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Surgical treatment of peripheral lung cancer adherent to the parietal pleura

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Abstract

Objectives: The objective of this paper is to assess the results of surgical treatment retrospectively in a consecutive series of 85 patients with peripheral non-small cell lung cancer (NSCLC) invading parietal pleura and chest wall. **Methods**: From 1994 to 1998, of the 572 patients having pulmonary resection for NSCLC, 29 patients with neoplasm involving the parietal pleura (group I) and 56 with that invading the chest wall (group II) underwent resection. **Results**: The operative mortality rate was 3.4% in group I and 1.8% in group II. In groups I and II, pathologic N status was N0 in 20 (69%) cases, N1 in five (17%), N2 in four (13.8%) and 44 (78.6%), seven (12.5%), five (8.9%), respectively. An incomplete resection (R1) was performed in two (6.9%) patients in group I and seven (12.5%) in group II. Postoperative radiotherapy was carried out in 18 patients in group I and 46 in group II. Systemic chemotherapy was also administered in seven patients in group I and eight in group II. There was a significant difference in adjuvant therapy between the groups ($P < 0.05$). Two patients (R1) in group I (7.4%) and 12 patients (seven patients R1 + 5 R0) in group II (24%) had local recurrence. There was no significant difference in local recurrence between the groups ($P = 12$). Follow-up was completed in 79 cases (28 in group I and 51 in group II). Median survival for groups I and II were 27 ± 6 and 16 ± 4.6 months, respectively. Five-year survival was longer in group I than in group II (33 vs. 14%), but there was no significant difference ($P = 13$). **Conclusions**: We found similar survival rates for extrapleural resection in limited parietal pleura invasion and chest wall resection in exceeded-beyond-parietal pleura invasion. The completeness of resection is important in both groups. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Peripheral lung cancer; Surgical treatment

1. Introduction

Chest wall invasion of lung cancer is rare, occurring in 5–8% of patients with non-small cell lung carcinoma (NSCLC) undergoing surgical treatment [1–4]. Early reports considered chest wall invasion as a relative contraindication to pulmonary resection [2,5]. Over the past 40 years, the operative techniques of chest wall resection and reconstruction have evolved [3]. However, recent reports have been more optimistic. In these reports, many authors have stressed that survival after resection of an NSCLC invading the chest wall is significantly related to the completeness of resection and to the lymph node involvement [1,6–11].

Although, the surgical management of tumors adherent to the parietal pleura has been controversial and varies from radiation treatment alone, there is a pulmonary resection with extrapleural dissection around the area where the tumor is adherent to the parietal pleura, to en bloc resection of lung and chest wall [9].

In this study, our experience with peripheral carcinoma of the lung adherent to the parietal pleura (group I) and invasion to the chest wall (group II) was reviewed.

2. Patients and methods

We retrospectively reviewed patients, with NSCLC invading the parietal pleura or chest wall, who underwent lung resection at the Department of Thoracic Surgery, Ankara University School of Medicine, from 1994 to 1998. Medical history, physical examination, complete blood cell count, blood chemistry, electrocardiography, posteroanterior and lateral chest radiograms were evaluated in all patients. In addition, computed tomographic (CT) scans of chest, upper part of abdomen and brain were performed. Bone scans were obtained if indicated by clinical examination, abnormal laboratory values, or both. Pulmonary function tests were performed routinely. Quantitative pulmonary ventilation and perfusion scans were

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carried out in patients with marginal pulmonary function. All the patients had preoperative or intraoperative bronchoscopic examination. When enlarged mediastinal lymph nodes (10 mm or more in the shortest axis) were detected in the CT scans, cervical mediastinoscopy was added to the standard preoperative evaluation process.

