Gen Thorac Cardiovasc Surg (2014) 62:522–530
DOI 10.1007/s11748-014-0425-7

CURRENT TOPICS REVIEW ARTICLE

Surgical management of locally advanced lung cancer

Kohei Yokoi · Tetsuo Taniguchi · Noriyasu Usami · Koji Kawaguchi · Takayuki Fukui · Futoshi Ishiguro

Received: 28 March 2014 / Published online: 29 May 2014
© The Japanese Association for Thoracic Surgery 2014

Abstract Majority of cases of lung cancer are detected at an advanced stage; such patients are usually treated with chemotherapy and radiotherapy, and the prognosis is frequently poor. Surgical resection remains the only reliable curative method for the treatment of lung cancer, and combined resection of the primary tumor and involved neighboring structures is performed when possible in patients with locally advanced disease. In the TNM classification, tumors with direct extrapulmonary extension are subdivided based on the anatomic extent of disease and its potential for surgical treatment: T3 lesions with limited, circumscribed extension are thought to be potentially surgically resectable, whereas T4 tumors with extensive extension are considered unresectable. Although surgical treatment for T3 lesions is generally accepted, the outcome is frequently not satisfactory. On the other hand, advanced surgical techniques are now being applied for T4 lesions due to improvements in surgery and anesthesiology and progress in combined treatment modalities. In the present staging, T4N0–1M0 lesions are categorized as stage IIIA disease, and T4 tumors without mediastinal nodal metastasis are now considered to be potentially curable if complete resection is possible. This article reviews the modern surgical management of patients with lung cancer invading neighboring structures, including the chest wall, superior sulcus, diaphragm, tracheal carina, left atrium, superior vena cava, aorta and vertebrae. Furthermore, the surgical treatment of carcinomatous pleuritis, which was categorized as T4 disease in the previous TNM classification, is also assessed, and the role of surgical resection in cases of locally advanced lung cancer is discussed.

Keywords Lung cancer · Locally advanced disease · Surgical treatment · Combined resection

Introduction

Lung cancer is the leading cause of cancer death worldwide [1]. Surgical resection remains the gold standard for curative treatment of early-stage lung cancer. Although patients are often diagnosed with advanced disease at presentation, surgical management is employed in cases of selected locally advanced T3 and T4 disease. According to a report of a nationwide registry study of surgical lung cancer cases during 2004, which was conducted by the Japanese Joint Committee of Lung Cancer Registry, 8.7 % of patients underwent combined resection of involved neighboring structures [2].

T3 lesions with limited, circumscribed extrapulmonary extension are thought to be potentially surgically resectable, whereas T4 tumors with extensive extrapulmonary extension are considered unresectable. However, the Union for International Cancer Control revised the TNM staging in the seventh edition published in 2009; that is, T4N0–1M0 lesions, which were classified as stage IIIB disease in the sixth edition, are now categorized as stage IIIA disease [3]. This modification indicates that T4 tumors without mediastinal nodal metastasis are potentially curable if complete resection is possible. Although carcinomatous pleuritis is now classified as M1a and stage IV disease, this condition was categorized as T4 disease in the

This review was submitted at the invitation of the editorial committee.

K. Yokoi (✉) · T. Taniguchi · N. Usami · K. Kawaguchi · T. Fukui · F. Ishiguro
Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan
e-mail: k-yokoi@med.nagoya-u.ac.jp

previous TNM classification and several results of the surgical treatment have been reported to date.

Therefore, we herein review the modern surgical management of locally advanced non-small cell lung cancer including carcinomatous pleuritis, with reference to the involved organs, and discuss the role of such treatment.

Chest wall

In 1947, Coleman first reported the curative treatment with pneumonectomy and simultaneous block resection of the chest wall for primary carcinoma of the lung with invasion of the ribs [4]. Since then, surgical treatment for lung cancer with chest wall invasion has been reported with acceptable morbidity and mortality rates.

Table 1 shows the recently reported outcomes of patients treated with surgical resection for lung cancer with chest wall invasion [5–8]. Complete resection and lymph node metastasis have been reported to be implicit prognostic factors in patients with such locally advanced lung cancer, whereas the depth of invasion and extent of combined resection remain controversial. A few investigators have emphasized the routine application of en bloc resection of the lung and ribs, regardless of the depth of chest wall invasion, from the viewpoint of obtaining a safe margin [9, 10], while others have recommended the use of extrapleural resection for lung cancer with invasion limited to the parietal pleura due to the lower morbidity and mortality rates [5, 6, 11]. Extrapleural resection is generally selected in cases of lung cancer with shallow invasion limited to the parietal pleura, and the high rate of complete resection demonstrates that experienced surgeons are able to make a correct judgment regarding the extent of combined resection during surgery in such cases. Consequently, patients with N0–1 disease are considered to be good candidates for surgical treatment, which is required to achieve complete resection with a negative surgical margin. Furthermore, combined resection of the chest wall has been shown to be a very high-risk procedure in elderly patients [6].

