margin after injection of 1 mL heparin (5,000 U/mL). Maintenance therapy with low-molecular-weight heparin (LMWH) was continued in the early postoperative period. Proximal control of the main PA was usually achieved extra-pericardially with the

help of a Satinsky clamp. On the right side, proximal control was achieved posterior to the superior vena cava, whereas on the left side it was achieved just distal to the ligamentum arteriosum to prevent laryngeal recurrent nerve injury. Distal control of the PA was achieved with a bulldog vascular clamp through the fissure (Figure 1a). The pulmonary vein of the lobe to be removed was cut using a vascular stapler (Figure 1b). Systemic anticoagulation was performed with heparin sodium 5,000 IU and not reversed with protamine at the end of reconstruction. Since the targeted resection was block removal of the lobe and the invaded portion of the PA, PA resection and reconstruction was performed as the first step to reduce arterial clamping time in patients requiring both bronchial and arterial sleeve resection (Figure 1c). While selecting the appropriate surgical technique for patients, careful examination of the extent of PA involvement is critical. The goal of angioplasty is to obtain a PA of appropriate length and a smooth lumen. In 45 patients who underwent partial resection, primary suturing was preferred in 33 patients due to residual arterial caliber of 50% or more. Autologous pericardial patch prepared according to the size of the defect was used in seven patients with caliber less than 50% (Figure 2a). In addition, 4/0 polypropylene suture was used to fix the patch and before tying the arterial suture, the distal clamp was opened and intravascular air was evacuated to help remove air from the PA (Figure 2b), and then the proximal vascular clamp was removed to ensure hemostasis of the sutured line (Figure 2c). In five patients who required circular resection of the PA, end-to-end vascular anastomosis was performed with 4/0 polypropylene suture (Figure 3). Before completion of arterial suturing, the distal clamp was opened and intravascular air was evacuated to remove air from the PA as in primary suturing, and then the proximal vascular clamp was removed.

If the patient is scheduled to undergo bronchial sleeve resection, the bronchial dissection should be ready for bronchotomy prior to clamping the artery. Following PA resection, bronchial resection is initiated, and the bronchus is typically closed using a stapler. In all cases, a pedicled flap was placed between the two structures, even when PA reconstruction and bronchoplasty were associated. The lobar bronchi of both bronchotomy sides with bronchial sleeve resection and standard resections without sleeve resection were examined by frozen-section pathological examinations. Pulmonary vascular margins were also analyzed in frozen-section analysis (circular single margin for arterial patch patients and both margins in patients with circular resection). In case of positive arterial margins, complementary pneumonectomy was performed proximal to the graft and patients who underwent pneumonectomy were excluded from the study.

Follow-up

Postoperative antithrombotic prophylaxis with a protective dose of LMWH was administered for approximately two weeks. Complications and mortality were recorded. All patients were monitored in the outpatient clinic with contrast-enhanced thoracic CT scans at three, six, nine,

