Surgery on Extracorporeal Circulation in Early and Advanced Non-Small Cell Lung Cancer

Matthias Kauffmann[1] Tobias Krüger[1] Hermann Aebert[1]

[1] Department of Thoracic, Cardiac and Vascular Surgery, University Hospital of Tübingen, Tübingen, Germany

Thorac Cardiovasc Surg 2013;61:103–108.

Address for correspondence Tobias Krüger, MD, Department of Thoracic, Cardiac and Vascular Surgery, University of Tübingen, Hoppe-Seyler-Str. 3, 72076 Tübingen, Germany (e-mail: krueger-tobias@web.de).

Abstract

Background Locally advanced (T4) non-small cell lung cancer (NSCLC) is principally amenable to surgery. For radical resection of cardiovascular structures, extracorporeal circulation (ECC) may be required. Tumor dissemination is a concern in this situation. In this study, we evaluate the long-term results of T4 NSCLC surgery with ECC and compare them with combined cardiopulmonary surgery for early-stage NSCLC and heart disease.

Methods We retrospectively analyzed 16 patients undergoing surgery on ECC over a 13-year period. Eight patients suffered from T4 NSCLC (group A), and another eight patients suffered from coincidental T1–T2 NSCLC and heart disease (group B).

Results In group A, five patients received neoadjuvant radiochemotherapy. Complete resection was achieved in all patients. Thirty-day mortality was one patient (12.5%) in each group. Six patients died from recurrent cancer with a median survival of 13.6 months in group A. Prognosis in patients with direct tumor invasion of the aortopulmonary window was a lot worse compared to those with atrial infiltration. One T4 patient who had only received surgery survived for 155 months without relapse. In group B, no NSCLC relapse occurred, and median survival was 21.6 months. All but one death in group B occurred due to cardiovascular incidents.

Conclusions Surgery on ECC for T4 NSCLC gives satisfactory results. The site of infiltration appears to be most important for local tumor relapse. Long-term survival is possible in some cases. Simultaneous cardiac and pulmonary surgery resulted in good early and midterm outcomes without surgery-induced tumor propagation.

Keywords
- lung cancer
- NSCLC
- cardiopulmonary surgery
- extracorporeal circulation
- cardiopulmonary bypass ECC

Introduction

Lung cancer is the deadliest neoplasm in the EU and is growing into this position in the populous countries of Asia. Prognosis even in the Western World is poor with an overall 5-year survival rate (5YSR) of 16%.[1] Non-small cell lung cancer (NSCLC) accounts for more than 80% of pulmonary neoplasms. Early stages are often missed and most patients are diagnosed in advanced stages (UICC III and IV). With systemic therapy, prognosis of locally advanced NSCLC is dismal. Two-year survival rate and 5YSR decrease to 25 and 6 to 8%, respectively, and the median survival time is approximately 1 year.[2,3]

In the UICC-TNM-7 system, T4N1 tumors are now classified as stage IIIa, implicating surgical resectability. Surgery for T4 NSCLC with invasion of cardiovascular structures may require extracorporeal circulation (ECC). The reported number of such procedures is limited and this is even more true for long-term results. The main concerns hindering surgical intervention are the supposedly high risk of extended combined cardiopulmonary operations and fear of tumor cell dissemination and immunosuppression by cardiopulmonary

received
January 20, 2012
accepted after revision
May 8, 2012
published online
December 4, 2012

DOI http://dx.doi.org/10.1055/s-0032-1331041.
ISSN 0171-6425.

bypass. To address these questions, we additionally enrolled patients undergoing combined cardiac and pulmonary surgery due to coincidental T1–T2 NSCLC and heart disease. We comparatively present perioperative and long-term results of both groups.

Patients and Methods

Inclusion Criteria

A series of 16 patients was treated between 1997 and 2010. All suffered from histologically proven NSCLC and underwent surgery utilizing ECC. Eight of them underwent extended resections of mediastinal structures for T4 tumors (group A). Those were compared with another eight patients receiving lung resection for T1–T2 NSCLC and combined cardiac procedures such as coronary or valve surgery (group B). We included all patients treated in the mentioned timeframe who met these criteria without patient selection or matching.

