Completion pneumonectomy for non-small cell lung cancer: experience with 59 cases [☆]

A. Terzi[a,*], A. Lonardoni[a], G. Falezza[a], P. Scanagatta[a], A. Santo[b], G. Furlan[a], F. Calabrò[a]

[a]Division of Thoracic Surgery , Ospedale Maggiore, Azienda Ospedaliera, Verona, Italy
[b]Division of Medical Oncology, Azienda Ospedaliera/University of Verona, Verona, Italy

Abstract

Objective: The objective of this study was to assess the results of completion pneumonectomy performed for non-small cell lung cancer, classified as second primary or recurrence/metastasis. **Methods**: From 1982 to 2000, 59 patients underwent completion pneumonectomy for lung cancer, classified second primary or recurrence/metastasis according to a modified form of Martini's criteria, after a mean interval from first resection of 60 months for second primary lung cancers and 19 months for recurrences/metastases. **Results**: Operative mortality was 3.4% and complications occurred in 30% of patients. Five-year survival rate for completely resected patients was 25% (median 20 months). No significant difference in long-term survival was detected between second primary and recurrent tumors; survival was not adversely affected by a resection interval of less than 2 years or less than 12 months. **Conclusions**: Completion pneumonectomy for non-small cell lung cancer is a safe surgical procedure in experienced hands; long-term survival is acceptable and the best results are obtained for stage I lung cancer. Distinction between second primary lung cancer and recurrence failed to demonstrate a prognostic value. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Lung cancer; Completion pneumonectomy; Second primary lung cancer; Local recurrence

1. Introduction

Completion pneumonectomy (CP) for non-small cell lung cancer (NSCLC) may be required for a second primary lung cancer (2nd Pr.), a local recurrence or a lung to lung metastasis. The risk of developing a 2nd Pr. is approximately 2% per patient per year in early stage lung cancer [1] while the frequency of recurrence in the same area as the first site of failure after resection ranges from 3 to 9% for stage IA [2,3] to 32% for stage IIIA with positive surgical margins [4]. Although it is difficult to distinguish a new cancer from a recurrence or a lung to lung metastasis when the histology is the same, some criteria have been developed [5].

Technical difficulties, although substantial, are not considered per se a limiting factor to perform a CP. The limiting factor, when distant metastases are absent and the tumor is resectable, is the functional status of the patient; if his/her cardiopulmonary reserve is enough, a CP can be performed. We reviewed our experience with this operation for lung cancer and evaluated early- and long-term results.

2. Materials and methods

From 1982 through 2000, 59 patients underwent a CP for NSCLC out of 85 who had a CP for any reason in our Division. These patients represent 6% of pneumonectomies performed during the same period for NSCLC. There were 57 males and two females, mean age was 62 years (range 41–79). First resection was on the right side in 32 patients (14 upper lobectomies, 11 lower lobectomies, 5 bi-lobectomies, one middle lobectomy plus wedge resection and one wedge resection) and on the left side in 27 patients (15 upper lobectomies, 10 lower lobectomies, one resesction of lingula and one wedge resection); resection was considered complete in all patients but two operated on in other institutions. We used the criteria proposed by Martini [5] to distinguish a 2nd Pr. cancer from a local recurrence/metastasis. A 2nd Pr. was a tumor of a different histology or if histology was the same, the disease-free interval between cancers was at least 2 years or the second cancer was in a different lobe but with no cancer in common lymphatics or extrapulmon-

