Surgical resection for lung cancer with infiltration of the thoracic aorta

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Objective: The purpose of this study was to evaluate the results of a combined resection of the thoracic aorta and primary lung cancer.

Methods: Sixteen patients underwent thoracic aorta resection along with a left pneumonectomy (n = 6), left upper lobectomy (n = 9), or partial lung resection (n = 1), of whom 10 also received preoperative induction therapy. Cardiopulmonary bypass was used in 10 patients, and a passive shunt between the ascending aorta and the descending aorta was used in 4 patients.

Results: Six postoperative major complications occurred in 5 patients, including postoperative bleeding (n = 3), intraoperative bleeding (n = 1), chylothorax (n = 1), and respiratory failure (n = 1). The postoperative morbidity rate was 31%, and the mortality rate was 12.5% (2/16). Furthermore, 4 patients died of systemic tumor relapse, and 1 patient died of intrapleural recurrence. Nine patients were alive after a median follow-up of 54 months (range, 12-199 months). The median survival time of patients with postoperative pathologic N0 disease was 31 months, whereas it was 10 months for those with pathologic N2 or N3 disease. Five-year survivals were 70% for patients with N0 disease and 16.7% for patients with N2 or N3 disease (P = .0070).

Conclusions: Although pulmonary resection with the involved aorta might cause high surgical morbidity and mortality rates, encouraging long-term survivals were obtained in patients without mediastinal nodal involvement.

Many studies have described a combined resection of the thoracic aorta in patients with thoracic malignancies¹⁻⁵ and provided information regarding prognostic factors, surgical techniques, and early postoperative results. However, long-term benefits have been rarely attained with an extended operation, and thus lung cancer with aortic invasion has been considered inoperable.⁶⁻⁸

Preoperative induction therapy has been recommended for treatment of tumors invading the aorta, as well as other types of T4 lung cancer, to improve survival.^{1,5,9,10} In addition, the hemi-clamshell approach has been proposed as a suitable method to obtain a wide mediastinal view.^{1,5} We have used both as effective methods for complete and en bloc resections of tumors and the involved aorta.

Although en bloc resection, especially after preoperative treatment, is technically demanding, it is not more complicated than resection of other types of T4 lung cancer, such as tumors with infiltration to the trachea, carina, superior vena cava, or vertebrae. The goal of the present study was to determine the effect of a combined resection of primary non-small cell lung cancer and the involved thoracic aorta on patient outcome.

Patients and Methods

Sixteen patients (all men; age range, 30-66 years; mean age, 55 years) underwent a radical resection of primary lung cancer and the affected aorta between 1986 and 2002 (Table 1). Histologically, the tumors consisted of adenocarcinoma (n = 8), squamous cell carcinoma (n = 5), and large cell carcinoma (n = 3). At the time of initial staging, all patients were given a diagnosis of infiltration of the aorta (clinical T4) on the basis of the findings of chest computed tomography (CT), which were confirmed by a clinical radiologist. All patients underwent a bone scan, abdominal CT imaging, and magnetic resonance imaging or CT imaging of the head to rule out distant metastasis. We did not use thoracoscopy, mediastinoscopy, or thoracotomy for the staging of T and N status before the surgical resection. Mediastinal lymphadenopathy was diagnosed as clinical N2 disease without histologic confirmation when the lymph node had a short diameter of greater than 1.0 cm on the CT image.

Nine patients underwent preoperative chemoradiotherapy, and one underwent preoperative chemotherapy alone. Chemotherapy regimens consisted of 4 different platinum-based combinations, whereas radiation therapy was performed with an average dose of 45 Gy (range, 30-60 Gy), with the radiation field encompassing the primary tumor, ipsilateral hilum, and mediastinum. In cases of chemoradiotherapy, the 2 modalities were initiated concurrently. Four patients who did not undergo preoperative treatment received postoperative chemotherapy. Staging of the entire patient population resulted in classification as postoperative pathologic stage IV (n = 2), IIIB (n = 9), IIIA (n = 1), IIB (n = 2), and IB (n = 1) disease. One patient showed no viable tumor cells after surgical intervention.

Treatment Strategies

The first 7 patients in the present series were treated on an ad hoc basis between 1986 and 1994. Of those, 5 underwent surgical resection as the first therapy, and 2 underwent chemoradiotherapy with subsequent surgical resection (patients 1-7 in Table 1).

On the basis of the surgical results from these first 7 patients, subsequent patients (ie, from 1995) underwent induction therapy before surgical resection. Patients with tumor infiltration at the origin of the left pulmonary artery or with left atrial invasion alongside the pulmonary vein underwent a resection of the primary tumor and involved aorta. Other patients were not considered for operative management, including those with tumor infiltration over the aorta to the trachea, distant metastasis, or local disease progression after induction therapy. One patient (patient 9) with chronic hepatitis was treated surgically without any adjuvant therapy.