Patients' Enrolment

The indication to offer surgery was based on the technical possibility to achieve R0 resection and the patients' general condition and motivation to undergo such an extensive procedure. For evaluation, the patients received an extensive work-up including cardiac catheterization in all and positron emission tomography (PET) or PET-computed tomography (CT) in all but one case. All patients were pre- and postoperatively presented to the institutional tumor board.

We retrospectively analyzed the patients' medical records and evaluated the present status by interviews with patients, patients' relatives, and family physicians. We collected demographic data, pathological staging, and details of surgical therapy, postoperative course, and complications. We further recorded the cancer relapse time and the time point and cause of death. This study was reviewed and approved by the local ethical committee (No. 83/2011A). All interviewed people were informed about the scientific purpose of the questioning and they gave their consent.

TNM Staging

All cancer stages are given in accordance with the actual UICC-TNM-7 system. Staging of all patients was revised retrospectively.

Statistical Analysis

Median and range are given for continuous variables. Endpoints of the study were perioperative complications, tumor relapse, and death. The Kaplan–Meier estimator was applied for survival analysis. The PASW-18 (SPSS Inc., Chicago, Illinois, United States) software was used for statistical analysis.

We entirely waived specification of inferential statistics due to small number of patients.

Results

Demographics Data

Group A consisted of patients with T4 NSCLC invading the mediastinal structures, and group B consisted of patients suffering from T1 or T2 tumors with coincidental cardiac disease. In group A, all patients were men, median age 65.1 years (range: 51.8 to 70.9 years). In group B, all but one patient were men, median age 68.7 years (range: 57.6 to 78.1 years). Patients' additional demographics, diagnoses, and surgical procedures are shown in ►**Table 1**. Five patients (nos. 2 to 6) in group A had received neoadjuvant radiochemotherapy consisting of cisplatin plus docetaxel or vincristine and a minimum of 45 Gy of local radiation, details are described elsewhere.[4] In group B, two patients had a history of previous malignancies, that is, breast and rectal cancers, with no apparent recurrence during preoperative staging. The cumulative observation period for group A was 251.5 patient-months, and 193.6 patient-months in group B, respectively.

Surgical Techniques

All patients were managed with double-lumen endotracheal intubation. The use of ECC was preoperatively planned in all cases. All patients were operated with mild hypothermia except nos. 2 and 13 who underwent hypothermic circulatory arrest for aortic arch procedures.

All resections were performed with curative intent. Surgical access was achieved either via median sternotomy or lateral thoracotomy (►**Table 1**). For the cardiac procedures in group B, the ascending aorta and the right atrium were cannulated in seven patients. One patient with adenocarcinoma of the left lower lobe was operated via lateral thoracotomy with cannulation of the ascending aorta and pulmonary artery. For resection of T4 tumors, cannulation and ECC strategies were more versatile: the femoral vessels were cannulated in one case (no. 8) and the main pulmonary artery and aortic arch were used in two cases (nos. 2 and 6). The circuit for ECC was standard, for left heart bypass (patient nos. 3 and 5) it was equipped with a pump sucker, a reservoir, and a heat exchanger for cannulas in the left atrium and the descending aorta. With these two exceptions and patient no. 8, who received crystalloid cardioplegia, the other patients undergoing cardiac arrest were managed with blood cardioplegia.

In group A, all patients received en bloc resections with the cardiovascular resection and reconstruction on ECC performed as the last step. In all cases of group B, the pulmonary procedure was done first, followed by the cardiac procedure. For reconstruction of the aorta, prosthetic material was used and all other reconstructions were performed with autologous pericardium. Closure of bronchial stumps in group B was heterogeneous but mainly by sole stapling without covering. In patient no. 12 and in all patients of group A, bronchial stumps were closed by staples and additional manual sutures and were covered with a pericardial flap. A polyglactin mesh (Ethicon, Norderstedt, Germany) served for closure of pericardial defects. Surgical procedures are indicated in detail in ►**Table 1**. All patients except nos. 9, 10, and 13 were operated by a single surgeon (H.A.).

