Surgical results and staging of non-small cell lung cancer with interlobar pleural invasion

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Abstract

The aim of this study was to compare the survival rates of non-small cell lung cancer (NSCLC) with interlobar pleural invasion (IPI) with that of patients with other T2 and T3 diseases according to the seventh TNM staging system. One thousand and one patients with pathologic T2 and T3 NSCLC (according to the seventh staging criteria) treated between 1980 and 2004 were retrospectively evaluated. Among these, 682 patients were pathologically staged as T2 without IPI (T2 group), 25 as T2 with IPI (IPI group) and 294 as T3 (T3 group). The 5-year survival rate for the T2, IPI and T3 groups were 52.0, 31.1 and 36.3%, respectively. In patients without nodal involvement, the 5-year survival rates of the T2N0, IPI0 and T3N0 groups were 60.9, 40.0 and 45.9%, respectively. The survival rate was significantly different between the T3N0 and T2N0 groups (P < 0.001) and between the IPI0 and T2N0 (P = 0.020) groups. There was no significant difference in the survival rate between the IPI0 and T3N0 groups (P = 0.644). In patients without nodal involvement, the survival of NSCLC with IPI is similar to that of the T3 disease.

Keywords: Lung cancer • Diagnosis • Staging • Pathology

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths in the Western world [1]. Effective staging systems for lung cancer are needed to stratify the patient survival and to assess treatment results of defined patient subgroups. The seventh TNM Classification of Malignant Tumors dealt with various problems related to the sixth edition, and the proposed changes better differentiate tumours associated with different prognoses [2–4].

However, there is no agreement on whether non-small cell lung cancer (NSCLC) with interlobar pleural invasion (IPI) should be classified into T2 or T3 [5–7].

In the present study, we compared the survival rates of patients with NSCLC with IPI with that of patients with other T2 and T3 diseases according to the seventh TNM staging system. We also compared the surgical results of NSCLC with IPI with those of subgroups of T3 tumours.

PATIENTS AND METHODS

From January 1980 to December 2004, 1989 patients were operated on for NSCLC in our surgical department. Available for analysis is a database that encompasses the medical, surgical and pathology records of these patients. In our hospital, the completeness of the interlobar fissure is generally recorded in the surgical records. Pathologic staging were evaluated according to the seventh International Union Against Cancer (UICC) TNM staging system [2]. Each tumour was examined histopathologically according to the World Health Organization classification [8]. In addition to the haematoxilin and eosin stains, elastic stains are generally used to confirm the presence of IPI. In our hospital, lobectomy or larger resection with hilar and mediastinal lymph node dissection through posterolateral was performed as a standard treatment for lung cancer in this period. Patients with co-morbidities such as cardiovascular diseases or impaired pulmonary function underwent sublobar resection. Of the 1989 patients, those who underwent lobectomy or larger resection with hilar and mediastinal lymph node dissection were included while those who underwent sublobar resection were excluded. Cases of operative death or death within 30 days after the operation were excluded. Patients who underwent incomplete resection or induction of chemo- or chemoradiotherapy, patients with synchronous or metachronous multiple lung cancer, T1, T4, N3 or M1 diseases were excluded. Patients whose tumours were subsequently classified pathologically as a low-grade malignant tumour were also excluded. Thus, 1001 patients with pathologic T2 and T3 NSCLC were enrolled in this retrospective study. Among the 1001 patients, those with IPI were confirmed (based on our data base (IPI group)). Then, the presence of interlobar pleural invasion was examined carefully in this group.
In the present study, IPI was regarded as a T factor in order to compare the surgical results of the IPI group with that of T2 without IPI or T3 diseases. For the purpose of comparison of the survival rates of patients with NSCLC with IPI with that of patients with other T2 and T3 diseases, patients without nodal involvement were analysed to exclude the influence of nodal involvement.

The surgical results of the IPI group were also compared with the T3 subgroups (i.e. tumours measuring >7 cm, tumour with invasion of the mediastinal structures, chest wall, diaphragm or tumours with separate nodule in the same lobe).

Patients of the IPI group underwent lobectomy with adjacent lobe segmentectomy, lobectomy with partial resection, bilobectomy or pneumonectomy. The type of resection was selected based on pulmonary reserve and localization of the tumour. Lobectomy with partial resection was preferred if complete resection with adequate margin was ensured.