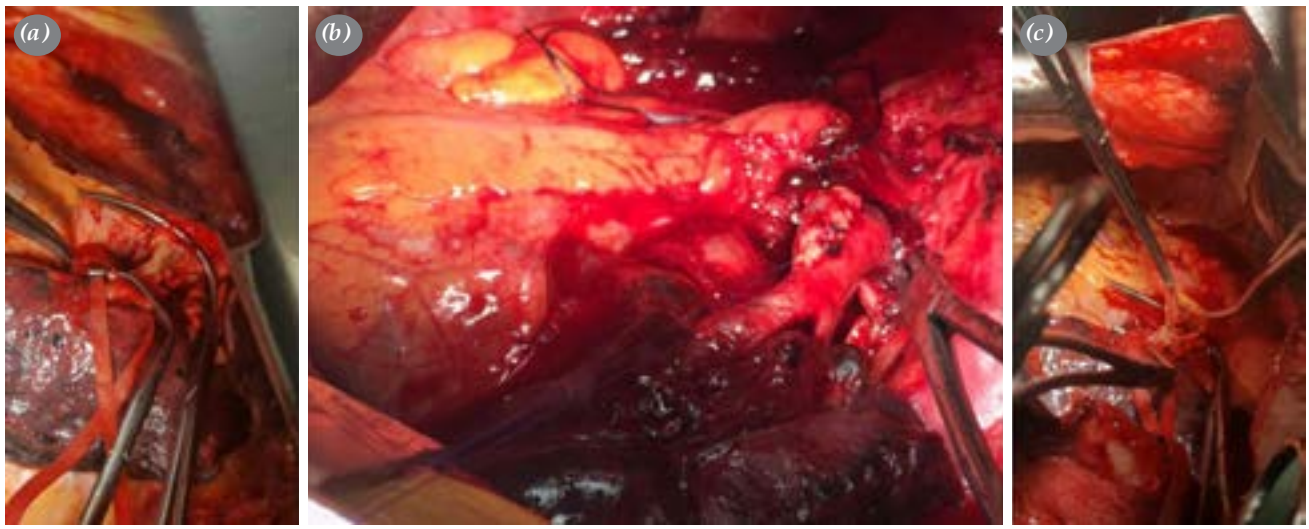

Figure 1. (a) Distal control of the PA was achieved with a bulldog vascular clamp through the fissure. **(b)** After pulmonary vein incision. **(c)** Pulmonary artery segment cut after clamping.

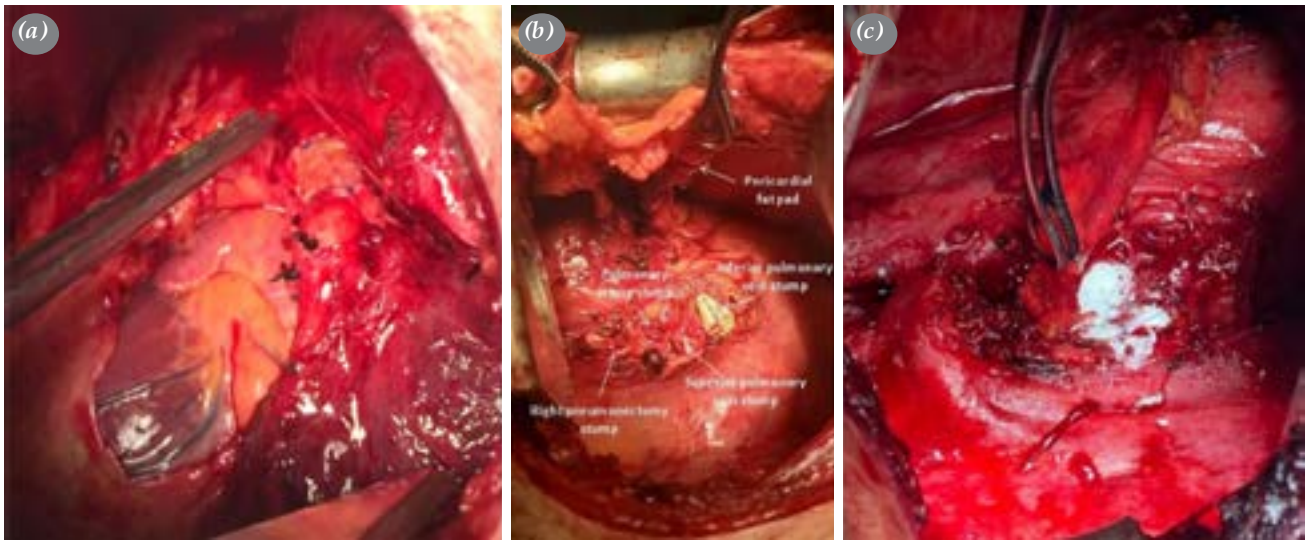

Figure 2. (a) Preparation of autologous pericardial patch. **(b)** Suturing of autologous pericardial patch. **(c)** Removing the vascular clamp after suturing.

and 12 months during the first year after surgery, every six months for the subsequent two years and annually thereafter. During the study, the latest status of all patients was updated from the National Health Data System. All mortality and relapses were included in the survival analysis. The overall survival was calculated as the period from the date of surgery to the date of death or the date of the most recent record update.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). The conformity of numerical variables to normal distribution was analyzed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were expressed in mean ± standard deviation (SD) or median (min-max), while categorical variables were expressed in number and frequency. The chi-square test was applied for categorical variables. Two group comparisons in terms of numerical variables were performed with the Mann-Whitney U test. The Kaplan-Meier and Cox regression analysis were used for survival analysis. A p value of <0.05 was considered statistically significant.