ary metastasis at time of diagnosis. However, when the cancer of the same histology appeared on the bronchial stump or on the margins of parenchymal resection of lobar resections, we considered it a local recurrence even 2 years after the resection. All patients were carefully restaged by means of a computed tomogrpahy (CT) scan of the chest, abdomen and brain and a bone scintigraphy. Pulmonary function tests and when required, a lung perfusion scintiscan and occasionally an oxygen consumption test, were obtained to ascertain whether they could tolerate the complete removal of the residual lung and only patients with a predicted postoperative Fev1 of more than 1.0 L and acceptable cardiac function underwent CP. Mediastinoscopy was performed not routinely, but to exclude N3 disease or in case CT scan demonstrated accessible mediastinal nodes with a diameter larger than 1 cm. According to Martini's (modified) criteria, 32 patients had a CP for a 2nd Pr. and 27 for a local recurrence/metastasis (19 recurrences and eight metastases of which two were multiple); recurrences were hilar and on the bronchial stump in 10 cases, into lung parenchima in five cases, involving chest wall in three cases and diaphragm in one case). Mean interval between the first resection and CP was 38 months overall (range 5–304); the interval was 60 months (range 6–304) for 2nd Pr. and 19 months (range 5–84) for local recurrences/ metastases ($P = 0.01$ Mann–Whitney test). In 37 patients, the cancer reappeared less than 2 years after the first resection and in 22 patients after more than 2 years. CP was on the right side in 31 cases and on the left in 28 cases. At first resection 43 patients were in stage IA-B, nine in stage II A–B and seven in stage IIIA. Histology at first resection was epidermoid carcinoma in 32 cases, adenocarcinoma in 25 cases, diffuse bronchioloalveolar carcinoma in one case and carcinoid in one case. Radiation therapy for R1 disease had been administered in two patients with an N0 disease operated on in other institutions but data on doses and fields employed were not available. Follow up of the patients who survived CP was complete, mean follow up was 28 months (range 2–160) . The Kaplan–Meier method was used to calculate the expected survival rates after CP and the data included operative mortality; statistical significance was calculated with the log-rank test and a *P* less than 0.05 was considered significant. Survival analysis was performed for the entire group of patients, for 2nd Pr. and recurrence, for stage, and for interval from first resection to CP for completely resected patients.

3. Results

CP was performed through a posterolateral approach even in those patients who had an anterolateral thoracotomy at first resection and a rib was sometimes removed. Intrapericardial approach to pulmonary vessels was obtained in most patients, even if occasionally an extrapericardial ligature was possible, mainly in patients with previous lower lobectomy. Extrapleural dissection was sometimes required; generally patients with a previous upper lobectomy had dense scar tissue around the pulmonary artery and main bronchus, making the resection more difficult. The resection was also difficult in those two patients who had previous radiation therapy although the pericardial cavity had not been completely obliterated. CP was associated with chest wall resection in seven patients, carinal resection in two patients and pericardial resection in another two (in one case associated to marginal left atrial resection). The bronchial stump was always hand-sutured and reinforced with a pedicled pericardial fat pad in most cases, in two cases a flap of the serratus anterior muscle, that was not transected at previous anterolatreral toracothomy, was used to reinforce the bronchial stump. Chest wall reconstruction was performed using a 2 mm thick PTFE patch. Intraoperative mean blood loss was 743 ml (range 270–2650 ml) and 32 patients required intra or postoperative blood transfusions (mean 3 units of packed cells), although no one needed reoperation for bleeding. The mean resection time was 167 minutes (range 90–240).