The surgical methods used for chest wall resection are common and non-specific. In general, detachment from the chest wall is first performed in order to avoid congestion of the lung to be excised. It is essential to maintain an adequate margin from the tumor when cutting the ribs. The indications of and methods for chest wall reconstruction vary among institutions. Generally, the indication for reconstruction is as follows: a large defect of caudal chest wall, which area is not covered with scapula, including resection of more than three ribs or measuring at least 4.0 × 4.0 cm in area. Weyant et al. [12] emphasized that the incidence of respiratory failure in their series was lower than that previously reported, which may be related to their routine use of a rigid prosthesis for reconstruction of large, anteriorly or laterally located defects causing a flail chest.

Concerning perioperative therapy, lung cancer with chest wall invasion is mostly staged as IIB or IIIA disease; therefore, the administration of adjuvant chemotherapy after surgical resection is recommended in many modern guidelines. On the other hand, a few reports have been published regarding the efficacy of induction therapy for lung cancer with chest wall invasion, whereas preoperative chemoradiotherapy has become a standard strategy for treating superior sulcus tumors (SSTs). In patients with chest wall invasion, we have conducted a phase II study, the Central Japan Lung Study Group Trial 0801, under the hypothesis that induction chemoradiotherapy followed by surgery can improve the prognosis such as in patients with SST [13].

Superior sulcus

SSTs or apical chest tumors, sometimes referred to as Pancoast tumors, were first described by a radiologist, Pancoast [14]. These tumors are located in the apex of the thoracic cavity and often detected at an advanced stage. Due to their anatomical location, involvement of the surrounding structures, such as the brachial plexus, subclavian vessels and/or spine, is usually observed in association with involvement of the first rib. Therefore,

Table 1 Surgical outcomes of patients with lung cancer involving the chest wall

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)			
					N0	N1	N2	All patients
Downey [5]	1999	269	65	5.7	49[a]	27[a]	15[a]	32[a]
Magdeleinat [6]	2001	201	83	7.0	25[a]	20[a]	21[a]	21 (24[a])
Doddoli [7]	2005	309	100	7.8	40	24	8	31
Kawaguchi [8]	2012	407	86	NR	49	36	21	43

NR not reported

[a] The data indicate 5-year survival rates of patients with complete resection of the tumor

this disease was considered a contraindication for surgery until Chardack and Maccallum [15] reported the case of a long-term survivor treated with en bloc resection of the right upper lobe, chest wall and nerve roots followed by adjuvant radiotherapy. Subsequently, the strategy of applying induction radiation at a dose of 30–35 Gy followed by surgery with curative intent was introduced by Shaw et al. [16]. The standard treatment strategy for SST remained unchanged for approximately 30 years until trimodality therapy consisting of induction chemoradiation followed by surgical resection was developed.

Based on the findings of recent reports, as shown in Table 2, concurrent chemoradiotherapy prior to resection has become the standard treatment for resectable SST [17–20]. The Southwest Oncology Group and Japan Clinical Oncology Group both conducted prospective phase II studies of induction chemoradiation followed by surgery in SST patients and reported significantly superior results with respect to the rates of complete resection and survival compared to that observed in the previous literature, despite the use of a multi-institutional setting [18, 19]. Candidates for the trimodality therapy are thought to include patients with N0–1 or ipsilateral N3 (supraclavicular) disease and/or T3–4 tumors, such as those with tumor invasion to the subclavian vessels, Th1 and C8 nerve roots or spine, when potentially resectable.

The surgical approach is the most interesting aspect with respect to the treatment of SST due to anatomical difficulties. The standard approach of creating a higher posterolateral incision for SST invading the middle or posterior compartments of the thoracic inlet was first reported by Shaw et al. [16]. Dartevelle et al. [21] later reported the use of the anterior approach to treat subclavian vessels exhibiting tumor involvement, and the evolution of surgical treatment, particularly that employing the anterior approach, was ignited. Other surgical approaches for SST have been reported by a number of thoracic surgeons [22–25], and the appropriate approach should be selected according to the locoregional extension of the tumor [26].

Pericardium

A few studies have assessed tumors invading the pericardium, and patients with such tumors have been reported to generally have a worse prognosis (Table 3) [8, 27, 28]. However, due to the small number of patients, the current results remain equivocal. Because prognostic factors have not yet been determined, the optimal operative indications for patients with tumor invading the pericardium remain an open question.

En bloc resection of the pericardium along with the tumor is usually possible. At the time of pericardial resection, it is necessary to obtain a sample of the pericardial effusion for a cytological examination. If malignant findings are observed, resection must be abandoned. Following resection of the pericardium, reconstruction may be performed using non-absorbable material to prevent cardiac herniation, if necessary.

Diaphragm

Because lung cancer involving the diaphragm is also rare, only a few reports with a relatively small number of cases have been published concerning the surgical treatment of patients with these tumors (Table 4) [8, 27, 29, 30]. The frequency of diaphragmatic invasion of lung cancer is extremely low, at 0.3–0.4 % [8, 29, 30].

Patients with N0 disease are considered to be good surgical candidates. Because the number of patients with N1 disease totaled less than 20 in all previous reports, it remains controversial whether to recommend surgery in such cases. Incomplete resection of lung cancer with diaphragmatic involvement offers no curative benefits. In patients with complete resection, combined resection of other organs has been reported to have an adverse effect on survival [30].