Operative Procedures

The surgical approach used was a hemi-clamshell thoracotomy (n = 10) or posterolateral thoracotomy (n = 6). Partial cardiopulmonary bypass (CPB) between the femoral vein and femoral artery was used in 9 patients, a temporary bypass graft from the ascending aorta to the descending aorta was used in 3 patients, and isolated brain perfusion and deep hypothermia was used in 1 patient, whereas the remaining 3 patients did not require any bypass technique (Table 1). The aorta was replaced with a prosthetic graft in 10 patients, a partial defect of the aortic wall was closed with a prosthetic patch in 5 patients, and direct closure of a small defect was performed in 1 patient. Seven patients underwent reconstruction of the subclavian artery, 2 patients underwent reconstruction of the common carotid artery, and 1 patient underwent partial vertebral resection. We attempted to avoid recycling blood aspirated from the pleural cavity during the procedure.

All patients were informed that the operative morbidity and mortality were high and that chemotherapy and chemoradiotherapy were alternative treatments with lower treatment-related morbidity and mortality. Written informed consent was obtained from all 16 patients.

Major complications were defined as those that would be lethal unless treated adequately. Survival was calculated by the Kaplan-Meier method from the start of preoperative therapy for 10 patients and from the time of the operation for the 6 patients who did not undergo induction therapy. Differences among the curves were analyzed by a log-rank test. Postoperative pathologic N and T status were evaluated as predictors of survival.

Results

Major complications occurred in 5 patients (Table 2). Three patients had intrapleural bleeding after the operation, and one of those died from the complication. Another patient had an aortic laceration just distal to the left subclavian artery and bled to death. One patient had respiratory failure requiring mechanical ventilation. Thus, the morbidity rate was 31% (5/16), and the mortality rate was 12.5% (2/16).

In 5 patients who received preoperative induction therapy, no histologic evidence of aortic involvement was found after the operation. Three patients with clinical N2 disease (patients 12, 15, and 16) and 1 patient with clinical N1 disease (patient 13) had a marked reduction in lymphadenopathy after induction therapy and showed no metastasis on postoperative histologic examination. Therefore, a possible downstaging of TNM status was observed in 7 of 10 patients who underwent induction therapy (patients 3, 10-13, 15, and 16).

Twelve (75%) patients underwent complete surgical resection. Postoperative adjuvant therapy was performed for 4 patients in whom complete resection could not be achieved or who did not receive preoperative therapy. Follow-up was completed for all patients in 12 to 199 months (mean, 43 months) after the initial treatment. Four patients died of systemic metastasis, and 1 died of intrapleural recurrence within 33 months of the operation. Nine patients were alive after a median follow-up period of 54 months.

TABLE 1. Patient demographics

Patient no.	Age (y)	Histology*	Preoperative therapy†	Postoperative therapy	Approach‡	TNM status after the operation	Cardiopulmonary bypass§	Survival time (mo)
1	65	Ad	-	PV	PL	420	FF	12
2	54	La	-	PV	HCS	420	FF	3
3	59	Sq	MVP + 50 Gy	-	HCS	300	(AA bypass)	199
4	62	Ad	-	PV	PL	420	-	33
5	64	Ad	-	-	PL	430	-	7
6	65	Sq	MVP + 30 Gy	-	PL	301	(AA bypass)	36
7	48	Ad	-	PV	PL	400	FF	101
8	30	La	MVP + 50 Gy	-	HCS	421	(AA bypass)	3
9	52	Ad	-	-	HCS	220	FF	64
10	47	La	MVP + 40 Gy	-	HCS	0	FF	67
11	63	Sq	PV + 40 Gy	-	PL	300	FF	54
12	66	Sq	PV + 50 Gy	-	HCS	200	-	26
13	55	Sq	CTG	-	HCS	400	FF	24
14	55	Ad	MVP + 40 Gy	-	HCS	400	FF	27
15	50	Ad	NP + 60 Gy	-	HCS	400	FF	19
16	59	Ad	PT + 40 Gy	-	HCS	400	CPB, hypothermia	12

*Ad, Adenocarcinoma; La, large cell carcinoma; Sq, squamous cell carcinoma.

†MVP, Cisplatin, vindesine, and mitomycin; PV, cisplatin and vindesine; CTG, carboplatin, paclitaxel, and gemcitabine; NP, cisplatin and vinorelbine; PT, cisplatin and docetaxel.

‡PL, Posterolateral thoracotomy; HCS, hemclamshell thoracotomy.

§FF, Femoro-femoral partial cardiopulmonary bypass; AA bypass, temporary bypass from the ascending aorta to the descending aorta; CPB, cardiopulmonary bypass.

||Patient who died.