The type of resection was primarily dictated by the local extent of the tumor and secondarily by the cardiorespiratory function and general condition. However, the decision to use extended segmentectomy and/or wedge resection as the primary therapy for peripheral lung cancer depended on the surgeon's impression that significant impairment in the patient's physiologic condition precluded lobectomy as an option for resection. Complete resection of the tumor combined with mediastinal lymph node dissection or sampling was performed. In the presence of fixation of parietal pleura to deeper structures (groups II), full-thickness chest wall resection was performed. On the other hand, in the presence of adherence to parietal pleura, an extrapleural resection was defined as extrapleural mobilization of a tumor at the chest wall with removal of lung parenchyma in continuity with a portion of the overlying parietal pleura (group I). Excision of adherent to parietal pleura was performed to include at least a 4 cm margin of normal tissue on all sides. Intraoperative frozen sections were done if there were doubts concerning the margins. In case of suspected incomplete (R1) resection, metal clips are placed in the surgical margin of parietal pleura as a marker for postoperative radiotherapy. Resection specimens were routinely examined pathologically for histological diagnosis and the determination of the extent of lymph node spread. In histopathologic examination, if invasion exceeded beyond parietal pleura, it was defined as incomplete (R1) resection in group I. The pathological stages were determined according to the American Joint Committee on Cancer (AJCC) staging system [12].

Postoperative radiotherapy or chemotherapy was performed under the care of referring physicians, so no uniform protocol was employed. For those patients who received thoracic radiation, a median dose of 50 Gy (30–70 Gy) with conventional fractionation (five fractions per week of 1.8–2.0 per fraction) was given to incomplete resection (R1, R2) and N2 disease.

Major complications were defined as hemorrhage causing re-exploration, pulmonary embolus, bronchopleural fistula, empyema, and chylothorax. Minor complications were wound infection, prolonged air leak, and sputum retention. Operative mortality was defined as death from any cause during hospitalization for lung resection or within 30 days of operation. Follow-up information was obtained for all survivors, either during periodic clinic visits or telephonic interview with the patients or their relatives.

Patients in groups I and II were evaluated for age, cigarette consumption, clinical findings, operation, histology, operative morbidity, operative mortality, local recurrence, and survival. The distributions of these variables were compared between groups and between cell types using the Chi-square test and Fisher's Exact test for discrete variables. Age analyses were performed using the Student's *t*-test. Cigarette consumption was compared between groups using the Mann–Whitney *U* test. Survival was measured from the date of operation, and median survival rates were calculated according to the Kaplan–Meier analysis. Differences in survival rates between groups were tested for significance using the log–rank test. All survival comparisons and analyses were performed using SPSS for Windows 6.0 (SPSS, Inc., Chicago, IL). Data were expressed as mean ± SD and differences were considered statistically significant when the P value was less than 0.05.

3. Results

Lung resections were performed in 85 patients with parietal pleura and chest wall invasion. There were 29 (34.1%) patients in group I and 56 (65.9%) in group II. There was only one female patient in group I. All patients were male in group II. The mean ages were 57 ± 10.8 years (mean ± SD; range, 24–87) in groups I and 56.3 ± 9.7 years (range, 34–75 years) in groups II. Although the patients in group II were younger than the patients in group I, this was not statistically significant ($P = 0.5$). The mean value of cigarette consumption was greater in group I than in group II but it was not statistically significant ($P = 0.3$). However, respiratory function values were similar in two groups.

Twelve (41.4%) patients with parietal pleura and 34 (60.7%) patients with chest wall invasion had symptoms of chest pain that had been present from 1 to 12 months prior to diagnosis. The chest pain was detected more frequently in group II than in group I but it was not statistically significant ($P = 0.45$).

Tumor and lymph node status in preoperative evaluation with CT were shown in Table 1. Chest wall invasion was evident preoperatively on CT in two (7%) patients in group I and 30 (53.6%) patients in group II. There was a significant

Table 1
Preoperative and postoperative pathologic stage of tumor and lymph node status in groups I and II

	Group I ($n = 29$)	Group II ($n = 56$)	P value
Preoperative T status			
T1	1 (3.4)[a]	1 (1.8)	$P < 0.001$
T2	26 (89.6)	25 (44.6)	
T3	2 (7)	30 (53.6)	
Preoperative N status			
N0	20 (69)	41 (73.2)	$P > 0.05$
N1	2 (7)	6 (10.7)	
N2	7 (24)	9 (16.1)	
Pathologic N status			
N0	20 (69)	44 (78.6)	$P > 0.05$
N1	5 (17.2)	7 (12.5)	
N2	4 (13.8)	5 (8.9)	

[a] Numbers in parentheses are percentages.