En bloc resection of the diaphragm along with the tumor should be attempted whenever possible. Generally, more than 2 cm of the macroscopically uninvolved diaphragm is excised from all tumor borders. If the defect

Table 2 Surgical outcomes of patients with superior sulcus tumor

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	Chemotherapy	Radiation dose (Gy)	Pathological complete response (%)	5-Year survival (%)
Kwong [17]	2005	36	97	2.7	CDDP based	57	41	59 (2-Year survival)
Rusch [18]	2007	110	76	2.3	CDDP + etoposide	45	36	44
Kunitoh [19]	2008	76	68	2.0	MVP	45	21	56
Kappers [20]	2011	19	100	2.0	CDDP	66	53	33

CDDP cisplatin, *MVP* mitomycin + vindesine + cisplatin

Table 3 Surgical outcomes of patients with lung cancer involving the pericardium

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)			
					N0	N1	N2	All patients
Sakakura [27]	2008	14	79	NR	NR	NR	NR	21
Riquet [28]	2010	32	81	15.6	NR	NR	NR	15
Kawaguchi [8]	2012	20	NR	NR	50	80	38	54

NR not reported

Table 4 Surgical outcomes of patients with lung cancer involving the diaphragm

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)			
					N0	N1	N2	All patients
Rocco [29]	1999	15	93	0	27	0	0	20
Yokoi [30]	2000	63	87	1.6	28[a]	20[a]	0	19 (23[a])
Sakakura [27]	2008	12	75	NR	NR	NR	NR	33
Kawaguchi [8]	2012	31	NR	NR	55	0	19	43

NR not reported

[a] The data indicate 5-year survival rates of patients with complete resection of the tumor

Table 5 Surgical outcomes of patients with lung cancer involving the main bronchus within 2 cm of the carina

Investigator	Year	No. of patients	Complete resection (%)	5-Year survival (%)			
				N0	N1	N2	All patients
Riquet [34]	2002	68	76	NR	NR	NR	35
Sakakura [27]	2008	33	85	NR	NR	NR	49
Kawaguchi [8]	2012	45	NR	92	46	36	55

NR not reported

area in the diaphragmatic muscle is smaller than the size of a fist, it is possible to perform direct suturing with non-absorbable bladed sutures. In cases of large defects, diaphragmatic reconstruction using non-absorbable material may be necessary to prevent herniation of the abdominal organs.

Trachea, carina and main bronchus

Lung cancer sometimes lies in the main bronchus within 2 cm of the carina (T3 lesions) and/or involves the trachea or carina (T4 lesions). Surgical intervention for these lesions requires challenging techniques for thoracic surgeons.

Main bronchus within 2 cm of the carina

Pneumonectomy and sleeve lobectomy are conducted for the surgical treatment of tumors located in the main bronchus within 2 cm of the carina [31]. In order to avoid pneumonectomy, which results in a substantial loss of the lung function and quality of life, bronchoplastic techniques combined with various surgical methods, such as pulmonary artery reconstruction, have been performed [32]. The operative mortality for sleeve lobectomy is approximately 2 % [33]. The modern surgical outcomes for T3 tumors invading the central main bronchus are shown in Table 5 and appear to be superior to those of other T3 tumors [8, 27, 34].

Trachea and carina

Surgical treatment for tumors with tracheal and/or carinal invasion has been performed using sleeve pneumonectomy and tracheocarinal resection. Encouraging results have been reported in recent series, in particular an excellent survival rate in pN0 patients (Table 6) [35–39]. Patients with N2 involvement exhibit a poor prognosis, even when treated with aggressive surgical resection. The long-term survival has been reported to be influenced by the pathologic nodal status and completeness of resection, not age, sex or pre- or postsurgical oncologic treatment [39]. The operative mortality has recently been reported to be 3–8 % [36, 38, 39], which is similar to that noted for conventional pneumonectomy, ranging from 5 to 15 %.

Right sleeve pneumonectomy is the most common procedure for treating these tumors, and the safe limit of

Table 6 Surgical outcomes of patients with lung cancer involving the trachea and carina

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)			
					N0	N1	N2	All patients
Mitchell [35]	2001	60	85	15	51	32	12	42
Regnard [36]	2005	65	94	7.7	38		5.3	27
de Perrot [37]	2006	119	94	7.6	53		15	44
Yıldızeli [38]	2008	92	90	6.5	50		17	43
Eichhorn [39]	2013	64	83	3.1	70	35	9	31

resection is approximately 4 cm between the lower trachea and left main bronchus [40]. A variety of carinal resection and reconstruction procedures have been performed according to the tumor characteristics in practice, and the use of careful patient selection and anesthetic and surgical techniques is advocated in order to minimalize morbidity and mortality [41].

Left atrium

The optimal management of patients with lung cancer invading the left atrium remains controversial. Nevertheless, some tumors have occasionally been removed, with reported 5-year survival and operative mortality rates of 14–30 and 0–10 %, respectively (Table 7) [42–46]. The survival rates are less favorable than those associated with resection of other T4 structures. The nodal status, type of operation and completeness of resection have been found to have a significant impact on survival [45, 46]. Therefore, in carefully selected NSCLC patients with left atrium invasion, candidates for surgical resection are only those with N0–1 disease.