Intraoperative Data

Median operative time was 315 minutes in group A (range: 269 to 430 min) and 362 minutes in group B (range: 230 to 427 min). Median ECC time was 55 minutes in group A (range:

Table 1 Demographics, diagnoses, surgical procedures, and perioperative outcome

	Patient no.	Age	Sex	Diagnosis	Stage	Surgical procedure	Exposure	Cannulation	ICU stay (days)	Perioperative complications
Group A: T4 tumors, extended surgery, ECC	1	71	M	AC	pT4N0M0 IIIa	Right intrapericardial pneumonectomy, partial resection of both atria and reconstruction	T	A.asc/biCaval	8	Sepsis, exitus
	2	59	M	AC	pT4N0M0 IIIa	Left intrapericardial pneumonectomy with pulmonary artery resection from the bifurcation, distal aortic arch replacement	T	A.arch/PA	2	None
	3	57	M	SCC	pT4N0M0 IIIa	Left intrapericardial pneumonectomy, replacement of the descending aorta, tangential esophageal resection and repair	T	A.desc/LA	1	None
	4	52	M	SCC	pT4N2M0 IIIb	Left intrapericardial pneumonectomy with open pulmonary artery resection of the bifurcation and reconstruction	T	A.asc/RA	1	None
	5	64	M	SCC	pT4N0M0 IIIa	Left intrapericardial pneumonectomy, replacement of the descending aorta	T	A.desc/LA	1	Empyema
	6	64	M	SCC	pT4N1M0 IIIa	Left intrapericardial pneumonectomy, open pulmonary artery resection of the bifurcation and reconstruction	T	A.arch/PA	1	None
	7	67	M	SCC	pT4N1M0 IIIa	Lower right bilobectomy, partial resection of the left atrium, reconstruction with pericardial patch	T	A.asc/biCaval	2	None
	8	70	M	SCC	pT4N1M0 IIIa	Ex situ sleeve resection and autotransplantation of the left lower lobe; partial resection of the left atrium[20]	T	A/V femoral	1	None
Group B: T1 and T2 tumors, combined cardiac surgery	9	69	M	AC; CAD	pT1aN0M0 Ia	Right middle lobectomy, ACB4	S	A.asc/RA	5	Ventricular fibril., exitus
	10	63	M	SCC; CAD	pT2aN0M0 Ib	Left upper lobe lobectomy, ACB5	S	A.asc/RA	1	None
	11	69	F	SCC; CAD; AS	pT2bN0M0 IIa	Right upper bilobectomy, aortic valve replacement, ACB1	S	A.asc/RA	1	None
	12	57	M	AC; CAD	pT2aN0M0 Ib	Left lower lobectomy, ACB3	T	A.asc/PA	1	None
	13	66	M	SCC; AA	pT2aN0M0 Ib	Right upper sleeve lobectomy, replacement of the A.asc, hemiarch	S	A.asc/RA	5	None
	14	78	M	AC; CAD	pT1bN1M0 IIa	Left upper lobectomy, lower lobe wedge resection, ACB3	S	A.asc/RA	1	None
	15	68	M	AC; CAD	pT2aN0M0 Ib	Left upper lobectomy, ACB4	S	A.asc/RA	1	None
	16	69	M	SCC; CAD	pT2aN0M0 Ib	Right lower lobectomy, upper lobe wedge resection, ACB2, carotid endarteriectomy	S	A.asc/RA	1	Pneumonia

Abbreviations: AA, aortic aneurysm; A. arch, aortic arch; A.asc, ascending aorta; AC, adenocarcinoma; ACB, aortocoronary bypass; A.desc, descending aorta; AS, aortic valve stenosis; CAD, coronary artery disease; LA, left atrium; PA, main pulmonary artery; RA, right atrium; S, sternotomy; SCC, squamous cell carcinoma; T, lateral thoracotomy.

42 to 176 min) and 99 minutes in group B (range: 69 to 146 min). Tumor diameters ranged from 3.5 to 11.0 cm in group A and 1.0 to 5.5 cm in group B. In group A, an average of 15 lymph nodes and in group B an average of 7 lymph nodes were resected. In group A, a median of three packed red blood cells (PRBCs) was administered intraoperatively, whereas in group B, a median of 1.5 PRBCs was needed. However, in both groups major transfusion was necessary in one patient each, 17 PRBCs in patient no. 3 and 8 PRBCs in patient no. 13, respectively.

There was no intraoperative mortality. Weaning from ECC was uncomplicated in all patients with low-dose catecholamine administration. Clear resection margins (R0) were achieved in all patients.