Data are expressed as mean ± SD. The overall survival was analysed by the Kaplan–Meier method. Differences between groups were analysed by the log-rank test. \( P < 0.05 \) was considered statistically significant. Statistical analysis was performed using StatView 5.0 software (SAS Institute, Berkley, CA, USA).

### RESULTS

Among the 1001 patients with pathological T2 and T3 NSCLC, 738 patients were males and 263 were females. The mean age was 65.1 ± 9.4 years (median, 67 years; range, 26–87 years). The histopathological diagnosis was squamous cell carcinoma in 391, adenocarcinoma in 521, large cell carcinoma in 60 and adenosquamous carcinoma in 29 patients. The pathological stage was T2 without IPI in 682 patients (T2 group), T2 with IPI in 25 patients (IPI group) and T3 in 294 patients (T3 group). The incidence of IPI among all the 1989 patients who were operated on for NSCLC in our department during that period was 1.3%. Table 1 shows the relation between pathological T factor and N factor. The median follow-up interval was 46 months (range, 1–301 months). Of all the 1001 patients, 596 patients underwent surgery alone, 308 patients underwent surgery and adjuvant chemotherapy, 55 patients underwent surgery and adjuvant radiotherapy, and 42 patients underwent surgery, adjuvant chemotherapy and radiotherapy.

Among the IPI group, the interlobar fissure was present and the tumour invaded across the interlobar fissure in 23 patients while the tumour invaded directly the adjacent lobe through an incomplete interlobar fissure in two patients. The primary tumour was located in the right lung in 15 patients (upper lobe in 11, middle lobe in 2 and lower lobe in 2) and in the left lung in 10 patients (upper lobe in 6 and lower lobe in 4). Fourteen (56%) patients had no lymph node metastasis, 4 (16%) had hilar-interlobar nodal metastasis (N1 disease) and 7 (28%) had mediastinal nodal metastasis (N2 disease). The type of resection was pneumonectomy in 4 patients, bilobectomy in 2, lobectomy with segmentectomy in 2 and lobectomy with partial resection in 17.

In patients without nodal involvement, the 5-year survival rates of the T2N0, IPI0N0 and T3N0 groups were 60.9, 40.0 and 45.9%, respectively (Fig. 1). The survival rate was significantly different between the T3N0 and T2N0 groups (\( P < 0.001 \)) and between the IPI0N0 and T2N0 (\( P = 0.020 \)) groups. There was no significant difference in the survival rate between the IPI0N0 and T3N0 groups (\( P = 0.644 \)).

Table 2 shows the results of analysis of T3 tumour subgroups: 87 patients had tumours >7 cm (size group), 39 with tumours invading the mediastinal structures (mediastinal pleura, parietal pericardium, the main bronchus <2 cm distal to the carina; mediastinal group), 96 with tumours invading the chest wall (chest wall group), 5 with tumours invading the diaphragm (diaphragm group) and 67 with separate nodule in the same lobe (pulmonary metastasis group).

The 5-year survival rates of the size, mediastinal, chest wall, diaphragm and pulmonary metastasis T3 subgroups were 32.5, 49.9, 40.7, 0 and 28.4%, respectively. The survival rate of the IPI group was significantly different from that of the diaphragm subgroup (\( P = 0.027 \)), while that of the IPI group was not significantly different from the rate of the size, mediastinal, chest wall and pulmonary metastasis subgroups (\( P = 0.489, 0.097, 0.774 \) and 0.577, respectively).

### DISCUSSION

Although there is still a debate on whether NSCLC with IPI are classified as T2 or T3, the seventh TNM staging system classifies these tumours as T2. This issue is complicated by the fact that in some cases with no interlobar fissure, invasion of the adjacent lobe can occur across the lung parenchyma without involvement of the pleura [4]. In the present study, we examined the surgical results of NSCLC with IPI according to the seventh TNM staging system and also carefully examined whether the interlobar pleura was present at the point of invasion.