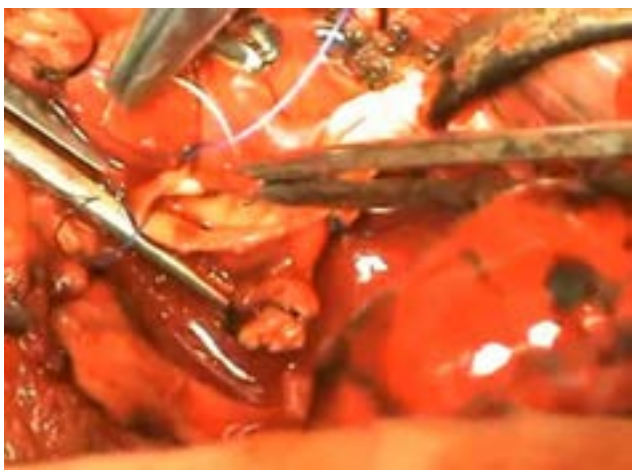

Figure 3. End-to-end vascular anastomosis was performed during circular resection of the pulmonary artery.

RESULTS

During the study period, 50 patients underwent PA reconstruction. Bronchial sleeve resection was performed in 20 (40%), lobectomy in 47 (94%), and bilobectomy in three patients (6%). Sixteen resections (32%) were performed on the right side and 34 (68%) on the left side. Demographic data of the patients are given in Table 1. Partial resection was performed in 45 (90%) patients (n=7 pericardial patch resection, n=33 primary suture, n=5 tangential resection with vascular stapler) and circular PA resection in the remaining five (10%) patients. All patients were operated through thoracotomy with proximal and distal Satinsky clamps. Pulmonary artery invasion originated from the tumor itself in 35 (70%) and from the lymph node in 15 (30%) patients.

Table 1. Demographic data and clinical characteristics of the patients

	n	%	Mean±SD	Min-Max
Age (year)			60.5±8	43-83
Age group (year)				
≥60	26	52.0		
<60	24	48.0		
Sex				
Female	3	6.0		
Male	47	94.0		
Side				
Right	16	32.0		
Left	34	68.0		
Reason of PA resection				
Direct tumor invasion	35	70.0		
Lymph node invasion	15	30.0		
Histology				
Squamous cell carcinoma	38	76.0		
Adenocarcinoma	10	20.0		
Large cell carcinoma	2	4.0		
Tumor group (cm)				
≤3	22	44.0		
3-7	23	46.0		
>7	6	12.0		
N status				
N0	13	26.0		
N1	25	50.0		
N2	12	24.0		
Type of PA resection				
Partial	36	72.0		
Circumferential	5	10.0		
Tangential	9	18.0		
Type of arterial reconstruction				
Running suture	38	76.0		
Vascular stapler	5	10.0		
Pericardium	7	14.0		

PA: Pulmonary artery.

Histopathologically, 38 (76%) patients had squamous cell carcinoma (SCC), 10 (20%) had adenocarcinoma, and two (4%) had large cell carcinoma. Eight (16%) patients were Stage 1, 23 (46%) were Stage 2 (2A n=3, 2B n=20), and 19 (38%) were Stage 3 (3A n=16, 3B n=3). Due to the relatively low number of patients among the groups, two groups in Stages-2 were combined for survival analysis. Preoperatively, 12 (24%) patients received neoadjuvant therapy, while 38 (76%) patients did not receive neoadjuvant therapy. The bronchial sleeve rate was 44% across all patients and bronchial sleeve resection was performed concurrently in patients who underwent right-sided resections, while this rate was 60% in left lung resections (p=0.08).

The overall survival rate of all patients was 46.0% and the median overall survival time was 32.4 (range, 0.0 to 89.4) months. Survival analyses showed that the survival rates of SCC and non-squamous cell carcinoma (NSCC) patients was 50.0% and 33.3%, respectively (p=0.357). The overall survival was 16.7% in patients who received neoadjuvant treatment and 55.3% in those who did not (p=0.023). Due to the low number of patients in the groups, two groups in Stages 1-2 were combined for survival analysis.

