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Surgical treatment of lung cancer invading chest wall: a retrospective analysis of 110 patients[☆]

Stefano Elia^{*}, Salvatore Griffo, Maria Gentile, Raimondo Costabile, Giovanni Ferrante

Department of Thoracic Surgery, Medical Faculty, University Federico II, Naples, Italy

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Abstract

Objective: To retrospectively assess the results of surgical treatment in a consecutive series of 110 patients with Stage IIb and IIIa non small cell lung cancer (NSCLC) invading chest wall. **Methods:** A series of 110 patients underwent surgery for Stage IIb and IIIa NSCLC with involvement of chest wall. There were 101 male and 9 female patients, mean age was 61.4 (range 32–74), 52 (47.3%) of them complaining for chest pain. Surgical procedures were pneumonectomy in seven patients (6.4%), lobectomy in 73 (66.4%), bi-lobectomy in six (5.4%) and wedge resection in 24 (21.8%). In 63 patients (57.3%) an extrapleural resection was performed while in the other 47 (42.7%) an ‘en bloc’ resection of tumor with chest wall was required. In 22 patients (76.3%) repair was achieved by muscle flap while in 8 (26.7%) a prosthesis was required. Five-year survival was computed using the Kaplan–Meier method; *P* values correspond to the log-rank test. **Results:** There were neither intraoperative nor postoperative deaths. Postoperative staging revealed 83 T3N0M0, 17 T3N1M0 and 10 T3N2M0. Mean postoperative hospital stay was 17.7 days (range 5–40). For N0 patients 5 year survival was 47% (39/83) and no significant difference was noted when extrapleural and ‘en bloc’ resection groups were compared (*P* = 0.08). In N1/N2 patients no survival was observed (0/27) and comparison between surgical procedures was not statistically significant (*P* = 0.41). Moreover when N0 patients were compared with N1 patients the difference in survival was significant for both extrapleural (*P* = 0.02) and ‘en bloc’ (*P* = 0.04) groups. No difference was noted when the two surgical procedures were compared independently from N status (*P* = 0.94). Within the group of patients undergone ‘en bloc’ resection survival was significantly better for N0 patients as in the group of extrapleural resection. **Conclusion:** Surgical treatment of Stage IIb and IIIa NSCLC invading chest wall by extrapleural or ‘en bloc’ resection is widely adopted and justified by the good results in terms of morbidity and relief of pain. Survival is always depending on the *N* status. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Lung cancer; Chest wall invasion; Surgical treatment; Survival

1. Introduction

Bronchogenic carcinoma of the lung remains the leading cause of death due to cancer. Pulmonary resection is presently the most appropriate treatment for lung cancer. Overall 5-year survival ranges from about 70% for Stage I non small cell lung cancer (NSCLC) to less than 10% for patients with bulky N2–3 disease [1]. Invasion of the chest wall, vertebral body, mediastinum or diaphragm is not rare and the prognostic value of this finding has always been controversial. In approximately 5% of patients with lung cancer a peripheral primary tumor will invade the parietal pleura and, in several of these patients, extend into ribs and

soft tissues of the chest wall [2]. Patients who have bronchogenic carcinoma with invasion of chest wall make up a particular subset of patients that has a potential long-term survival, provided that complete resection is achieved and mediastinal node involvement is not present.

Parietal pleura and Luschka’s fascia make up a natural barrier to cancer involvement and usually are interested by an ‘adhering’ more than ‘infiltrating’ process and therefore quite a few of these tumors may be detached from chest wall by extrapleural dissection. The overcoming of such a barrier by the neoplasm requires a more extended procedure that will encompass all involved ribs and chest wall soft tissue with a safety resection edge of at least 3–4 cm.

Presently survival for patients undergone surgery for NSCLC invading chest wall ranges from 15 to 38% and seems being affected by mediastinal lymph node involvement, histology and extent of invasion [3–5].