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Table 2
Pulmonary resection according to groups

	Group I	Group II
Lobectomy	19 (65.5)[a]	32 (57.1)
Pneumonectomy	6 (20.7)	3 (5.4)
Segmentectomy and/or wedge resection	4 (13.8)	21 (37.5)

[a] Numbers in parentheses are percentages.

difference in T status between groups ($P < 0.001$). There was no significant difference in preoperative or pathologic N status (Table 1). The diameter of the tumors ranged from 2.5 to 15 cm (mean ± SD, 7.5 ± 3.5) and 2–13 cm (mean ± SD, 5.9 ± 2.2) in groups I and II, respectively. The diameters of the tumors were greater in group I than in group II; this finding was statistically significant ($P < 0.05$). Seventy-nine percent (23/29) of the tumors in group I and 84% (47/56) of tumors in group II occurred in the upper lobe. The most frequent type of operation was lobectomy in both groups (Table 2). There was no significant difference in resection type between groups ($P = 0.08$). In group II, the number of resected ribs ranged from one to five. After chest wall resection, the residual defect required reconstruction in 36 (64.3%) patients. Prosthetic material (generally Mersilene mesh combination with methyl methacrylate) was employed in 16 cases; in the remaining 20, a myoplastic procedure was performed.

The operative morbidity rate was 31% ($n = 9$) in group I and 25% ($n = 14$) in group II (Table 3). The operative mortality rate was 3.4% ($n = 1$) and 1.8% ($n = 1$), respectively. The postoperative length of stay was similar between two groups.

Postoperative radiotherapy was carried out in 18 (62.1%) patients in group I and 46 (82.1%) in group II. Systemic chemotherapy was also administered in seven cases of group I and eight cases of group II. There was a significant difference in adjuvant therapy between the groups ($P < 0.05$).

Table 4 shows the distribution of cell types with respect to the groups. There was no significant difference in the distribution of histology between the groups ($P = 0.14$). N status of all patients was shown in Table 1. Pathologic stages for groups I and II are as follows: for group I, T3N0 = 69%, T3N1 = 17.2%, T3N2 = 13.8% and for group II; T3N0 = 78.6%, T3N1 = 12.5%, T3N2 = 8.9%. There was

Table 3
Postoperative complications

Complication	Group I	Group II
Wound infection	3 (10.3)[a]	3 (5.3)
Prolonged air leak	2 (6.9)	9 (16)
Re-explored for hemorrhage	2 (6.9)	1 (1.8)
Empyema	–	3 (5.3)
Chylothorax	1 (3.4)	–

[a] Numbers in parentheses are percentages.

Table 4
Distribution of cell type according to groups

Cell type	Group I	Group II
Squamous cell carcinomas	12 (41.4)[a]	27 (48.2)
Adenocarcinomas	11 (37.4)	24 (42.9)
Large cell carcinomas	2 (6.9)	3 (5.3)
Adenosquamous carcinomas	4 (13.8)	2 (3.6)

[a] Numbers in parentheses are percentages.

no significant difference in the stage distribution between the groups ($P = 0.47$). An incomplete resection was performed in two (6.9%) patients in group I and seven (12.5%) patients in group II. In all these patients, despite en block resection of tumors with macroscopic clearance of tumor, subsequent pathological examination revealed microscopic residual disease in the chest wall margin (R1). None of the patients who underwent gross incomplete resection (R2) belonged to this series. Two patients (R1) in group I (7.4%) and 12 patients (seven patients R1 + five patients R0) in group II (24%) had local recurrence. There was no significant difference in local recurrence between the groups ($P = 0.12$).

Survival analysis was recorded for 79 cases (28 patients in group I and 51 patients in group II). Five patients in group II and one patient in group I were lost to follow-up and were not included in this study. The status at follow-up of the patients group I was as follows: 10 patients (37%) were alive without evidence of disease, one patient (3.7%) died without evidence of disease, one patient (3.7%) was alive with disease and 15 patients died of disease (55.6%); in group II, it was eight (16%) patients, two (4%) and three (6%), 37 (74%), respectively (Table 5). Mean survival of patients in groups I and II were 37.8 ± 5.6 (median ± standard error, range 1–71 months) and 28.3 ± 4.5 (range, 1–81) months, respectively. Median survival for groups I and II were 27 ± 6 and 16 ± 4.6 months, respectively. Five-year survival was longer in group I than group II (33% vs. 14%). There was no

Table 5
Status of patients at last follow-up

Status at last follow-up	Group I ($n = 28$)	Group II ($n = 51$)
Died postoperatively	1 (3.4%)	1 (1.8%)
No recurrence	11 (40.7%)[a]	10 (20%)
Alive, no evidence of disease	10	8
Dead, no evidence of disease	1	2
With recurrence	16 (59.3%)[b]	40 (80%)[c]
Alive, with disease	1	3
Dead, with disease	15	37
Total	28	51

[a] The patients with operative mortality and lost to follow-up were excluded.
[b] Two local recurrences, three mediastinal recurrences and 13 metastatic diseases.
[c] Twelve local recurrences and 32 metastatic diseases.