Although combined resection of the lung and left atrium is performed using vascular clamps, cardiopulmonary bypass (CPB) is required in cases of intraluminal polypoid tumor growth. However, as reported in the literature, the application of CPB has only rarely been used [45] and is frequently avoided [42–44]. In patients with right tumors, the Sondergaard technique is useful for lengthening the left atrial cuff [44].

Table 7 Surgical outcomes of patients with lung cancer involving the left atrium

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)
Tsuchiya [42]	1994	44	NR	NR	22
Ratto [43]	2004	19	58	0	14
Spaggiari [44]	2005	15	100	0	39 (3-Year survival)
Kuehnl [45]	2010	35	69	9	16
Stella [46]	2012	31	94	10	30

NR not reported

Table 8 Surgical outcomes of patients with lung cancer involving the superior vena cava

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)
Shargall [48]	2004	15	93	14	57 (3-Year survival)
Suzuki [49]	2004	40	70	10	24
Spaggiari [50]	2007	52	NR	8	31
Yıldızeli [38]	2008	39	85	8	29

NR not reported

Superior vena cava

Lung cancer with invasion of the superior vena cava (SVC) has been considered to be a contraindication for surgery [47]. However, over the last 20 years, several reports regarding the surgical resection in selected patients have shown improved results, with acceptable perioperative morbidity, mortality and 5-year survival rates (Table 8) [38, 48–50].

Which type of SVC resection and reconstruction is performed depends on the degree of venous involvement [50]. Following partial SVC resection, the pattern of reconstruction includes the use of simple running sutures, vascular staplers or patch replacement. In cases of SVC infiltration of more than 50 % of the circumference of the vessel, total prosthetic replacement of the SVC is required using an extraluminal shunt placed between the left brachiocephalic vein and the right atrium and the cross-clamping technique.

Suzuki et al. [49] identified SVC invasion by metastatic lymph nodes to be a significant poor prognostic factor. On the other hand, several studies have reported that the lymph node status and completeness of resection do not

significantly affect survival [38, 48]. Clinically, among carefully selected NSCLC patients with SVC invasion, candidates for surgical resection are considered to include those with N0–1 disease and the potential for complete resection [51].

Aorta

Aortic involvement by lung cancer has long been considered to be a relative contraindication for surgical resection. However, in recent years, the publication of several reports regarding aortic resection and replacement has increased interest in the application of extended procedures. Among studies focusing specifically on aortic resection, the overall 5-year survival rate has been reported to be 17–48 %, with an operative mortality of 0–13 % (Table 9) [52–55]. The encouraging long-term survival rates obtained in patients with N0 disease and complete resection are essential in selected patients with aortic involvement.

The type of aortic resection depends on the degree of tumor involvement and consists of subadventitial dissection and aorta en bloc resection and reconstruction. In cases in which segmental resection of the descending aorta is necessary, partial cardiopulmonary bypass between the femoral vein and artery or temporary bypass grafting from the ascending to the descending aorta is used. Recently, some reports have shown that pulmonary resection with combined resection of the aortic wall can be successfully accomplished after thoracic aorta endovascular stent graft placement without the use of cardiopulmonary bypass support [56, 57]. The placement of an endovascular stent is an alternative in selected patients with aortic invasion.

Spine

Lung cancer that invades to the spine is classified as T4 disease, which has long been considered to be unresectable. However, due to the development of innovative approaches for performing vertebral resection and spinal reconstruction and the combined use of multimodality therapy since the late of 1980s, low mortality with encouraging 5-year survival rates of 31–61 % has been reported in several series (Table 10) [58–61].

Table 9 Surgical outcomes of patients with lung cancer involving the aorta

Investigator	Year	No. of patients	Complete resection (%)	Operative mortality (%)	5-Year survival (%)
Ohta [52]	2005	16	75	13	48
Shiraishi [53]	2005	16	50	13	17
Mithos [54]	2007	13	100	0	31
Wex [55]	2009	13	85	0	45

Surgery alone is almost never an adequate treatment for this disease and must be combined with other modalities. Recently, the introduction of concurrent chemoradiation prior to surgery for SST, which often exhibits upper spinal involvement, has been reported to yield relatively favorable rates of complete resection and overall survival [18, 62].

There are several thoughts as to the resection technique for performing vertebrectomy. The technique introduced by Grunenwald et al. [63] involves en bloc total vertebrectomy, in which the transmanubrial approach [24] is used, followed by the creation of a posterior midline incision. After performing laminectomy one level above and below the tumor, the vertebral body is rotated into the chest toward the tumor and subsequently removed en bloc along with the lung and chest wall. Anraku et al. [64] introduced their 'staged surgery' for multiple-level total vertebrectomy based on the principle of en bloc resection. Recently, long-term favorable outcomes of this procedure were reported, with a 5-year survival rate of 61 % in 48 patients [61]. The authors also reported that the response to induction therapy was found to be an independent prognostic factor in a multivariate analysis.