Table 2. Overall survival assessment (Kaplan Meier Analysis)

		Survival rate		Overall survival (months)		
	n	n	%	Mean±SD	Min-Max	*p*
Age (year)						0.379
<60	24	10	41.7	22.7±1.6	19.5-25.9	
≥60	26	13	50.0	82.3±38.4	7.1-157.6	
Sex						0.433
Male	47	21	44.7	27.9±13.5	1.3-54.4	
Female	3	2	66.7	N/A	N/A	
Side						0.061
Right	16	6	37.5	20.8±7.6	5.8-35.7	
Left	34	17	50.0	82.3±40.3	3.3-161.4	
Histology						0.357
Squamous cell carcinoma	38	19	50.0	82.3±42.0	0.03-164.6	
Non-squamous cell carcinoma	12	4	33.3	24.2±2.7	19.0-29.4	
Stage						0.371
1-2	31	15	48.4	82.3±42.7	0.0-166.1	
3-4	19	8	42.1	24.2±3.6	17.1-31.4	
Tumor size (cm)						0.313
≤3	22	8	36.4	23.4±8.3	7.0-39.8	
3-7	23	11	47.8	27.9±31.5	0,0-89.6	
>7	5	4	80.0	N/A	N/A	
Neoadjuvant treatment						**0.023**
No	38	21	55.3	84.4±56.3	0.0-194.6	
Yes	12	2	16.7	15.3±6.8	2.1-28.6	
N status						**0.030**
N0	13	7	53.8	82.3±N/A	–	
N1	25	13	52.0	84.4±43.8	0.0-170.2	
N2	12	3	25.0	15.3±6.8	2.1-28.6	
PA resection reason						**0.017**
Tumor invasion	35	19	54.3	82.3±N/A	–	
Lymph node invasion	15	4	26.7	15.3±7.1	1.4-29.2	
Sleeve resection						**0.008**
No	30	16	53.3	84.4±35.6	14.6-154.1	
Yes	20	7	35.0	13.8±1.5	10.8-16.8	
Type of PA resection						**0.022**
Partial	36	19	52.8	82.3±26.2	30.9-133.7	
Circumferential	5	2	40.0	13.7±10.5	0.0-34.2	
Tangential	9	2	22.2	15.3±1.3	12.8-17.9	
Type of arterial reconstruction						0.741
Running suture	38	19	50.0	32.4±24.9	0.0-81.2	
Vascular stapler	5	2	40.0	22.7±11.9	0.0-46.0	
Pericardium	7	2	28.6	44.9±40.7	0.0-125.0	
Recurrence						0.607
Yes	46	21	45.7	32.4±28.9	0.0-89.0	
No	4	2	50.0	15.3±1.4	12.7-18.0	

SD: Standard deviation; PA: Pulmonary artery.

As shown in Table 2, the five-year survival rate was 48.4% in Stage 1-2 and 42.2% in Stage 3-4 (p=0.371).

Recurrence was observed in four (8%) patients, while 46 (92%) patients showed no recurrence. There was no statistically significant difference in survival rates between the groups with and without recurrence (p=0.607). When survival rates of the groups were evaluated according to the

reason for PA resection, a significant difference was found between the groups (p=0.017). In addition, a statistically significant difference was found between the survival rates of patients with and without sleeve resection and between the PA resection type groups (p=0.008 and p=0.022, respectively).

There was no significant difference between the survival rates for age groups, sex, and tumor size groups. The median overall survival times and the comparison of survival rates determined by Kaplan-Meier analysis are shown in Table 2.

In the univariate Cox regression analysis, neoadjuvant treatment (hazard ratio [HR]=2.4 and p=0.027), N2 status (HR=3.6 and p=0.018), reason for PA resection (HR=2.5 and p=0.022), sleeve resection (HR=2.7 and p=0.011), and type of PA resection (HR=2.7 and p=0.032) were found to be statistically significant as variables affecting survival (Table 3). According to the results of multivariate Cox regression analysis, N2 disease and sleeve resection were the most significant factors affecting survival (p=0.035 and p=0.020, respectively) (Table 3).

Considering disease-free survival, the median disease-free survival time for all patients was 27.9 (range, 4.5 to 51.2) months. According to Kaplan-Meier analysis, side (p=0.037), neoadjuvant treatment (p=0.009), N status (p=0.002), reason for PA resection (p=0.032), sleeve resection (p=0.009) and type of PA resection (p=0.001) were statistically significant factors (Table 4).

The evaluation of risk factors for disease-free survival is shown in Table 5. According to the univariate and multivariate Cox regression analysis, N2 disease, sleeve resection and circumferential PA resection were the most significant factors affecting disease-free survival time.