Postoperative Course

In the early postoperative period, one patient died in each group (30-day mortality: 12.5%). Patient no. 1 died of pneumonia and septic shock on the eighth postoperative day. Reintubation had been required on the day after operation.

Patient no. 9 experienced ventricular arrhythmias and died in shock on the fifth postoperative day. No neurological complications, no major bleeding, and no early revisions occurred. Late revisions were required in patient no. 5 with descending aortic replacement who developed a left pleural empyema. After rinsing the thoracic cavity with iodine solution, he underwent successful thoracomyoplasty. All surviving patients were transferred from the intensive care unit to the ward after a median of 1 day (range: 1 to 5 days) and discharged from the hospital after a median of 13 days (range: 10 to 24 days). All survivors were discharged in good condition and did not receive adjuvant radio- or chemotherapy.

Endpoint: Relapse

►**Fig. 1** shows the Kaplan–Meier estimator of the relapse of the NSCLC, either in form of local recurrence or distant metastasis. All but one patient with T4 tumors (group A) experienced recurrent disease. Median time to relapse was 6.5 months (range: 3 to 31 months). This is despite the fact that five patients (nos. 2 to 6) had received neoadjuvant radiochemotherapy). Patient nos. 3, 4, and 6 experienced early local recurrence after 4, 7, and 6 months, respectively. Of note, all had direct infiltration of the aortopulmonary window area. Patient nos. 2, 5, and 7 experienced distant metastasis of the liver, brain, esophagus, spine, and the adrenal gland after 3, 12, and 31 months, respectively. Only patient no. 8 never experienced a relapse of the disease and survived for 155 months after surgery. No relapse at all was documented in group B (T1 and T2 tumors).

Endpoint: Survival

►**Fig. 2** shows the Kaplan–Meier estimator of survival. Median survival was 13.6 months in group A (range: 0.3 to 155.4 months) and 21.1 months (range: 0.3 to 61.2 months) in group B. In group A, all patients died during the observation period. There was one long-term survivor (no. 8) in group A, who died after 155 months of disease-free survival from ventricular arrhythmias probably secondary to myocardial ischemia. All other patients died due to complications secondary to recurrence of their cancer.

In group B, two patients (nos. 11 and 16) were alive at the end of the observation period; one of them survived more than 5 years. Both live in good general condition. There was one perioperative death (no. 9). Another patient, no. 13, died of metastasized rectal carcinoma. The other four patients died due to cardiovascular incidents.

In both groups the estimated 5YSR amounted to 12.5%.

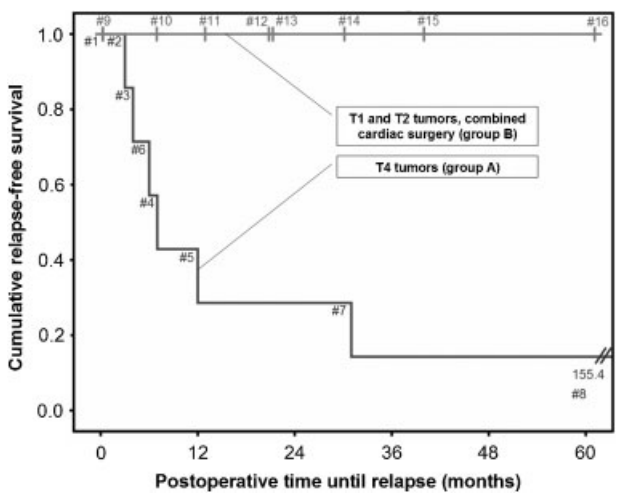

Fig. 1 Kaplan–Meier estimator of relapse-free survival from NSCLC; small figures indicate individual patients, corresponding to ►**Table 1**. NSCLC, non-small cell lung cancer.