Carcinomatous pleuritis

Carcinomatous pleuritis in patients with lung cancer is usually found to accompany frank malignant pleural effusion and is associated with a short-term survival [65]. The present TNM classification categorizes this condition as M1a and stage IV disease and suggests that patients with carcinomatous pleuritis are candidates for non-surgical treatment. However, this disorder is sometimes discovered with or without a small amount of pleural effusion during thoracotomy in patients with resectable lung cancer, with a reported incidence of 1.5–4.5 % [66–68]. Surgical treatment has been applied in affected patients at some institutions, achieving long-term survival in selected cases [66–70]. On the other hand, the outcome of chemotherapy for patients with pleural dissemination detected during surgery was recently reported, and the result was more favorable than that of patients with preoperatively diagnosed stage IV disease [71]. Therefore, a part of carcinomatous pleuritis could be considered as a locally advanced disease.

The surgical procedures employed are diverse, including limited resection, lobectomy, pneumonectomy and extrapleural pneumonectomy. The median postoperative survival time and 5-year survival rate have been reported to be

Table 10 Surgical outcomes of patients with lung cancer involving the spine

Investigator	Year	No. of patients	Vertebrectomy		Multilevel (%)	Complete resection (%)	5-Year survival (%)
			Total	Hemi			
Grunenwald [58]	2002	19	4	15	3 (16)	79	14
Schirren [59]	2011	20	4	16	18 (90)	80	47
Fadel [60]	2011	54	5	49	54 (100)	91	31
Collaud [61]	2013	48	10	38	47 (98)	88	61

Table 11 Surgical outcomes of patients with lung cancer and carcinomatous pleuritis

Investigator	Year	No. of patients	Median survival (months)		5-Year survival (%)		
			N0–1	N2	N0–1	N2	All patients
Ichinose [66]	2001	100	21		NR	NR	23
Mordant [67]	2011	32	15		NR	NR	16
Okamoto [68]	2012	73	30		NR	NR	24
Yokoi [70]	2013	23	126	21	61	6	34

NR not reported

17–30 months and 13–24 %, respectively (Table 11) [66–68, 70]. We performed extrapleural pneumonectomy in 23 patients between 1988 and 2012, with a median survival time and 5-year survival rate of 34 months and 34 %, respectively [69, 70]. Among 12 patients with pathologic N0–1 disease, six remain alive without disease at four to 288 months after surgery, for a median survival time and 5-year survival rate of 126 months and 61 %, respectively. These results indicate that carefully selected patients with carcinomatous pleuritis may be candidates for surgical treatment including extrapleural pneumonectomy.

Nevertheless, at present, with the progression of chemotherapy and molecular targeted therapy, a few reports of the outcomes of patients with carcinomatous pleuritis detected during surgery are available [71]. Therefore, the appropriate treatment strategy for patients with minimal pleural carcinomatosis should be investigated.

Conclusion

Locally advanced lung cancer with involvement of the neighboring structures is usually treated with chemotherapy and radiotherapy, with the exception of T3N0–1M0 tumors. However, promising outcomes of surgical treatment have been reported in selected patients with more advanced T4 tumors, and the TNM classification has been revised according to these results. Furthermore, due to improvements in surgical techniques and perioperative management as well as progress in the development of combined treatment modalities, such as radiotherapy and chemotherapy including molecular targeted therapy, it is now possible to administer more aggressive multidisciplinary treatment. Therefore, the criteria for selecting candidates for surgical treatment of lung cancer involving the neighboring structures should be reevaluated.

Conflict of interest The authors declare no conflict of interest.

References

1. Alberg AJ, Ford JG, Samet JM. American College of Chest Physicians. Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007;132(3 Suppl):29S–55S.
2. Sawabata N, Fujii Y, Asamura H, Nomori H, Nakanishi Y, Eguchi K, et al. Lung cancer in Japan: analysis of lung cancer registry cases resected in 2004. Jpn J Lung Cancer. 2010;50:875–88 (Japanese).
3. Sobin LHG, Wittekind C, editors. International Union Against Cancer (UICC) TNM classification of malignant tumors. 7th ed. New York: Wiley-Liss; 2009.
4. Coleman FP. Primary carcinoma of the lung, with invasion of the ribs: pneumonectomy and simultaneous block resection of the chest wall. Ann Surg. 1947;126:156–68.
5. Downey RJ, Martini N, Rusch VW, Bains MS, Korst RJ, Ginsberg RJ. Extent of chest wall invasion and survival in patients with lung cancer. Ann Thorac Surg. 1999;68:188–93.
6. Magdeleinat P, Alifano M, Benbrahem C, Spaggiari L, Porrello C, Puyo P, et al. Surgical treatment of lung cancer invading the chest wall: results and prognostic factors. Ann Thorac Surg. 2001;71:1094–9.
7. Doddoli C, D'Journo B, Le Pimpec-Barthes F, Dujon A, Foucault C, Thomas P, et al. Lung cancer invading the chest wall: a plea for en-bloc resection but the need for new treatment strategies. Ann Thorac Surg. 2005;80:2032–40.
8. Kawaguchi K, Miyaoka E, Asamura H, Nomori H, Okumura M, Fujii Y, et al. Modern surgical results of lung cancer involving neighboring structures: a retrospective analysis of 531 pT3 cases in a Japanese Lung Cancer Registry Study. J Thorac Cardiovasc Surg. 2012;144:431–7.
9. Facciolo F, Cardillo G, Lopergolo M, Pallone G, Sera F, Mertelli M. Chest wall invasion in non-small cell lung carcinoma: a rationale for en bloc resection. J Thorac Cardiovasc Surg. 2001;121:649–56.