Operative mortality was seen in three (6%) patients. Minor complications were seen in 10 (20%) patients including prolonged air leak in eight patients and atelectasis in two and major complications including bronchopleural fistula in two (4%). Three (6%) patients with respiratory failure required mechanical ventilation for >5 days on postoperative Days 1, 2, and 4 and these patients died within 10 days postoperatively.

DISCUSSION

Pulmonary artery reconstruction indicates that the tumor or lymph node is associated with the

Table 3. Evaluation of risk factors for survival (Univariate and Multivariate COX regression analysis)

	Univariate Cox regression analysis			Multivariate Cox regression analysis		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (year)						
≥60 *vs.* <60	1.4	0.7-3.0	0.381			
Sex						
Female *vs.* Male	2.2	0.3-16.1	0.446			
Side						
Left *vs.* Right	2.1	1.0-4.6	0.067	2.0	0.8-5.0	0.127
Neoadjuvant treatment						
No *vs.* Yes	2.4	1.1-5.3	**0.027**	1.7	0.5-5.1	0.373
N status			0.040			0.088
N0 *vs.* N1	1.5	0.6-4.0	0.433	1.2	0.4-3.7	0.754
N0 *vs.* N2	3.6	1.2-10.7	**0.018**	3.5	1.0-11.9	**0.046**
PA resection reason						
Tumor invasion *vs.* lymph node invasion	2.5	1.1-5.4	**0.022**	2.3	0.9-5.4	**0.066**
Sleeve resection						
No *vs.* Yes	2.7	1.3-5.9	**0.011**	3.0	1.2-7.5	0.020
Type of PA resection			**0.032**			0.412
Partial *vs.* circumferential	3.5	1.0-12.2	**0.049**	2.9	0.6-14.2	0.185
Partial *vs.* tangential	2.7	1.1-6.8	**0.032**	1.5	0.4-5.0	0.553

PA: Pulmonary artery.

Table 4. Evaluation of disease-free survival (Kaplan Meier Analysis)

		Disease free survival (months) (DFS)		
	n	Mean±SD	Min-Max	*p*
Age (year)				0.348
<60	24	22.7±1.6	19.5-25.9	
≥60	26	44.9±25.6	0.0-95.1	
Sex				0.387
Male	47	27.9±5.9	16.3-39.4	
Female	3	N/A	N/A	
Side				**0.037**
Right	16	20.8±6.6	7.8-33.7	
Left	34	44.9±34.5	0.0-112.6	
Histology				0.199
Squamous cell carcinoma	38	44.9±29.1	0.00-101.9	
Non-squamous cell carcinoma	12	22.7±2.8	17.1-28.3	
Stage				0.161
1-2	31	82.3±42.7	0.0-166.1	
3-4	19	23.1±8.7	6.3-39.8	
Tumor size (cm)				0.260
≤3	22	23.4±6.7	10.2-36.6	
3-7	23	24.2±3.9	16.7-31.8	
>7	5	N/A	N/A	
Neoadjuvant treatment				**0.009**
No	38	84.4±46.3	0.0-175.1	
Yes	12	13.8±2.3	9.3-18.2	
N Status				**0.002**
N0	13	82.3±N/A	–	
N1	25	84.4±43.8	0.0-170.1	
N2	12	12.2±0.5	11.1-13.2	
PA resection reason				**0.032**
Tumor invasion	35	44.9±30.9	0.0-1105.5	
Lymph node invasion	15	23.1±9.4	4.6-41.5	
Sleeve resection				**0.009**
No	30	82.3±27.9	27.6-137.1	
Yes	20	12.2±2.0	8.2-16.2	
Type of PA resection				**0.001**
Partial	36	82.3±26.2	30.9-133.7	
Circumferential	5	8.0±8.1	0.0-23.9	
Tangential	9	14.5±3.9	6.8-22.2	
Type of arterial reconstruction				0.502
Running suture	38	27.9±25.2	0.0-77.2	
Vascular stapler	5	22.7±11.9	0.0-46.0	
Pericardium	7	44.9±40.8	0.0-125	

SD: Standard deviation; PA: Pulmonary artery.