The aim of this study was to retrospectively assess the

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^{*} Corresponding author. Via Mariano D’Ayala, 181-80121 Naples, Italy. Tel.: +39-081-7462651; fax: +39-081-7462651.

E-mail address: elia@unina.it (S. Elia).

results of surgical treatment in a series of 110 patients with NSCLC invading the chest wall.

2. Materials and methods

A retrospective review of the data recorded at the Thoracic Surgery Department of the University 'Federico II', Naples, Italy, performed to determine patterns of failure and overall survival, identified a series of 110 evaluable patients who underwent surgical exploration for NSCLC with T3 chest wall involvement between January 1980 and December 1994. Recurrences, metastatic cancer, residual disease after resection, synchronous primary tumors, non bronchogenic carcinoma and superior sulcus tumors were excluded from this study. Operative reports, pathology reports and hospital records were analysed for the following potential prognostic factors: tumor size, tumor location, tumor grade, histology, patient age, use of adjuvant radiation therapy and type of surgical procedure performed (en bloc or extrapleural resection). A review of pathological reports and operative notes determined the depth of invasion and the degree of nodal involvement while no review of actual pathologic samples was performed.

Preoperative diagnostic/staging procedures included clinical history, physical examination, complete blood cell count, liver function tests, chest roentgenogram, fiberoptic bronchoscopy with cytology and computed tomography (CT) of the chest and CT assisted fine needle aspiration biopsy (FNAB) of the lung, abdominal CT. Brain CT and bone scan were performed whenever required.

All patients with recent cardiac ischemia (<3 months), unstable angina pectoris, heart failure or arrhythmia were excluded from surgery. Moreover the following respiratory function values taken at rest would contraindicate a surgical procedure: VC < 40%, FEV1/FVC < 35%, FEV1 < 1.5 l, Pao₂ < 55 mmHg and PaCO₂ > 45 mmHg.

There were 101 male and nine female patients, mean age was 61.4 (range 32–74). Main symptom was chest pain (47.3%) followed by haemoptysis (15.4%), cough (13.6%) and effort dyspnoea (2.7%) while in 25 patients (22.7%) the finding was occasional. Surgical procedures were pneumonectomy in seven patients (6.3%), lobectomy in 73 (66.4%), bi-lobectomy in 6 (5.4%) and wedge resection in 24 (21.8%). This last procedure was performed in patients whose respiratory function would not allow a major surgery. In 63 patients (57.3%) an extrapleural resection was performed with an extrapleural mobilisation of the tumor at the level of its attachment to chest wall and removal of lung tissue in continuity with the overlying pleura. In the other 47 (42.7%) an 'en bloc' resection of tumor with chest wall was required. In this latter subset of patients the number of resected ribs was four in five patients (10.6%), 3 in 24 (51%), 2 in 14 (29.7%), and one in four (8.5%). The resection was defined as complete (R0) by pathologic demonstration of negative tissue margins and by the judge-

ment of the operating surgeon who had removed all detectable disease and performed a mediastinal lymph node dissection. Patients having complete gross resection at surgery but with positive margins at pathology were defined as having undergone microscopically incomplete resection (R1). No patient undergone grossly incomplete resection (R2) belongs to this series.

The involvement of chest wall was lateral or anterolateral in 30 patients (63.8%) and posterior in 17 (36.2%). In 22 patients (73.3%) repair was achieved by muscle flap while in eight (26.7%) a prosthesis was required. The mean size of chest wall defect was 6.8 × 4.5 cm. Median follow up was 60 months (range 1–179). The final event was patient's death for neoplasm or other causes while the starting time was the day of surgery. Clinical (TNM) and pathological (pTNM) were assigned in agreement with the New International System for Staging Lung Cancer as applied by the American Joint Committee on Cancer and Union Internationale Contre le Cancer [6]. Calculation of survival used the Kaplan–Maier method and included operative deaths defined as intraoperative, within 30 days of surgery or within the same hospitalisation. Groups were compared using the log-rank test. A probability level of less than or equal to 0.05 was considered significant.