TABLE 2. Complications and causes of death

Complication	
Pleural bleeding after operation	3 (1*)
Aortic laceration	1*
Chylothorax	1
Respiratory failure	1
Morbidity	31% (5/16)†
Mortality	12.5% (2/16)
Cause of death	
Systemic metastasis	4
Local recurrence	1

*Patient who died.

†There were 6 complications among 5 patients.

The median survival time of all patients was 26 months, and the 5-year survival was 48.2%. The median survival time and 5-year survival were 31 months and 70%, respectively, for the 10 patients with postoperative pathologic N0 disease and 10 months and 17%, respectively, for the 6 patients with pathologic N2 or N3 disease ($P = .0070$, Table 3 and Figure 1). Pathologic T factor ($P = .0539$) did not appear to have an influence on survival (Table 3).

Discussion

A malignant thoracic tumor with infiltration of the aorta carries a poor prognosis, and thus surgical resection is contraindicated in these cases.¹¹ However, previous studies have shown that long-term survival is possible after limited

resection of the aortic adventitia along with the primary tumor.^{6,9,10,12} Moreover, in 4 separate studies,^{1,2,5,10} 7 of 20 patients who underwent resection of the involved aortic wall with subsequent graft replacement survived for at least 3 years, and each report recommended complete resection of the entire tumor.

Preoperative induction therapy is an effective method for achieving complete resection of lung cancer and has been applied extensively for treatment of stage IIIA and IIIB disease.^{13,14} In those studies mediastinal lymph node status after induction treatment showed prognostic significance for surgical treatment.^{7,13,14} Those reports are consistent with findings from the present study, which demonstrated that survival outcome was relatively favorable for patients with postoperative pathologic N0 disease, although outcome was still poor for those with pathologic N2 or N3 disease; and these results underscore the importance of accurate diagnosis of mediastinal lymph node involvement before surgical treatment. On the basis of our results, we suggest the following operative strategy. Patients with a T4 tumor infiltrating the aorta, as confirmed by CT imaging, and with or without clinical N2 disease should undergo preoperative induction therapy. When these patients show no tumor progression after therapy, further examinations, such as video-assisted thoracoscopy, a Chamberlain procedure, or mediastinoscopy, are required for assessment of the para-aortic, subaortic, or paratracheal lymph nodes before definitive surgical management. When no histologic evidence of

Figure 1. Survival of patients with T4 non-small cell lung cancer infiltrating the thoracic aorta. **Solid lines and dotted lines** represent survival curves and their E bars, respectively, for patients with postoperative pathologic N0 disease (5-year survival, 70%) or N2 or N3 disease (5-year survival, 16.7%).

mediastinal nodal involvement is found after these examinations, a radical resection of the affected aorta should be performed.

Some surgeons prefer the use of a passive shunt between the ascending and descending aorta to avoid extracorporeal circulation^{1,2} and to maintain perfusion in the lower part of the body. However, recent technical advances and implementation of a vortex pump with a low dose of heparin have allowed for safe and reliable circulatory support without renal failure, cerebral complications, or spinal cord injury.¹⁵ In the present study 10 patients underwent surgical intervention with CPB without critical complications, and the intensive care unit stay was less than 3 days for each. Operations with CPB usually use a cell salvage system, which washes and concentrates erythrocytes aspirated from the surgical field for subsequent transfusion to the patient. However, in lung cancer operations, blood in the pleural cavity might be contaminated with tumor cells. Therefore, although evidence is limited, we consider that blood aspirated from the surgical field should not be transfused back into the patient.

Radical en bloc resection of the tumor and invaded organ is essential for preventing intrapleural local recurrence.¹⁶ One of our patients (patient 13), who underwent discontinuous resections of the lung and tumor during CPB, had local recurrence in the chest wall pleura approximately 1 year after the operation. We suspected that the local recurrence was due to intrapleural tumor spread resulting from the discontinuous resection.

TABLE 3. Survival time on the basis of the pathologic T factor and N factor

	T0, T2, or T3 (n = 7)	T4 (n = 9)	P value
Median survival time (mo)	66	12	
5-year survival (%)	67	37	.0539
	N0 (n = 10)	N2 or N3 (n = 6)	
Median survival time (mo)	31	10	
5-year survival (%)	70	17	.0070

In conclusion, surgical morbidity and mortality rates were high in patients who underwent resection of the tumor and involved aorta, although similar to those of patients with other T4 organ involvement^{7,13,14} treated with preoperative induction therapy. The encouraging long-term survivals obtained in patients with N0 disease suggest that radical resection is a valid intervention for selected patients with aortic involvement of non-small cell lung cancer.

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