10. Burkhart HM, Allen MS, Nichols FC III, Deschamps C, Miller DL, Trastek VF, et al. Results of en bloc resection for bronchogenic carcinoma with chest wall invasion. J Thorac Cardiovasc Surg. 2002;123:670–5.
11. Kawaguchi K, Mori S, Usami N, Fukui T, Mitsudomi T, Yokoi K. Preoperative evaluation of the depth of chest wall invasion and the extent of combined resections in lung cancer patients. Lung Cancer. 2009;64:41–4.
12. Weyant MJ, Bains MS, Venkatraman E, Downey RJ, Park BJ, Flores RM, et al. Results of chest wall resection and reconstruction with and without rigid prosthesis. Ann Thorac Surg. 2006;81:279–85.
13. Kawaguchi K, Yokoi K, Niwa H, Ohde Y, Mori S, Okumura S, et al. Trimodality therapy for lung cancer with chest wall invasion: initial results of a phase II study. Ann Thorac Surg. 2014 (in press).
14. Pancoast HK. Importance of careful roentgen-ray investigations of apical chest tumors. JAMA. 1924;83:1407–11.
15. Chardack WM, Maccallum JD. Pancoast tumor; five-year survival without recurrence or metastases following radical resection and postoperative irradiation. J Thorac Surg. 1956;31:535–42.
16. Shaw RR, Paulson DL, Kee JL. Treatment of superior sulcus tumor by irradiation followed by resection. Ann Surg. 1961;154:29–40.
17. Kwong KF, Edelman MJ, Suntharalingam M, Cooper LB, Gamliel Z, Burrows W, et al. High-dose radiotherapy in trimodality treatment of Pancoast tumors results in high pathologic complete response rates and excellent long-term survival. J Thorac Cardiovasc Surg. 2005;129:1250–7.
18. Rusch VW, Giroux DJ, Kraut MJ, Crowley J, Hazuka M, Winton T, et al. Induction chemoradiation and surgical resection for superior sulcus non-small-cell lung carcinomas: long-term results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160). J Clin Oncol. 2007;25:313–8.
19. Kunitoh H, Kato H, Tsuboi M, Shibata T, Asamura H, Ichinose Y, et al. Phase II trial of preoperative chemoradiotherapy followed by surgical resection in patients with superior sulcus non-small-cell lung cancers: report of Japan Clinical Oncology Group trial 9806. J Clin Oncol. 2008;26:644–9.
20. Kappers I, Klomp HM, Koolen MG, Uitterhoeve LJ, Kloek JJ, Belderbos JS, et al. Concurrent high-dose radiotherapy with low-dose chemotherapy in patients with non-small cell lung cancer of the superior sulcus. Radiother Oncol. 2011;101:278–83.
21. Dartevelle PG, Chapelier AR, Macchiarini P, Lenot B, Cerrina J, Ladurie FL, et al. Anterior transcervical-thoracic approach for radical resection of lung tumors invading the thoracic inlet. J Thorac Cardiovasc Surg. 1993;105:1025–34.
22. Masaoka A, Ito Y, Yasumitsu T. Anterior approach for tumor of the superior sulcus. J Thorac Cardiovasc Surg. 1979;78:413–5.
23. Niwa H, Masaoka A, Yamakawa Y, Fukai I, Kiriyama M. Surgical therapy for apical invasive lung cancer: different approaches according to tumor location. Lung Cancer. 1993;10:63–71.
24. Grunenwald D, Spaggiari L. Transmanubrial osteomuscular sparing approach for apical chest tumors. Ann Thorac Surg. 1997;63:563–6.
25. Korst RJ, Burt ME. Cervicothoracic tumors: results of resection by the "hemi-clamshell" approach. J Thorac Cardiovasc Surg. 1998;115:286–95.
26. de Perrot M, Rampersaud R. Surgical approaches to apical thoracic malignancies. J Thorac Cardiovasc Surg. 2012;144:72–80.
27. Sakakura N, Mori S, Ishiguro F, Fukui T, Hatooka S, Shimada M, et al. Subcategorization of resectable non-small cell lung cancer involving neighboring structures. Ann Thorac Surg. 2008;86:1076–83.
28. Riquet M, Grand B, Arame A, Pricopi CF, Foucault C, Dujon A, et al. Lung cancer invading the pericardium: quantum of lymph nodes. Ann Thorac Surg. 2010;90:1773–8.