Complications occurred in 18 patients (30%); there were 13 medical complications (atrial fibrillation in nine, respiratory failure in two, pericarditis in one and pulmonary edema in one) and eight surgical intra or postoperative complications (chylothorax in one, intraoperative massive bleeding from aorta in one, hemorrage from azygous cross laceration in two, left recurrent section in one, broncopleural fistula in one, empyema in one, incomplete wound dehiscence in one), there was no difference in the complication rates between the right and left sides. Operative mortality was 3.4% (2/59). One patient died intraoperatively after cardiac arrest due to acute myocardial infarction as detected by autopsy, the other died a few hours after CP due to massive bleeding from the right main pulmonary artery related to slipping of the tie. Six patients had an incomplete resection due to R1 disease in four cases (one carcinoma in situ and two mucosal residual disease on bronchial stump, one on left atrial resection margin) and R2 disease in two cases (one vertebral body and one esophagus); all cases of incomplete resection were in the group with a local recurrence of disease, five out of the six patients refused further adjuvant treatment (mean survival time 132 days) and the patient with a carcinoma in situ was followed-up until death for distant recurrence after 61 months. At CP, eight patients were in stage IA–B, 25 in stage IIA–B, 25 in stage IIIA–B (11 for N2 disease) and one in stage IV for a single brain metastasis; all stage I patients had a second primary lung cancer. Histology at CP was different from the first resection for five patients in the 2nd Pr. group; so we had 33 epidermoid carcinomas, 25 adenocarcinomas and one diffuse bronchiolo-alveolar carcinoma. Completely resected patients with a N2 disease underwent radiation therapy on mediastinum. Cumulative 3- and 5-year survival rates were 34.5 and 23% overall. For completely resected patients, survival rates were 38 and 25% overall (Fig. 1), while the
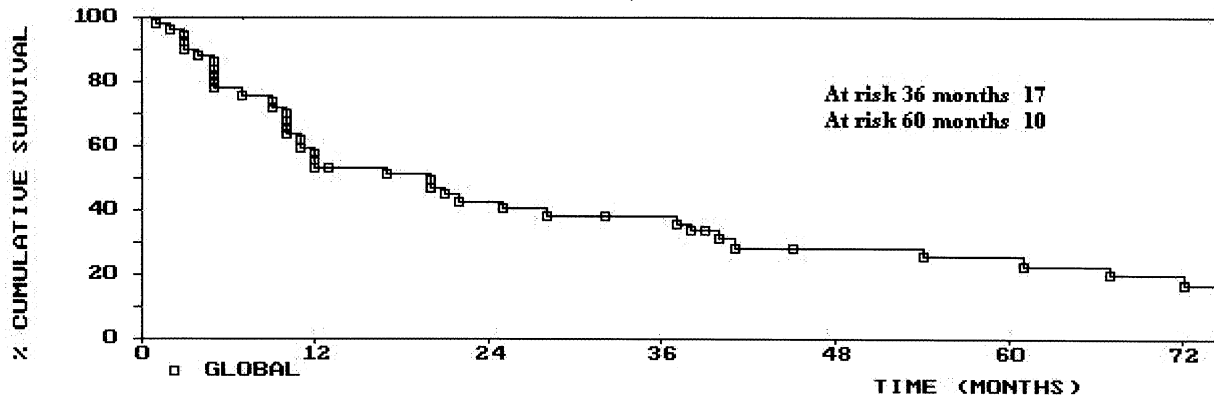
Fig. 1. Cumulative survival rate for all completely resected patients.

rates were 42 and 30% for patients with a 2nd Pr. and 28 and 14% for the recurrence/metastasis group ($P = 0.2$) (Fig. 2). Survival by stage in completely resected patients showed a 3- and 5-year survival of 71.5% for stage I, 32 and 20% for stage II, 35 and 15% for stage III ($P = 0.03$) (Fig. 3). In completely resected patients in whom the cancer reappeared less, or more, than 2 years after the first operation, the cumulative 3- and 5-year survival rates were 33–27%, and 44–24%, respectively ($P = $ NS) overall. They were 40% and 43–26% ($P = $ NS) for 2nd Pr. lung cancer only. Again patients who had the recurrence less, or more, than 12 months after the first resection did not have a significantly different 5-year survival rate (14 versus 19%).

4. Discussion

CP for lung cancer is an uncommon procedure performed both for second primary lung cancer and local recurrence. It is a technically demanding procedure in which massive intraoperative bleeding can occur accounting for most cases of intraoperative mortality [6–8]. To overcome the increased risk of massive haemorrhage, intrapericardial control of pulmonary vessels is usually recommended, and