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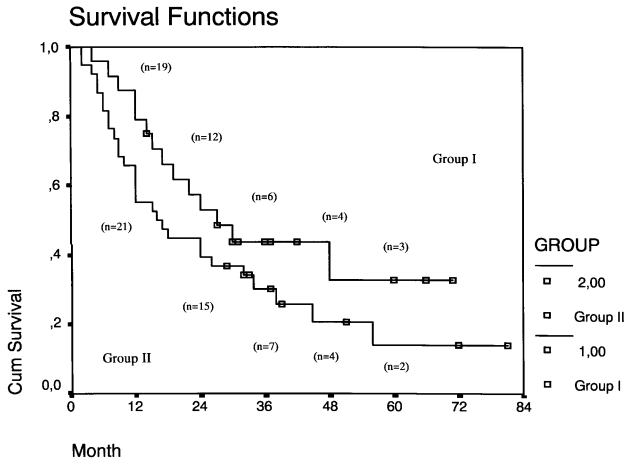


Fig. 1. Survival according to groups.

significant difference ($P = 0.13$) with respect to survival between the groups. Survival curves after pulmonary resection were shown in Fig. 1.

4. Discussion

Although chest wall invasion of the lung cancer has been known for a long time and many advances have been made in thoracic surgery, the optimal approach to lung cancer with limited parietal pleura invasion remains controversial. This report aims at evaluating subgroup analyses with chest wall invasion of peripheral lung cancer and survival curves for patients who underwent en bloc chest wall resection compared to extrapleural procedures. Today, it is accepted that long-term survival is related to the extent of nodal involvement and completeness of resection in lung cancer with chest wall invasion [2,3,11]. We did not use N factor and resection type in the current study for survival analysis because there was no significant difference in preoperative, pathologic N status and resection type in our series (Table 1).

The complaint of persistent localized chest pain is a strong indication of parietal pleura and chest wall involvement in NSCLC [3,9]. However, the absence of pain does not exclude the possibility of parietal pleura and chest wall invasion in that 17 of 29 (58.6%) patients in group I and 22 of 56 (39.3%) patients in group II did not have pain in our series.

Preoperative diagnosis of chest wall invasion by NSCLC is still a matter of debate. Preoperative evaluations (chest X-ray films, ultrasound examinations, CT scans, and magnetic resonance imaging (MRI)) lack specificity and sensitivity except in the presence of extensive bone destruction [1,4,13,14]. Glazer et al. [15] using various combinations of criteria for assessing parietal pleura and chest wall invasion, found that the sensitivity for chest wall invasion was 87% and the specificity was 59%. CT and MRI for assessing chest wall invasion were compared and no statistically significant differences were found between the two modalities [14]. In our series, chest wall invasion was evident in CT in two (7%) patients in group I and in 30 (53.6%) patients in group II. According to our experience in this study, CT scan can be inaccurate in assessing direct parietal pleura invasion of lung cancer [16]. However, the presence of parietal or chest wall invasion is not critical for proper surgical treatment.

In our series, nodal involvement was quite few in both the groups and we did not find any differences in terms of survival between groups with respect to N factor. This finding is in accordance with some previous reports [2,5,17]. In our series, the presence of mediastinal lymph node metastasis significantly reduces both groups, 69 versus 13.8% in group I, 78.6 versus 8.9%, respectively. This rate for some other series was 58–75.4% vs. 9.1–24% (Table 6) [1,2,5,6,9,10,18]. Our data suggest that mediastinal lymph node involvement is not frequent in peripheral lung cancer.