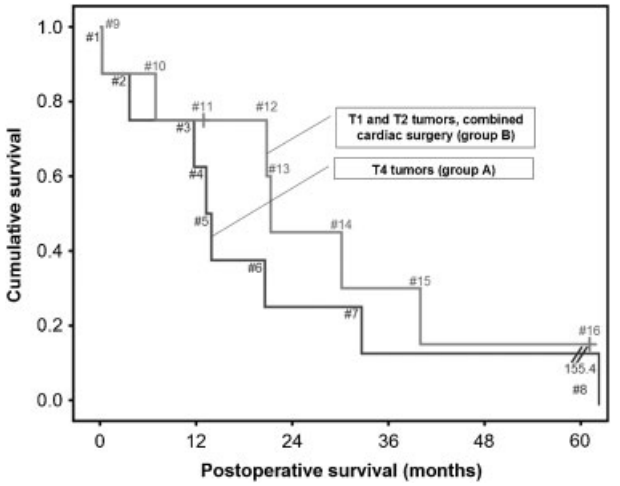

Fig. 2 Kaplan–Meier estimator of survival from NSCLC; small figures indicate individual patients, corresponding to ►**Table 1**. NSCLC, non-small cell lung cancer.

Discussion

Intraoperative cancer cell dissemination by ECC especially by pump suckers is a concern in T4 surgery for invasion of cardiovascular structures. Tumor cells have been observed in arterial ECC-filters.[5] We tried to reduce this risk by en bloc resection and avoiding pump suction and re-transfusion from cell-saving devices during the pulmonary part of surgery.

T4N0–1 tumors are supposed by some authors to have a substantially different biological behavior compared with small tumors (T1–T2) with advanced nodal involvement (N2–N3) or distant metastases.[6] Further, in locally advanced tumors, the prognosis is thought to depend predominantly on the nodal status.[7,8] In our experience, these assumptions hold true only for direct invasion of the atria and pulmonary veins. This is concordant to others who found that in such T4 cases, prognosis is not worse compared with tumor invasion of just the pericardium (T3).[8] The lack of distant metastases in spite of large direct exposure of tumor cells to the blood stream in atrial invasion also indicates a different biological behavior. In a recent systematic review on NSCLC resection with ECC, nodal status was without significance for long-term survival.[9]

In contrast, the prognosis of direct tumor invasion of the aortopulmonary window appears dismal. Three out of five patients with this entity in our series died within half a year postoperatively due to local recurrence. We attribute these

early recurrences to the fact that in the aortopulmonary window resection margins to other vital mediastinal structures are too narrow for effective radical resection in spite of en bloc resection of cardiovascular structures and pathological R0 status. All these patients had received neoadjuvant radiochemotherapy which apparently had no major influence in this respect. This is in contrast to our experience in other stage III NSCLC.[4] In the two patients with the longest survival, the aortopulmonary window was not infiltrated and the indication for ECC was direct invasion of the left atrium. One of these patients who survived for 13 years did not receive additional chemo- or radiotherapy.

Relating to intraoperative tumor cell dissemination and possible immunosuppressive effects of ECC, it is remarkable that no patient of group B experienced relapse of his NSCLC. Further, seven out of eight patients in group B were operated via sternotomy with its limited access to mediastinal lymph nodes. The number of removed lymph nodes was only half of those in group A, indicating a disadvantage of this approach in respect to systematic lymphadenectomy. Because no NSCLC relapse was observed in this group and because all but one patient not surviving the observation period died due to cardiovascular incidents, the combined cardiopulmonary surgery for simultaneous early NSCLC and cardiac disease appears legitimate. The further course of these patients indicates the considerably poor prognosis of this constellation.

The disadvantages of a two-staged approach are the high cardiac risk if the pulmonary resection is done first, the risk of tumor progress during the delay of therapy if the cardiac procedure is done first, a longer total period of convalescence with two operations, and not the least, economic effects. Sustained bleeding and impaired lung function due to ECC-associated side effects were no problems in our experience. From an oncological point of view, the suboptimal access to lymph nodes via sternotomy is a disadvantage of a one-stage approach. However, at least in left-sided NSCLC, the pulmonary operation including full lymphadenectomy and concomitant bypass grafting with an internal thoracic artery graft can be performed via a lateral thoracotomy as in patient no. 12. Some authors report inferior results with a one-stage approach,[10] whereas others document satisfactory results with a low perioperative mortality and 5YSRs of 42.0 to 64.0%.[11] We observed neither perioperative bleeding complications nor perioperative tumor spread during combined surgery and favor a one-stage procedure for coincidental pulmonary and cardiac disease. The low rate of these complications can also be taken into account when entertaining catheter procedures for cardiac disease with its requirements for high-dose antiplatelet therapy rendering a secondary lung resection cumbersome. Some of the procedures possibly could have been done off-pump. We decided in the past against this technique because we estimated the cardiopulmonary situation to be more unstable after lung resection. In any case, ECC has to be readily available for rapid management of cardiac problems.