29. Rocco G, Rendina EA, Meroni A, Venuta F, Pona CD, Giacomo TD, et al. Prognostic factors after surgical treatment of lung cancer invading the diaphragm. Ann Thorac Surg. 1999;68:2065–8.
30. Yokoi K, Tsuchiya R, Mori T, Nagai K, Furukawa T, Fujimura S, et al. Results of surgical treatment of lung cancer involving the diaphragm. J Thorac Cardiovasc Surg. 2000;120:799–805.
31. Deslauriers J, Grégoire J, Jacques LF, Piraux M, Guojin L, Lacasse Y. Sleeve lobectomy versus pneumonectomy for lung cancer: a comparative analysis of survival and sites or recurrences. Ann Thorac Surg. 2004;77:1152–6.
32. Rendina EA, De Giacomo T, Venuta F, Ciccone AM, Coloni GF. Lung conservation techniques: bronchial sleeve resection and reconstruction of the pulmonary artery. Semin Surg Oncol. 2000;18:165–72.
33. Okada M, Yamagishi H, Satake S, Matsuoka H, Miyamoto Y, Yoshimura M, et al. Survival related to lymph node involvement in lung cancer after sleeve lobectomy compared with pneumonectomy. J Thorac Cardiovasc Surg. 2000;119:814–9.
34. Riquet M, Lang-Lazdunski L, Le PB, Dujon A, Souilamas R, Danel C, et al. Characteristics and prognosis of resected T3 non-small cell lung cancer. Ann Thorac Surg. 2002;73:253–8.
35. Mitchell JD, Mathisen DJ, Wright CD, Wain JC, Donahue DM, Allan JS, et al. Resection for bronchogenic carcinoma involving the carina: long-term results and effect of nodal status on outcome. J Thorac Cardiovasc Surg. 2001;121:465–71.
36. Regnard JF, Perrotin C, Giovannetti R, Schussler O, Petino A, Spaggiari L, et al. Resection for tumors with carinal involvement: technical aspects, results, and prognostic factors. Ann Thorac Surg. 2005;80:1841–6.
37. de Perrot M, Fadel E, Mercier O, Mussot S, Chapelier A, Dartevelle P. Long-term results after carinal resection for carcinoma: does the benefit warrant the risk? J Thorac Cardiovasc Surg. 2006;131:81–9.
38. Yıldızeli B, Dartevelle PG, Fadel E, Mussot S, Chapelier A. Results of primary surgery with T4 non-small cell lung cancer during a 25-year period in a single center: the benefit is worth the risk. Ann Thorac Surg. 2008;86:1065–75.
39. Eichhorn F, Storz K, Hoffmann H, Muley T, Dienemann H. Sleeve pneumonectomy for central non-small cell lung cancer: indications, complications, and survival. Ann Thorac Surg. 2013;96:253–8.
40. Dartevelle P, Macchiiarini P. Carcinal resection for bronchogenic cancer. Semin Thorac Cardiovasc Surg. 1996;8:414–25.
41. Mitchell JD, Mathisen DJ, Wright CD, Wain JC, Donahue DM, Moncure AC, et al. Clinical experience with carinal resection. J Thorac Cardiovasc Surg. 1999;117:39–53.
42. Tsuchiya R, Asamura H, Kondo H, Goya T, Naruke T. Extended resection of the left atrium, great vessels, or both for lung cancer. Ann Thorac Surg. 1994;57:960–5.
43. Ratto GB, Costa R, Vassallo G, Alloisio A, Maineri P, Bruzzi P. Twelve-year experience with left atrial resection in the treatment of non-small cell lung cancer. Ann Thorac Surg. 2004;78:234–7.
44. Spaggiari L, D'Aiuto M, Veronesi G, Pelosi G, de Pas T, Catalano G, et al. Extended pneumonectomy with partial resection of the left atrium, without cardiopulmonary bypass, for lung cancer. Ann Thorac Surg. 2005;79:234–40.
45. Kuehnl A, Lindner M, Hornung HM, Winter H, Jauch KW, Hatz RA, et al. Atrial resection for lung cancer: morbidity, mortality, and long-term follow-up. World J Surg. 2010;34:2233–9.
46. Stella F, Dell'Amore A, Caroli G, Dolci G, Cassanelli N, Luciano G, et al. Surgical results and long-term follow-up of T(4)-non-small cell lung cancer invading the left atrium or the intrapericardial base of the pulmonary veins. Interact CardioVasc Thorac Surg. 2012;14:415–9.
47. Burt ME, Pomerantz AH, Bains MS, McCormack PM, Kaiser LR, Hilaris BS, et al. Results of surgical treatment of stage III