there are other technical artifices well known to experienced thoracic surgeons which achieve safe control of pulmonary vessels [6,8,9]. Reported operative mortality ranges from 0 to 15.2% [10], although in most reports it is below 10%, and in our experience it is 3.4%. Our rate of mortality is comparable to the operative mortality of standard pneumonectomy [11]. Although morbidity is not higher than for standard pneumonectomy, postoperative bleeding is common [8] and the most dreaded complication, broncopleural fistula, is best prevented by bronchial stump coverage, even with skeletal muscles in cases of previous radiation therapy. Bleeding was greater than usual in most of our patients, although no one required rethoracotomy, and a broncopleural fistula occurred only in one patient. Five-year survival was 25% in completely resected patients, and was not significantly different between patients operated on for a second primary lung cancer or a local recurrence, and this is in agreement with data reported by others [12,13] although a more favourable trend is shown for 2nd Pr.; our data are comparable with those of McGovern et al. [7] and Al-Kattan et al. [14], who reported a 5-year survival of 26.5 and 23%, respectively. A significant difference was present by stage, although the difference was not significant when stages II and III were compared. It is known that
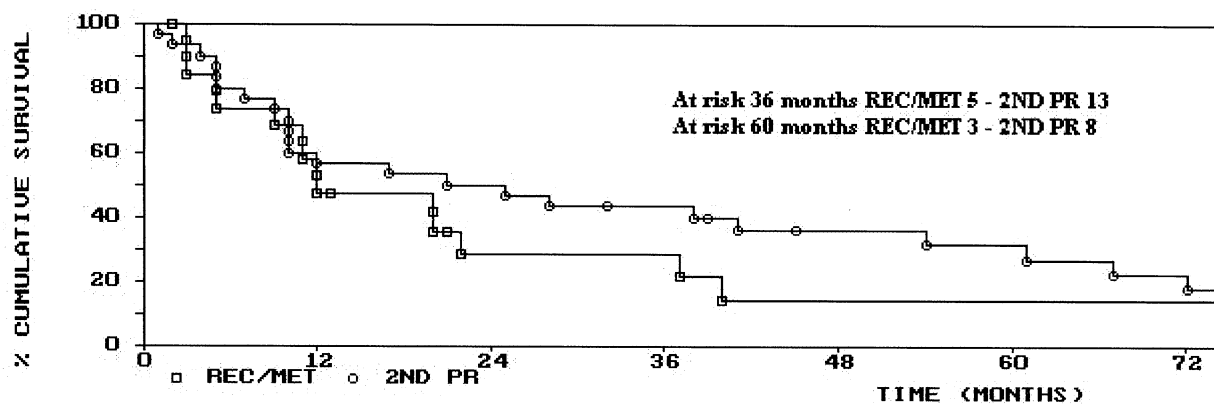

Fig. 2. Cumulative survival rates for completely resected patients with a second primary lung cancer and recurrence/metastasis.
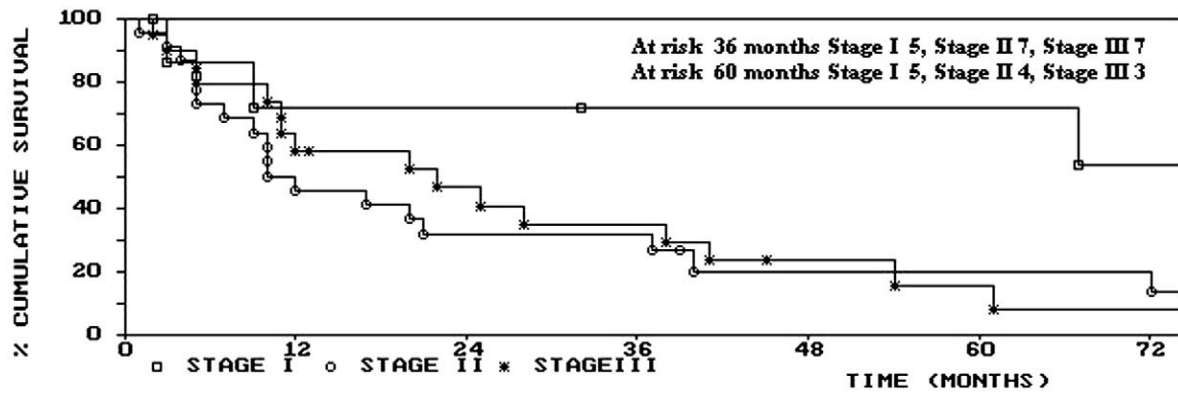
Fig. 3. Cumulative survival rate by stage for completely resected patients.