PA and resection cannot be completed with simple lobectomy.[6] Its involvement can vary from partial infiltration to peripheral invasion and full-thickness invasion. This variability in vascular involvement necessitates the use of different techniques for repair, such as pericardial patch plasty, primary suturing, end-to-end anastomosis, or vascular resection.[7]

Since the first half of the 19th century, numerous authors have reported interventions involving limited lung resection treatments for lung cancer, aimed at reducing the morbidity and mortality rates associated with pneumonectomy. D'Abreu and Mac Hale[8] demonstrated the feasibility of pulmonary arterioplasty in 1952, Allison[9] in 1954, and Wurnig[10]

Table 5. Evaluation of risk factors for DFS (Univariate and Multivariate Cox regression analysis)

	Univariate Cox regression analysis			Multivariate Cox regression analysis		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (year)						
≥60 *vs*. <60	1.4	0.7-3.0	0.351			
Sex						
Female *vs*. Male	2.3	0.3-17.3	0.402			
Side						
Left *vs*. Right	2.2	1.0-4.7	**0.042**	2.3	1.0-5.6	0.063
Neoadjuvant treatment						
No *vs*. Yes	2.6	1.2-5.6	**0.012**	1.7	0.6-4.9	0.321
N status			**0.005**			**0.016**
N0 *vs*. N1	1.5	0.6-4.0	0.422	1.2	0.4-3.8	0.716
N0 *vs*. N2	4.7	1.7-13.3	**0.004**	4.5	1.4-14.6	**0.011**
PA resection reason						
Tumor invasion *vs*. lymph node invasion	2.2	1.0-4.8	**0.037**	2.1	0.9-4.9	0.084
Sleeve resection						
No *vs*. Yes	2.6	1.2-5.5	**0.012**	2.8	1.1-6.7	0.024
Type of PA resection			**0.002**			0.090
Partial *vs*. circumferential	5.2	1.7-15.9	**0.004**	5.0	1.2-21.5	**0.028**
Partial *vs*. tangential	3.3	1.4-8.0	**0.008**	1.7	0.5-5.3	0.369

DFS: Disease free survival; PA: Pulmonary artery.

in 1967 with the tangential resection technique of PA. In 1971, Pichlmaier and Spelsberg[11] published a report on four successful cases of combined bronchial and vascular arm resections. Pulmonary angioplasty is rarely performed, as it is more demanding and requires more experience than bronchial sleeve resections. Another reason for its rare application is the lack of adequate studies on morbidity and mortality. Five-year survival rate in angioplastic resection was found to be 14% in previous studies[4] and 46.0% in our study.

Similar to other studies,[12] in our study, arterial resection and reconstruction was more frequently (68%) in the left-localized entities, and the predominant histology was SCC. Squamous cell carcinoma is more common in central type NSCLC, as larger bronchi are typically the primary localization sites of this type of tumor. Additionally, SCC frequently metastases to hilar lymph nodes in the early period. Compared to the right side, both the superior and posterior sides of the left upper lobe bronchus are closely surrounded by PA. Due to this anatomical configuration, the likelihood of direct invasion of the PA by primary tumor or metastatic lymph nodes originating from the lung hilum is higher on the left side. In our study, PA involvement was partial in most of the patients and partial resection, which is direct suturing of the arterial defect, or reinforcement with a pericardial patch was sufficient in treatment, consistent with the literature.[5] We believe that arterial resection and patch plasty alone may be sufficient to achieve a radical approach in combating the disease. Moreover, although the outcomes of end-to-end anastomosis performed in five (10%) patients in our study differed from those reported in the literature,[13] an analysis of the inclusion criteria revealed similarities to the findings of Rendina et al.,[14] particularly concerning patch reconstruction and circumferential resections.

Although Venuta et al.[6] suggested decreasing heparinization dose from 5,000 to 1,500 IU to reduce the amount of bleeding during surgery; in our study, we performed PA clamping and angioplasty rapidly without altering the heparinization dose with or without bronchoplasty. In the postoperative period, we adhered to standard protocols by administering subcutaneous LMWH to prevent embolism, and we did not observe any major bleeding.