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**Table 1:** Relationship between the pathological T and N factors

<table>
<thead>
<tr>
<th>T2 (n = 682)</th>
<th>IPI (n = 25)</th>
<th>T3 (n = 294)</th>
</tr>
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<tbody>
<tr>
<td>N0M0 375</td>
<td>N0M0 14</td>
<td>N0M0 139</td>
</tr>
<tr>
<td>N1M0 170</td>
<td>N1M0 4</td>
<td>N1M0 66</td>
</tr>
<tr>
<td>N2M0 137</td>
<td>N2M0 7</td>
<td>N2M0 89</td>
</tr>
</tbody>
</table>

**Figure 1:** The 5-year survival rates of the T2N0, IPI0N0 and T3N0 groups. The 5-year survival rate was significantly different between the T3N0 and T2N0 groups (\( P < 0.001 \)) and between the IPI0N0 and T2N0 (\( P = 0.020 \)) groups, but not between the IPI0N0 and T3N0 groups (\( P = 0.644 \)).
The survival of patients with NSCLC-IPI was significantly better than that of patients with NSCLC and VPI only. They concluded that NSCLC with IPI should be classified as T2. In contrast, two other investigators have reported that NSCLC with IPI should be classified as T3. Okada et al. [6] demonstrated that the survival rate of patients with NSCLC-IPI was similar to that of patients with NSCLC with invasion of the parietal pleura and chest wall (5-year survival rates: 37 vs. 14%, P < 0.001) and was not different from that of patients with NSCLC and VPI only. They concluded that NSCLC with IPI should be classified as T3. Okada et al. [6] demonstrated that the survival rate of patients with NSCLC-IPI was similar to that of patients with NSCLC >7 cm in size and NSCLC with a separate nodule in the same lobe. In the present study, the 5-year survival rates of the T2N0 and T3N0 groups were 60.9 and 45.9%, respectively. Patients with T2N0 disease were distributed as stage IB or IIA, and these with T3N0 disease were distributed as stage IIB according to the seventh edition of the TNM classification. Our data are comparable with the surgical results of the nearly the same period (1982–2002) by another institution in Japan according to the seventh edition of the TNM classification which shows 5-year survival rates of stage IB, IIA and IIB were 64.9, 65.9 and 44.7%. In the present study, the 5-year survival rate of the IPI group was 31.1%, which is comparable with those of previous reports (range: 34–37%) [5–7]. The survival rate of patients with IPINO was significantly different from that of the T2N0 group. The present study indicates that the survival of the IPINO group is similar to that of the T3N0 group.

When compared with subgroups of T3, the survival rate of the IPI group was significantly better than that of the diaphragm subgroup but not significantly different from that of the size, mediastinal, chest wall and pulmonary metastasis subgroups. These results are in agreement with those of previous reports. In Okada’s series [6], the survival rate of patients with NSCLC-IPI was similar to that of patients with NSCLC and parietal pleura or chest wall invasion. In the study of Demir et al. [7], the survival rate of patients with NSCLC-IPI was similar to that of patients with bronchial T3, peripheral T3 and mediastinal T3. The present study is the first to demonstrate that the survival of patients with NSCLC-IPI is similar to that of NSCLC >7 cm in size and NSCLC with a separate nodule in the same lobe.

The present study had certain limitations. First, the number of patients was relatively small. Secondly, the number of cases of NSCLC with direct invasion to an adjacent lobe through the incomplete interlobar fissure was probably underestimated. While the presence of IPI with intact interlobar fissure could be confirmed retrospectively by microscopic examination using elastic stains, which confirmed the pleural invasion of the adjacent lobe, direct invasion to an adjacent lobe through the incomplete interlobar could only be confirmed by precise description of the anatomical relationship between the tumour and the interlobar fissure. Thirdly, the study included patients who were treated over several decades and followed up with different radiological modalities and various techniques of perioperative care. Advancement of radiological modalities in this period such as multidetector computed tomography (CT) provides more accurate preoperative staging. Patients in the conventional CT era might be understaged. Adjuvant therapy might impact on the survival of patients. Unfortunately, the regimen and dose of adjuvant chemotherapy was not available in our database. Advancement of treatment for relapse, i.e. chemotherapy and radiotherapy, might influence on the survival. Patients in recent years might had better prognosis after recurrence. These factors could have influenced the results of analysis. Future data collection with precise pathological and anatomical description conducted in a multi-centre setting is needed to resolve these limitations.

**CONCLUSIONS**

In patients without nodal involvement, the survival of NSCLC with IPI is similar to that of the T3 disease.

**Conflict of interest:** none declared.

**REFERENCES**