controversy exists concerning the disease-free interval to be used to distinguish a local recurrence from a second primary lung cancer in cases of identical histology. Moreover, according to Massard [15], in stage IIIA patients the distinction between a hilar node recurrence or locally advanced 2nd Pr. cannot be easily stated in all cases. Although 2, 3 or 5 years have been considered the optimal interval [5,16,17] to separate a 2nd Pr. from a local recurrence or metastasis, no general agreement has been reached and other methods such as flow cytometry or DNA ploidity analysis have been suggested [18]. In a recent paper [19] it was shown that for 2nd Pr. survival was negatively affected by a resection interval of less than 2 years; these data confirm those reported by Rosengart et al. [20], who found a significantly lower 5-year survival rate in patients in whom the interval between two primary lesions was shorter than 2 years. A disease-free interval longer than 2 years was associated with significantly better survival in a group of patients with a local recurrence who were treated by radiation therapy by Yano [21]. In our patients we found no difference when comparing patients in whom the new cancer appeared after less or more than 2 years, either in patients with a 2nd Pr. or with a recurrence. Although a cancer occurring after 2 years is usually considered a 2nd Pr., there are cases which are probably recurrences with a very long doubling time [22] and it is for this reason that we considered those cases occurring on the bronchial stump or in the area of a previous sublobar resection (wedge or segmental resection) to be local recurrences, even after a time span longer than 2 years. It has been reported [22] that these late recurrence cancers with a long doubling time have an inherently good prognosis. But, looking at our data, we cannot agree with Lenner [22] that perhaps the prognosis is directly related to the length of the resection interval regardless of whether it is a 2ndPr. or a recurrent cancer. Recently Otha et al. [23] considered the role of microvessel density on outcome in patients with recurrent lung cancer and concluded that in patients with recurrence the mean vessel density was significantly higher than in those without recurrence; interestingly, patients who survived longer after CP had a lower vessel density when compared to other patients. Due to the small sample of patients, no definitive conclusion can be drawn from this study, although we agree with the authors that further investigations on that subject should be conducted. In the same paper, the authors report that patients who survived for a long period had a disease free interval of longer than 12 months, but in our patients with a local recurrence, no difference was detected even when an interval of 12 months was chosen. Radiation therapy as an alternative form of treatment for local recurrence fails to obtain results better than surgery and Yano [21] reported a 5-year survival of 8.5% in a group of patients with a local recurrence treated by radiation therapy and chemo/radiation therapy but a 0% 3-year survival in non-responder patients.

In conclusion, CP is a safe surgical procedure in the hands of an experienced thoracic surgeon. Long-term survival is really satisfactory only for stage I patients, although for higher stages it can be considered acceptable if we consider the poor results of alternative treatments and the operative mortality rate; distinction between a 2nd Pr. and a recurrence does not seem to influence the prognosis. So the problem is to evaluate the patients for a complete resection. After resection of a low stage lung cancer, an intensive follow-up might allow to detect a new lung cancer in an early stage thus allowing a curative CP to be performed. Resection interval does not seem to influence long-term survival although the small number of patients does not allow to draw definitive conclusions.

References

[1] Johnson BE, Cortazar P, Chute JP. Second lung cancers in patients successfully treated for lung cancer. Semin Oncol 1997;24:492–499.

[2] Ishida T, Yano T, Maeda K, Kaneko S, Tateishi M, Sugimachi K. Strategy for lymphadenectomy in lung cancer three centimeters or less in diameter. Ann Thorac Surg 1990;50:708–713.

[3] Thomas P, Rubenstein L. Cancer recurrence after resection: T1N0 non-small cell lung cancer. Ann Thorac Surg 1990;49:242–247.

[4] Kaiser LR, Fleshner P, Keller S, Martini N. Significance of extramucosal residual tumor at the bronchial resection margin. Ann Thorac Surg 1989;47:265–269.

[5] Martini M, Melamed MR. Multiple primary lung cancer. J Thorac Cardiovasc Surg 1975;70:606–612.