3. Results

We identified 110 patients between January 1980 and December 1994 who had undergone surgical exploration for NSCLC with T3 chest wall invasion and no known distant metastases (M0). There were neither intraoperative nor postoperative (30 days) deaths. Mean postoperative hospital stay was 17.7 days (range 5–40). In 12 patients (10.9%) a prolonged air leakage was observed (>7 days) which did not require further action, while in 19 patients (17.27%) a postoperative atelectasis and/or infection were observed. Histology showed a squamous cell in 61 patients (55.4%), adenocarcinoma in 39 (35.4%), large cell in four (3.6%) 'spindle cell' in two (1.8%) and mixed type in four (3.6%). Postoperative staging revealed 83 T3N0M0, 17 T3N1M0 and ten T3N2M0. Resection was complete (R0) in 94 patients (85.4%) and microscopically incomplete (R1) in 16 patients (14.5%). Of the 94 patients undergone R0 resection 79 were staged as T3N0, seven as T3N1 and eight as T3N2. Of the 16 patients undergone R1 incomplete resection four patients were staged as T3N0, 10 as T3N1 and two as T3N2. All R1 patients underwent postoperative adjuvant radiation therapy on surgical site in combination with mediastinal field in 12 cases with a median dose of 50 Gy (25–70 Gy) and conventional fractionation (five fractions per week of 2.0 Gy per fraction). In 15 patients undergone R0 resection a mediastinal postoperative radiation treatment was performed due to the pTNM according to the same modalities.

The local disease control after resection was good and the

resolution of pain was achieved in all patients. The status at last follow-up of all patients undergone complete (R0) resection was as follows: 36 patients (38.2%) were alive without evidence of disease, two were alive with disease (2.1%), nine died without disease (9.5%) and 51 died of disease (54.2%).

Overall 5-year survival for N0 patients was 47% (39/83) while no survival was reported for N1 patients (0/17) and among N2 patients (0/10) in both extrapleural and en bloc resection groups. No significant difference was noted when surgical procedures were compared ($P = 0.88$).

4. Discussion

Despite the improvements recorded in the last four decades, lung cancer continues to be an extremely lethal disease, responsible for more cancer deaths than any other solid tumor. Resection remains the best treatment option for patients with localized NSCLC provided that an early diagnosis is achieved. In about 5–8% of patients with lung cancer there is a parietal pleura or full thickness chest wall involvement. Notwithstanding the fact that this should be considered as an unfavourable outcome of the disease these patients must be evaluated carefully for surgical exploration with consideration of resection because chest wall invasion per se does not contraindicate resection. As a matter of fact in 1997 the International Staging System for Lung Cancer was revised to address the heterogeneity of end results within stage groups and the lack of specificity in stage classification [6]. Changes from the previous system would concern the division of stage I into stage IA and IB depending on tumor size and the division of stage II into stage IIA and IIB based on tumor size and nodal involvement. The group of T3N0 was moved from stage IIIA to stage IIB. Favourable survival is reported following extended resection of the chest wall in cases without lymph node involvement. An actuarial 5-year survival rate of up to 54% has been reported in chest wall resection for N0 disease [7]. Undoubtedly survival is mostly determined by the N status and the prognosis is worse for N1 and N2 patients.