The rate of extended segmentectomy and wedge resection in our series was slightly higher than other series [8,18]. In preoperative period, every patient's respiratory performance was evaluated and appropriated for pulmonary resection. The programmed major resection (lobectomy or pneumonectomy) was not feasible in the result of intraoperative evaluation for 25 patients. However, some investigations

Table 6
N status of patients with peripheral lung cancer with chest wall or parietal pleura invasion

Year	First author	Number of patients	Number of patients with N0	Number of patients with N1	Number of patients with N2
1982	Piehler [6]	50	31 (62)[a]	7 (14)	12 (24)
1984	Trastek et al. [5]	52	29 (55.8)	13 (25)	10 (9.2)
1991	Allen et al. [10]	52	43 (82.7)	9 (17.3)	NP[b]
1992	Albertucci et al. [9]	37	21 (56.8)	9 (24.3)	7 (18.9)
2001	Facciolo et al. [1]	104	83 (79.8)	5 (4.8)	16 (15.4)
2001	Elia et al. [18]	110	83 (75.5)	17 (15.4)	10 (9.1)
2001	Magdeleinat et al. [2]	195	116 (59.5)	52 (26.7)	27 (13.8)
2001	Present series	85	64 (75.3)	12 (14.1)	9 (10.6)

[a] Numbers in parentheses are percentages.
[b] NP, no patients in this group.

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have advocated that wedge resection can be an alternative procedure for peripheral lung cancer in poor-risk patients or small (T1) peripheral tumors [19].

In lung cancer, when invasion extends beyond parietal pleura, chest wall resection should be performed. Evidence of mediastinal lymph node metastases has been considered to be indicators of incurability and a surgical approach has not been recommended [7]. However, the extent of surgical resection necessary for peripheral carcinomas of the lung to have a parietal pleura invasion remains controversial. Some authors have recommended that en bloc resection of the lung and chest wall should be performed for all patients with invasion of the parietal pleura [5,9–11]. On the other hand, some investigators have advocated that in the case of the parietal attachment of trial of extrapleural, dissection is attempted if there is no evidence of extension of disease beyond the parietal pleura [2,7,8]. In our approach, in peripheral carcinomas of the lung found at thoracotomy to have a peripheral attachment, mobile and not fixed, to the chest wall, gentle blunt extrapleural dissection is attempted if this plane is easily dissected from the underlying osteomuscular structures and, no evidence of extension of disease lies beyond the parietal pleura. We did not hesitate in proceeding to chest wall resection when we suspected a tumor or found a tumor extending beyond the parietal pleura. After extrapleural resection, we performed pulmonary resection and mediastinal lymph node dissection. This procedure is much more related to the experience of the surgeon than to objective criteria. Using this approach, we have demonstrated a 93.1% (27/29) incidence of complete resection in patients with invasion of the parietal pleura and 87.5% (49/56) in patients with invasion of the chest wall. The incidence of complete resection in patients with invasion of the parietal pleura was similar to that reported by McCaughan et al. [7]. Local recurrence rates were found to be higher in group II than in group I. However, postoperative radiotherapy rate was 62.1% in group I and 82.1% in group II and there was a significant difference in adjuvant therapy between the groups ($P < 0.05$). Two patients (R1) in group I (7.4%) and 12 patients (seven patients R1 + five patients R0) in group II (24%) had local recurrence. Patients with R1 resection had postoperative radiotherapy. Radiation therapy was used in some patients after R0 resection. For those patients who received thoracic radiation, a median dose of 50 Gy (30–70 Gy) with conventional fractionation (five fractions per week of 1.8–2.0 per fraction) was given to incomplete resection (R1, R2) and N2 disease. Furthermore, the indications for radiotherapy for chest wall and parietal pleura invasion remain unclear [10,20].

When comparing patients in depth of invasion, we found similarity at a survival time between extrapleural resection in limited parietal pleura invasion and chest wall resection beyond parietal pleura invasion (Fig. 1). Downey et al. [8] reported similar results. When lymph nodes involvement was similar to our series, the depth of chest wall invasion and resection type (en bloc in chest wall invasion or extrapleural resection in parietal plevra involvement) does not significantly influence survival time. In our opinion, if the tumor is fixed to chest wall, en bloc resection of the chest wall should be performed. On the other hand, an extrapleural resection provides adequate tumor clearance for filmy adhesion between the tumor and chest wall tumor involving only parietal pleura.

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