Surgery for T4 NSCLC on ECC and combined cardiac and pulmonary procedures pose challenges in several respects. The indication for surgical intervention rests on accurate preoperative determination of resectability, general condition and motivation of the patient, and the ability of the surgeon for adequate resection and reconstruction. We believe that PET-CT studies are imperative for evaluation of NSCLC. Magnetic resonance tomography may assist in determining invasion of cardiovascular structures. However, infiltration of the aorta exceeding the mere adventitia is particularly difficult to determine preoperatively. In one of our patients, this was only possible by exploratory thoracotomy in another hospital before referral to our institution. Cardiac catheterization in addition to the routine work-up presently appears still necessary for adequate estimation of risks.

In respect to surgical strategy, some old techniques are worth mentioning: use of the pericardium for reconstruction in adults and pulmonary artery cannulation in left lateral thoracotomy. Pericardium confers optimal pliability and blood-tightness for reconstruction of cardiac cavities. It is an ideal regional flap for covering the bronchial stump and for separation of surrounding structures such as the esophagus. Cannulation of the main pulmonary artery trunk gives excellent venous drainage when the cannula is carefully advanced into the right ventricle while slowly commencing ECC to provide for an open pulmonary valve. Together with use of the ascending aorta or aortic arch as arterial cannulation sites, possible complications of groin cannulation are avoided and arterial flow is antegrade throughout the operation.

With the exception of the two early deaths and the patient with the successfully treated empyema, the postoperative course of our patients was rather uneventful. Of note, no revision for bleeding and no bronchial stump insufficiency were observed. Transfer from the ICU to the ward and discharge were quite rapid. So the risk appears calculable in both of our patients groups.

Few articles report on the long-term outcome of T4 NSCLC surgery. The variability of infiltration patterns in T4 tumors further hampers scientific analysis. For superior vena cava resections, 5YSRs of 24 to 31%,[6,12,13] for left atrium resections, 5YSR of 14%,[14] and for central pulmonary artery resections, 5YSR of 28%,[15] are reported without ECC use. For T4 resections without ECC in general, 30-day mortalities of ~12% and 5YSRs of ~15 to 37% are communicated.[8,9,14] The use of ECC is only required in a minority of T4-patients, Yildizeli et al observed an overall frequency of only 3.3% (TNM-6). However, in case of cardiovascular tumor infiltration, this share increased to 35%.[6] De Perrot et al[16] and Hasegawa et al[17] reported satisfactory perioperative and midterm results with use of ECC but very high rates of relapse. Ohta et al[18] reported a median survival of 26 months in a rather heterogeneous group of patients with infiltration of the descending thoracic aorta. However, assessment of infiltration was based on preoperative CT scans, a part of the patients was managed with temporary prosthetic bypass or without any bypass, and approximately one-third received just tangential resection of the aortic wall.

In a recent systematic review of lung resection for NSCLC with circulatory bypass, Muralidaran et al collected 72 patients from 20 publications over a 20-year period.[9] They

found a 5-year survival of 37% which seems to be much better than that in our patients. However, the average age was 10 years less than that in our group A and the authors suggest publication bias due to a "skewed population in the literature" with preponderant publication of positive outcomes.

The limited patient number presented here allows only for limited conclusions, but these emanate from a consecutive series in a single institution. Our postoperative results of ECC-assisted T4 surgery resemble the outcome of combined cardiopulmonary surgery. However, the midterm mortality in the T4-population clearly depended on the malignancy, whereas mortality in the group of low-stage NSCLC with coincidental heart disease depended on the cardiovascular disease. In this latter group, we observed a considerable risk for further cardiovascular incidents and death. The high rate of relapse in T4 NSCLC surgery with ECC we and others could document shows the clear limitation of its curative potential. This is in accordance with our experience in other cardiovascular tumor entities such as sarcomas.[19] Because perioperative complications are low and the midterm results are satisfactory, in our opinion T4-surgery may be indicated with palliative intention. Local complications by organ invasion can be reduced or deferred. Curative resection is feasible in some patients. However, direct tumor invasion of the aortopulmonary window carries in our experience a much worse prognosis than infiltration of the atria in spite of neoadjuvant radiochemotherapy. Caution and reluctance appear indicated when entertaining surgery for this entity.