[6] Gregoire J, Deslauriers J, Guojin L, Rouleau J. Indications, risks and results of completion pneumonectomy. J Thorac Cardiovasc Surg 1993;105:918–924.

[7] McGovern EM, Trastek VF, Pairolero PC, Spencer Payne W. Completion pneumonectomy: indications, complications and results. Ann Thorac Surg 1988;46:141–146.

[8] Watanabe Y, Shimizu J, Oda M, Tatsuzawa Y, Hayashi Y, Iwa T. Second surgical intervention for recurrent and second primary bronchogenic carcinoma. Scand J Thorac Cardiovasc Surg 1992;26:73–78.

[9] Mansour KA, Downey RS. Managing the difficult pulmonary artery during completion pneumonectomy. Surg Gynecol Obstet 1989;169:161–162.

[10] Tronc F, Grégoire J, Rouleau J, Deslauriers J. Techniques of pneumonectomy. Chest Surg Clin North Am 1999;9:393–404.

[11] Ginsberg RJ, Hill LD, Eagan RT, Thomas P, Mountain CF, Deslauriers J, Fry WA, Butz RO, Goldberg M, Waters PF, Jones DP, Pairolero P, Rubinstein L, Pearson FG. Modern thirty day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 1983;86:654–658.

[12] Regnard JF, Icard P, Magdeleinat P, Jauffret B, Farés E, Levasseur P. Completion pneumonectomy: experience in eighty patients. J. Thorac Cardiovasc Surg 1999;111:1095–1101.

[13] Fujimoto T, Zaboura G, Fechner S, Hillejan L, Schroeder T, Marra A, Krbek T, Hinterthaner M, Greschuchna D, Stamatis G. Completion pneumonectomy:current indications,complications,and results. J Thorac Cardiovasc Surg 2001;121:484–490.

[14] Al-Kattan K, Goldstraw P. Completion pneumonectomy: indications and outcome. J Thorac Cardiovasc Surg 1995;110:1125–1129.

[15] Massard G, Lyons G, Whilm J, Fernoux P, Dumont P, Kessler R, Roeslin N, Morand G. Early and long-term results after completion pneumonectomy. Ann Thorac Surg 1995;59:196–200.

[16] The Lung Cancer Study Group prepared by P.A. Thomas, L. Rubinstein. Malignant disease appearing late after operation for T1N0 non-small cell lung cancer. J Thorac Cardiovasc Surg 1993;106:1053–1058.

[17] VanBogedom PC, Wagenaar SS, Corrin B, Baak JPA, Berkel J, Vanderschuren RGJRA. Second primary lung cancer: importance of long-term follow-up. Thorax 1989;44:788–793.

[18] Olak J, Ferguson MK. Surgical management of second primary and metastatic lung cancer. In: Pass H, Mitchell JB, Johnson DH, Turrisi A, Minna JD, editors. Lung cancer principles and practice, Philadelphia, PA: Lippincot Williams and Wilkins, 2000. pp. 730–741.

[19] Doddoli C, Thomas P, Ghez O, Giudicelli R, Fuentes P. Surgical management of metachronous bronchial carcinoma. Eur J Cardiothorac Surg 2001;19:899–903.

[20] Rosengart TK, Martini N, Ghosen P, Burt M. Multiple primary lung carcinomas: prognosis and treatment. Ann Thorac Surg 1991;52:773–779.

[21] Yano T, Hara N, Ichinose Y, Asoh H, Yokoyama H, Otha M, Hata K. Local recurrence after complete resection for non-small cell lung cancer. J Thorac Cardiovasc Surg 1994;107:8–12.

[22] Lenner R, Teirstein A, Krellenstein DJ. Metachronous cancers or late recurrences after resection of stage I lung cancer. Ann Thorac Surg 1999;67:548–549.

[23] Otha Y, Hara T, Tanaka Y, Watanabe SI, Oda M, Murakami S, Watanabe Y. Completion pneumonectomy for patients with recurrent lung cancer: the impact of microvessel density on outcome. Surg Today 2000;30:134–138.