Previous reports attempted to identify patterns of failure and overall survival in patients undergone surgical exploration for a T3 non-small cell lung cancer but most of these studies would concern a quite heterogeneous group of patients with respect to nodal status, margins, radiation therapy and type of surgical resection (extrapleural or 'en bloc' chest wall resection). However most of them suggested that durable survival can be achieved with an acceptable mortality by resection and that survival is highly dependent not only on a complete resection but essentially on the extent of lymph node involvement [8]. Some authors stated that also the depth of chest wall invasion may be influencing the 5-year survival insofar as tumors involving only parietal pleura had survival differences approaching statistical

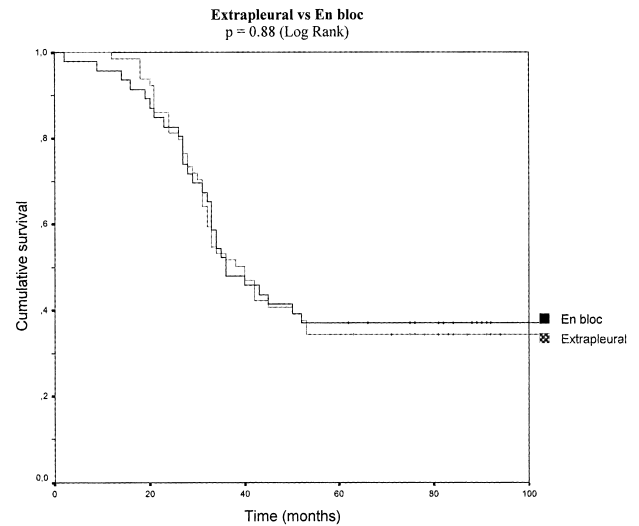


Fig. 1. Overall survival by type of surgical procedure: all patients.

significance when compared with those in which other chest wall components were involved [2,9].

This report aims at evaluating a more homogeneous subset of patients, namely patients with chest wall T3 N0 M0 classification in which a complete (R0) resection as judged by the surgeon had been performed even if a subgroup of them came out to be microscopically (R1) incompletely resected. Therefore macroscopically incomplete (R2) resection was purposely not included since we believed that this last subset may have jeopardized the overall evaluation.

Subgroup analyses were undertaken examining the association between chest wall invasion, type of resection and survival within nodal status categories [10]. The overall survival stratified by type of surgical procedure did not show any significant statistical difference between extra-

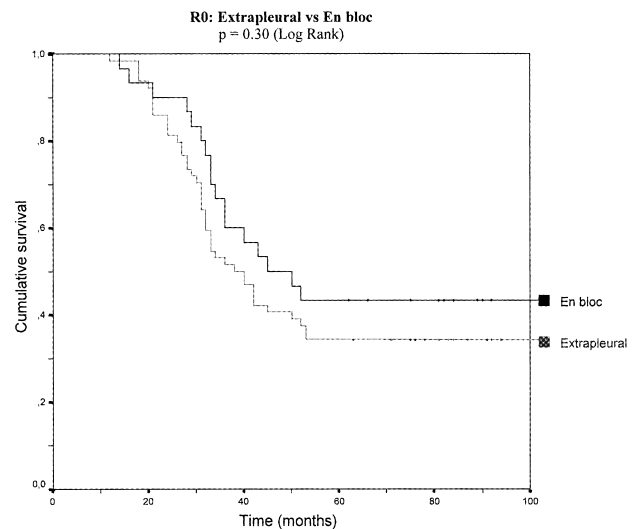


Fig. 2. Survival by type of surgical procedure in completely resected patients (R0).