Operative mortality was 6% (n=3) and morbidity rates were 24% (n=12) including minor complications in 20% and major complications in 4% in our study. Although morbidity and mortality data in the literature are quite variable, morbidity rates are between 7 and 45%, and mortality rates are between 0 and 17.2%.[5] This variability reflects differences in the overall condition of the study populations and the varying levels of surgical experience. It should also be kept in mind that the postoperative risk increases in patients who underwent arterial resection, as the disease is locally more advanced. Early mortality occurred in three (6%) patients within the first 10 days, primarily due to failure to wean from mechanical ventilation resulting from a fistula at the sleeve anastomosis line. In light of these three fatal complications, it is crucial to protect the sleeve anastomosis line with pericardial fatty tissue, intercostal muscle, or parietal pleura to reduce the risk of fistula formation. The literature contains limited data on the long-term outcomes of patients undergoing PA resection and reconstruction.[13] In our study, the median survival time of PA resection and reconstruction patients was 32.4 months and the five-year survival rate was 46.0%, which is similar to the study conducted by Rendina et al.[14] In a recent meta-analysis of 152 patients, the five-year survival rate was 38.7%, which was below the survival rate observed in our study.[4] This difference is likely attributable to variations in the characteristics of the study populations, disease stages, surgical techniques, and adjuvant treatments.

In another recent study, Alifano et al.[15] reported that the median survival was 40 months and the three- and five-year overall survival rates were 59.6% and 39.4%, respectively. These results were similar to Cerfolio and Bryant's study[12] in terms of having a very limited percentage of circumferential PA resections. Although there are few reports in the literature regarding the long-term survival of N2 disease in patients who underwent PA reconstruction, the five-year survival reported by Chunwei et al.[16] was 0% and by Obuchi et al.[17] was 23%. In our study, the overall five-year survival rate was 46.0%, but this rate was 48.4% in patients with Stage 3 disease and 42.1% in Stage 3. According to the N factor, the five-year survival rate was 57.8% for N0 and N1 disease and 25.0% for N2 disease. Furthermore, Cerfolio and Bryant[13] reported an overall five-year survival rate of 60% in a recently published study including different side preferences and pathological cell type. In our study, the five-year survival of SCC and NSCC patients was 50.0% and 33.3%, respectively.

In the study conducted by Toker et al.,[18] the authors identified female sex as a significant prognostic factor in patients who underwent PA resection, although they were unable to provide a sufficient explanation for this observation. They also showed that nodal involvement, side, histology and bronchial sleeve resections had no effect on survival, but adjuvant treatment and postoperative complication-free period were positive predictors for long-term survival.

In our study, five-year survival rate was 50.0% for patients with SCC and 33.3% for those with NSCC; however, this was not statistically significant. Our findings indicated that, among patients who underwent PA resection, early-stage disease, SCC histology, and nodal status of N0 or N1 were associated with a good prognosis.

Neoadjuvant therapy is typically administered to patients with N2 disease, and PA reconstruction often becomes technically more challenging after induction therapy due to its detrimental effects on bronchial healing, increased vascular fragility, and local devascularization. Given the more advanced stage of disease at the outset and the heightened risk of perioperative and postoperative complications, lower survival rates are usually expected in the neoadjuvant group. In our study, the five-year survival was 16.7% in patients who received neoadjuvant therapy, compared to 55.3% in those who did not.

Our recurrences are not local recurrences; metastatic recurrences were in the mediastinal lymph node in two patients, in the bone in one patient, and in the liver in one patient. In the literature, the five-year recurrence rate for completely resected NSCLC was 20%. In our study, the recurrence rate was 8% with four patients, which is lower compared to the literature.[19]

The main limitations to this study include the single-center, retrospective nature of the data analysis and the inability to implement randomization. Additionally, heterogeneities such as variations in preoperative stage, nodal status, and histological differences present further limitations. Expanding research through multi-center, larger patient groups may provide greater insight into the future of PA reconstructions.

In conclusion, pulmonary artery resections and reconstructions performed to avoid pneumonectomy are feasible and effective surgical procedures with acceptable morbidity and mortality rates. Our findings align with those reported in the literature and support

this technique as an effective option for patients with lung cancer. In addition, neoadjuvant therapy, N2 disease, and the reason and type of pulmonary artery resection are potential factors that may affect long-term survival. Taken together, pulmonary artery reconstruction seems to be safe in experienced clinics with promising long-term survival outcomes.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Made substantial contributions to the design of the work, made the creation of new software used in the work: B.A.S., S.Y.; Made the analysis of data: Y.T., B.G., E.Y.S.; Have drafted the work: B.A.S.; Revised: A.U., B.A.S.

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