lung cancer invading the mediastinum. Surg Clin N Am. 1987;67:987–1000.
48. Shargall Y, de Perrot M, Keshavjee S, Darling G, Ginsberg R, Johnston M, et al. 15 years single center experience with surgical resection of the superior vena cava for non-small cell lung cancer. Lung Cancer. 2004;45:357–63.
49. Suzuki K, Asamura H, Watanabe S, Tsuchiya R. Combined resection of superior vena cava for lung carcinoma: prognostic significance of patterns of superior vena cava invasion. Ann Thorac Surg. 2004;78:1184–9.
50. Spaggiari L, Leo F, Veronesi G, Solli P, Galetta D, Tatani B, et al. Superior vena cava resection for lung and mediastinal malignancies: a single-center experience with 70 cases. Ann Thorac Surg. 2007;83:223–9.
51. Kozower BD, Larner JM, Detterbeck FC, Jones DR. Special treatment issues in non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143:e369S–99S.
52. Ohta M, Hirabayasi H, Shiono H, Minami M, Maeda H, Takano H, et al. Surgical resection for lung cancer with infiltration of the thoracic aorta. J Thorac Cardiovasc Surg. 2005;129:804–8.
53. Shiraishi T, Shirakusa T, Miyoshi T, Yamamoto S, Hiratsuka M, Iwasaki A, et al. Extended resection of T4 lung cancer with invasion of the aorta: is it justified? Thorac Cardiovasc Surg. 2005;53:375–9.
54. Misthos P, Papagiannakis G, Kokotsakis J, Lazopoulos G, Skouteli E, Lioulias A. Surgical management of lung cancer invading the aorta or the superior vena cava. Lung Cancer. 2007;56:223–7.
55. Wex P, Graeter T, Zaraca F, Haas V, Decker S, Bugdayev H, et al. Surgical resection and survival of patients with unsuspected single node positive lung cancer (NSCLC) invading the descending aorta. Thorac Surg Sci. 2009;6:Doc02.
56. Collaud S, Waddell TK, Yasufuku K, Oreopoulos G, Rampersaud R, Rubin B, et al. Thoracic aortic endografting facilitates the resection of tumors infiltrating the aorta. J Thorac Cardiovasc Surg. 2014;147:1178–82.
57. Nagata T, Nakamura Y, Yamamoto H, Sato M. A fenestrated stent graft for surgical resection of lung cancer invading the aortic arch. J Thorac Cardiovasc Surg. 2013;146:238–9.
58. Grunenwald DH, Mazel C, Girard P, Veronesi G, Spaggiari L, Gossot D, et al. Radical en bloc resection for lung cancer invading the spine. J Thorac Cardiovasc Surg. 2002;123:271–9.
59. Schirren J, Donges T, Melzer M, Schonmayr R, Eberlein M, Bolukbas S. En bloc resection of non-small-cell lung cancer invading the spine. Eur J Cardiothorac Surg. 2011;40:647–55.
60. Fadel E, Missenard G, Court C, Mercier O, Mussot S, Fabre D, et al. Long-term outcomes of en bloc resection of non-small cell lung cancer invading the thoracic inlet and spine. Ann Thorac Surg. 2011;92:1024–30.
61. Collaud S, Waddell TK, Yasufuku K, Pierre AF, Darling GE, Cypel M, et al. Long-term outcome after en bloc resection of non-small-cell lung cancer invading the pulmonary sulcus and spine. J Thorac Oncol. 2013;8:1538–44.
62. Bolton WD, Rice DC, Goodyear A, Correa AM, Erasmus J, Hofstetter W, et al. Superior sulcus tumors with vertebral body involvement: a multimodality approach. J Thorac Cardiovasc Surg. 2009;137:1379–87.
63. Grunenwald D, Mazel C, Girard P, Berthiot G, Dromer C, Baldeyrou P. Total vertebrectomy for en bloc resection of lung cancer invading the spine. Ann Thorac Surg. 1996;61:723–5.
64. Anraku M, Waddell TK, de Perrot M, Lewis SJ, Pierre AF, Darling GE, et al. Induction chemoradiotherapy facilitates radical resection of T4 non-small cell lung cancer invading the spine. J Thorac Cardiovasc Surg. 2009;137:441–7.
65. Sugiura S, Ando Y, Minami H, Ando M, Sakai S, Shimokata K. Prognostic value of pleural effusion in patients with non-small cell lung cancer. Clin Cancer Res. 1997;3:47–50.
66. Ichinose Y, Tsuchiya R, Koike T, Kuwahara O, Nakagawa K, Yamato Y, et al. Prognosis of resected non-small cell lung cancer patients with carcinomatous pleuritis of minimal disease. Lung Cancer. 2001;32:55–60.
67. Mordant P, Arame A, Foucault C, Dujon A, Le Pimpec Barthes F, Riquet M. Surgery for metastatic pleural extension of non-small-cell lung cancer. Eur J Cardiothorac Surg. 2011;40:1444–9
68. Okamoto T, Iwata T, Mizobuchi T, Hoshino H, Moriya Y, Yoshida S, et al. Pulmonary resection for lung cancer with malignant pleural disease first detected at thoracotomy. Eur J Cardiothorac Surg. 2012;41:25–30.
69. Yokoi K, Matsuguma H, Anraku M. Extrapleural pneumonectomy for lung cancer with carcinomatous pleuritis. J Thorac Cardiovasc Surg. 2002;123:184–5.
70. Yokoi K, Matsuguma H. Surgical treatment of lung cancer with carcinomatous pleuritis. Nihon Geka Gakkai Zasshi. 2013;114:196–200 (Japanese).
71. Kimura M, Murakami H, Naito T, Kenmotsu H, Taira T, Akamatsu H, et al. Outcomes of platinum-based chemotherapy for non-small-cell lung cancer patients with pleural dissemination detected during surgery. Mol Clin Oncol. 2013;1:949–52.