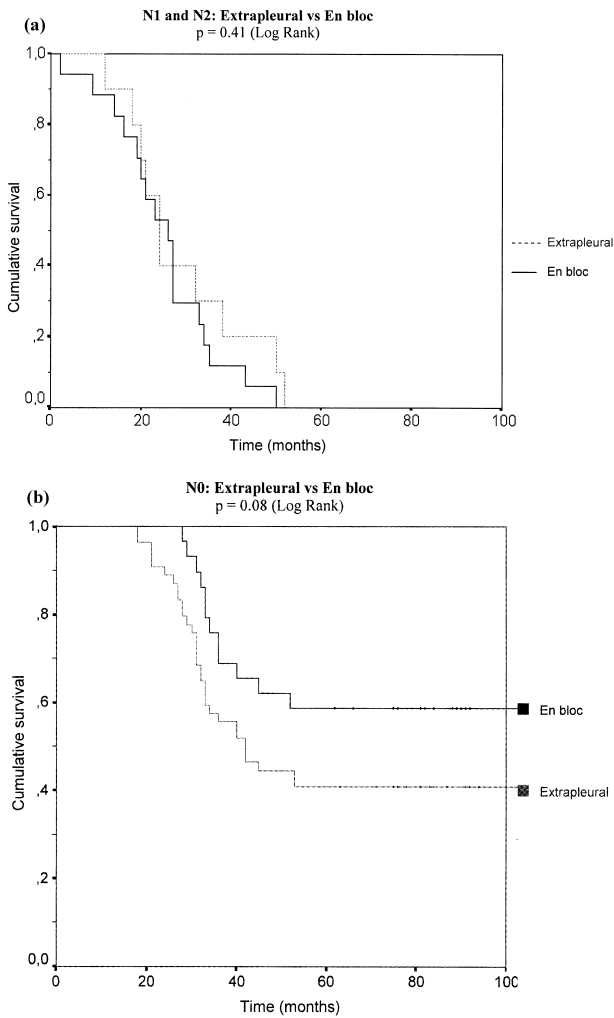


Fig. 3. (a) Survival by type of surgical procedure in N1 and N2 patients. (b) Survival by type of surgical procedure in N0 patients.

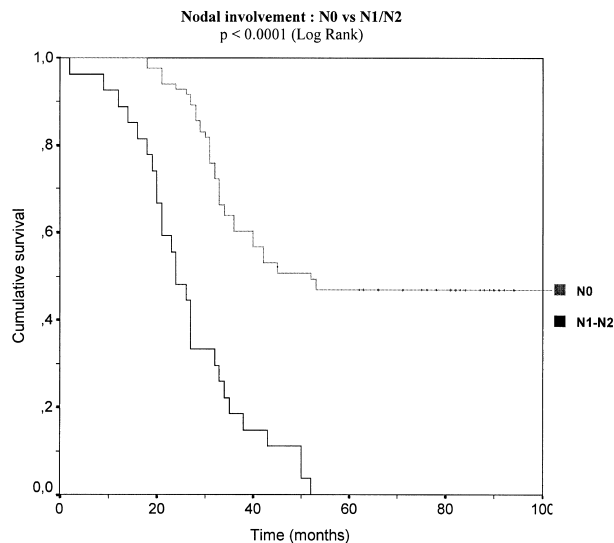


Fig. 4. Survival by nodal involvement: all patients.

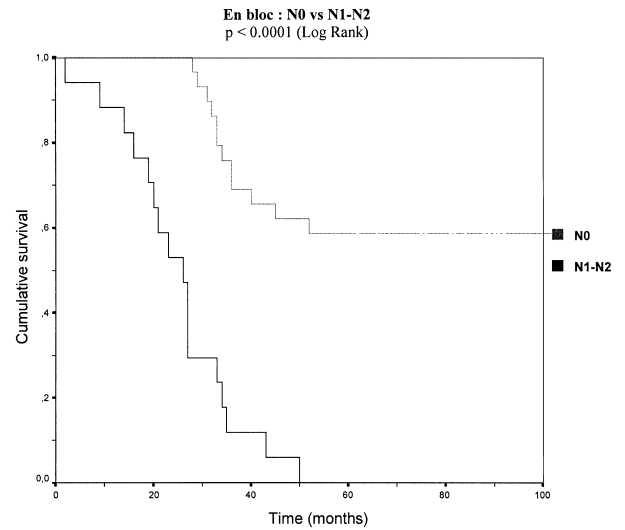


Fig. 5. Survival by nodal involvement: 'en bloc' resection.

pleural and en bloc resection (Fig. 1). Even when we considered all patients undergone complete (R0) resection no statistical difference was noted (Fig. 2). Without nodal involvement (N0) a prolonged survival time was found among patients receiving full thickness vs. extrapleural resection even though the value would only approach statistical significance ($P = 0.08$) while when a nodal involvement was present (N1 or N2), the survival curves were quite similar (Fig. 3a,b).