Competing Interests

The authors declare that they have no competing interests.

References

1 Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010;60(5):277–300

2 Aupérin A, Le Péchoux C, Pignon JP, et al; Meta-Analysis of Cisplatin/carboplatin based Concomitant Chemotherapy in non-small cell Lung Cancer (MAC3-LC) Group. Concomitant radio-chemotherapy based on platin compounds in patients with locally advanced non-small cell lung cancer (NSCLC): a meta-analysis of individual data from 1764 patients. Ann Oncol 2006;17(3):473–483

3 Jett JR, Scott WJ, Rivera MP, Sause WT; American College of Chest Physicians. Guidelines on treatment of stage IIIB non-small cell lung cancer. Chest 2003;123(1, Suppl):221S–225S

4 Friedel G, Budach W, Dippon J, et al. Phase II trial of a trimodality regimen for stage III non-small-cell lung cancer using chemotherapy as induction treatment with concurrent hyperfractionated chemoradiation with carboplatin and paclitaxel followed by subsequent resection: a single-center study. J Clin Oncol 2010;28(6):942–948

5 Akchurin RS, Davidov MI, Partigulov SA, et al. Cardiopulmonary bypass and cell-saver technique in combined oncologic and cardiovascular surgery. Artif Organs 1997;21(7):763–765

6 Yildizeli 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(4):1065–1075, discussion 1074–1075

7 Wang T, Nelson RA, Bogardus A, Grannis FW Jr. Five-year lung cancer survival: which advanced stage nonsmall cell lung cancer patients attain long-term survival? Cancer 2010;116(6):1518–1525

8 Riquet M, Grand B, Arame A, et al. Lung cancer invading the pericardium: quantum of lymph nodes. Ann Thorac Surg 2010;90(6):1773–1777

9 Muralidaran A, Detterbeck FC, Boffa DJ, Wang Z, Kim AW. Long-term survival after lung resection for non-small cell lung cancer with circulatory bypass: a systematic review. J Thorac Cardiovasc Surg 2011;142(5):1137–1142

10 Miller DL, Orszulak TA, Pairolero PC, Trastek VF, Schaff HV. Combined operation for lung cancer and cardiac disease. Ann Thorac Surg 1994;58(4):989–993, discussion 993–994

11 Rao V, Todd TR, Weisel RD, et al. Results of combined pulmonary resection and cardiac operation. Ann Thorac Surg 1996;62(2):342–346, discussion 346–347

12 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(4):1184–1189, discussion 1184–1189

13 Spaggiari L, Thomas P, Magdeleinat P, et al. Superior vena cava resection with prosthetic replacement for non-small cell lung cancer: long-term results of a multicentric study. Eur J Cardiothorac Surg 2002;21(6):1080–1086

14 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(1):234–237

15 Venuta F, Ciccone AM, Anile M, et al. Reconstruction of the pulmonary artery for lung cancer: long-term results. J Thorac Cardiovasc Surg 2009;138(5):1185–1191

16 de Perrot M, Fadel E, Mussot S, de Palma A, Chapelier A, Dartevelle P. Resection of locally advanced (T4) non-small cell lung cancer with cardiopulmonary bypass. Ann Thorac Surg 2005;79(5):1691–1696, discussion 1697

17 Hasegawa S, Otake Y, Bando T, Cho H, Inui K, Wada H. Pulmonary dissemination of tumor cells after extended resection of thyroid carcinoma with cardiopulmonary bypass. J Thorac Cardiovasc Surg 2002;124(3):635–636

18 Ohta M, Hirabayasi H, Shiono H, et al. Surgical resection for lung cancer with infiltration of the thoracic aorta. J Thorac Cardiovasc Surg 2005;129(4):804–808

19 Mayer F, Aebert H, Rudert M, et al. Primary malignant sarcomas of the heart and great vessels in adult patients—a single-center experience. Oncologist 2007;12(9):1134–1142

20 Hendrix H, Schmitt J, Aebert H. [Ex situ sleeve resection and autotransplantation of the left lower pulmonary lobe after extended pneumonectomy]. Chirurg 2000;71(7):820–823