On the other hand when all patients were stratified for N0 vs. N1/N2 there was a statistically significant advantage ($P < 0.0001$) when survival curves were compared independently from the depth of resection (Fig. 4).

An interesting controversy has been concerning the extent of surgical resection that is required for patients with parietal pleural involvement or invasion into the

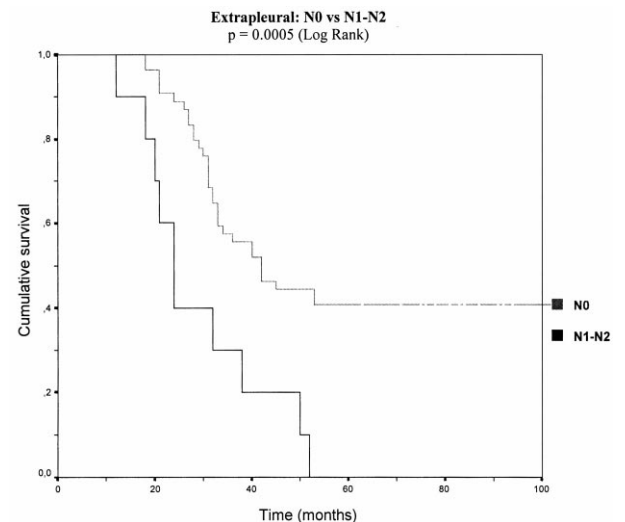


Fig. 6. Survival by nodal involvement: 'extrapleural' resection.

chest wall. Some of the previous reports have shown improved survival curves for patients undergone en bloc chest wall resection compared with extrapleural procedures [11,12]. Downey et al. [2] stated that an incomplete resection, even if leaving only microscopic disease, offers the patient no curative benefit. No patients with macroscopic residual disease has been included in present series and therefore we only took into consideration those patients that upon surgeon's judgement were completely resected since, as it is well known, frozen section on bone is not available. Sixteen out of our 47 patients undergone en bloc resection had microscopic residual disease (R1) at post-operative pathology and therefore underwent adjuvant radiation treatment according to the usual standard of treatment [13]. None of the patients undergone extrapleural resection showed residual disease thus a comparison could not be made. On the other hand within the R1 group the difference in survival between N0 and N1/N2 patients was highly significant ($P = 0.0012$).

When the group of patients undergone 'en bloc' resection was analyzed separately the comparison of survival between N0 and N1/N2 patients was highly significant (Fig. 5). The same statistical significance was detected when the group of extrapleural resection was taken into consideration (Fig. 6).

The rate of wedge resections in our series was slightly higher than in other series (21.8% vs. 10–15%) [2]. This was due in nine cases to the fact that the programmed major resection (lobectomy or pneumonectomy) was not feasible for the intolerance to single lung ventilation during surgery, and in other 15 cases with poor functional status, to the choice of treating the symptom (pain) and improving the quality of life.

This study confirms the results achieved by other authors [2,4,9] that patients with completely (R0) resected T3N0M0 non-small cell-lung cancer may be considered as a favourable subset of patients, to be more appropriately classified as stage IIB of the 1997 AJCC staging classification [6,14,15]. Our data suggest that even though there was a statistical advantage for node-negative disease with the involvement limited to parietal pleura this difference is small and the depth of chest wall invasion should not be considered as an independent indicator of survival as already observed in other series [2].

The likelihood of long-term survival is highly related to the extent of nodal involvement with a significant worsening from N0 to N1/N2 patients. The diffusion of effective neoadjuvant treatment for locally advanced NSCLC [16]

may result in an improvement of 5-year survival in patients with N2 nodal involvement who subsequently undergo a complete resection.

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