Surgical treatment of lung cancer with adjacent lobe invasion in relation to fissure integrity

Claudio Andreetti¹, Camilla Poggi², Mohsen Ibrahim¹, Antonio D’Andrilli¹, Giulio Maurizi¹, Matteo Tiracorrendo¹, Valentina Peritore¹, Erino Angelo Rendina¹, Marco Venuta²,3, Marco Anile², Andreina Pagini², Giovanni Natale⁴, Mario Santini⁴ & Alfonso Fiorelli⁴

¹ Division of Thoracic Surgery, Sant’Andrea Hospital, Faculty of Medicine and Psychology, University of Rome ‘Sapienza’, Rome, Italy
² Division of Thoracic Surgery, Policlinico Umberto I, Faculty of Pharmacy and Medicine, University of Rome ‘Sapienza’, Rome, Italy
³ Fondazione Eleonora Lorillard Spencer Cenci, Rome, Italy
⁴ Division of Thoracic Surgery, Università degli Studi della Campania “Luigi Vanvitelli”, Naples, Italy

Keywords
Adjacent lobe; fissure integrity; lung cancer; pleural invasion; surgery.

Correspondence
Alfonso Fiorelli, Thoracic Surgery Unit, Università degli Studi della Campania “Luigi Vanvitelli”, Piazza Miraglia, 2, I-80138 Naples, Italy.
Tel: +39 081 5665228
Fax: +39 081 5665230
Email: alfonso.fiorelli@unicampania.it

Received: 14 August 2019;
Accepted: 22 September 2019.

doi: 10.1111/1759-7714.13217
Thoracic Cancer 11 (2020) 232–242

Abstract

Background: Tumor with adjacent lobe invasion (T-ALI) is an uncommon condition. Controversy still exists regarding the optimal resection of adjacent lobe invasion, and the prognostic value in relation to fissure integrity at the tumor invasion point. The aims of this paper were to evaluate the prognosis of T-ALI with regard to fissure integrity, and type of resection.

Methods: This was a retrospective multicenter study which included all consecutive patients with T-ALI undergoing surgical treatment. Based on radiological, intraoperative and histological findings, T-ALI patients were differentiated into two groups based on whether the fissure was complete (T-ALI-A group) or incomplete (T-ALI-D Group) at the level of tumor invasion point. Clinico-pathological features and survival of two study groups were analyzed and compared.

Results: Study population included 135 patients, of these 98 (72%) were included into T-ALI-A group, and 37 (38%) into T-ALI-D Group. T-ALI-D patients had better overall survival than T-ALI-A patients (63.9 ± 7.0 vs. 48.9 ± 3.9; respectively, P = 0.01) who presented with a higher incidence of lymph node involvement (35% vs. 4%; P = 0.004), and recurrence rate (43% vs. 16%; P = 0.01). At multivariable analysis, T-ALI-D (P = 0.01), pN0 stage (P = 0.0002), and pT≤5 cm (P = 0.0001) were favorable survival prognostic factors.

Conclusions: T-ALI-D presented a better prognosis than T-ALI-A while extent of resection had no effect on survival. Thus, in patients with small T-ALI-D and without lymph node involvement, sublobar resection of adjacent lobe rather than lobectomy could be indicated.

Key points

- The extent of resection of adjacent lobe had no effect on survival while T-ALI-D, pN0 stage, and pT≤5 cm were significant prognostic factors.
- In patients with small T-ALI-D and without lymph node involvement, sublobar resection of adjacent lobe could be indicated as an alternative to lobectomy.
Introduction

Visceral pleural invasion (VPI) was adopted as a specific description in the Tumor, Node, Metastasis (TNM) classification of the International Union Against Cancer (IUAC) staging system in the mid-1970s as T2, and this classification remained unchanged in the further revisions. Tumor with adjacent lobe invasion (T-ALI) across the interlobar pleura was firstly defined as T2 in the sixth TNM classification of the Union for International Cancer Control (UICC), and in the seventh TNM classification proposed by the International Association for the Study of Lung Cancer (IASLC) it was classified as T2a unless other criteria assigned a high T category. The eighth edition of TNM classification revised the T category as follows: T2 tumor >5 cm and ≤7 cm are reclassified as T3, and T3 tumors >7 cm are reclassified as T4, but there has been no highlighted proposal for T-ALI, and thus this should still be classified as T2. However, the TNM classifications proposed in subsequent years (including the last eighth edition by IALCS) do not consider the fissure status (complete or incomplete) in the definition of T-ALI, and the data in the literature on this lack of classification is scarce and controversial.

The aims of our study were to: (i) Evaluate the prognosis of T-ALI with regard to the fissure integrity; and (ii) define the most appropriate surgical resection for these patients.

Methods

Study design

This was a retrospective multicenter study which included all consecutive patients with T-ALI undergoing surgical treatment in three different centers between January 2000 to January 2018. The data were extracted from the data base of each participating center. T-ALI patients were differentiated into two groups based on whether the tumor invaded the adjacent lobe across a complete fissure point (T-ALI-A group), or directly invaded the adjacent lobe through an incomplete fissure point (T-ALI-D group). Exclusion criteria were: (i) Patients with T-ALI simultaneously combined with invasion of chest wall, diaphragm, phrenic nerve, mediastinal pleura, and parietal pericardium. (ii) Patients with T-ALI suspected on radiological and/or intraoperative findings but not confirmed by histological studies (ie. tumor that invaded only to the visceral pleura, and not to the adjacent lobe). (iii) Patients with a different histological diagnosis from NSCLC (ie. neuroendocrine, carcinoid, small cell carcinoma, oat cell carcinoma, sarcoma, and mesothelioma histology) as the natural history, treatment, and/or outcome of these histologic subtypes differ from those of NSCLC. (iv) Patients who received any kind of neoadjuvant treatment. (v) Patients with a history of concurrent malignant disease or other previous primary cancers.

The end points of the study were to evaluate the prognosis of T-ALI in relation to the fissure integrity (primary end point), and to the extent of resection (secondary end point).

The study design was approved by local ethics committees of the coordinator center and approved by each participating center. All patients gave a written informed consent for the surgical treatment and were aware that all information could be used anonymously for scientific purposes only.

Histological examination

All specimens were fixed with 10% formalin and embedded in paraffin. The tumors were cut in the horizontal section at 5 mm intervals to examine the fissure status and the ALI, and serial 4 μm sections were stained with hematoxylin and eosin. The Victoria blue van Gieson method was used to visualize the elastic fibers. In addition, the distance between the tumor and the parenchymal suture margin was also measured. Each pathological specimen was reviewed by two pathologists who were blinded to the clinical outcome of the study.

Example of T-ALI-D and T-ALI-A are reported in Figs 1 and 2, respectively.
Follow-up

A follow-up examination was generally carried out every three months for the first two years, and six months thereafter. The examination included physical and radiological examination, either CT or PET, as indicated. Recurrences were defined by radiology and in some cases confirmed by pathology. As previously reported, loco-regional recurrence was defined as any recurrence into ipsilateral chest wall/pleural, parenchymal, bronchial stump, hilar and/or mediastinal lymph node. Distal recurrences were defined as any recurrence not located in the ipsilateral thorax. Recurrences in patients who had simultaneous loco-regional and distant recurrences were defined as distant recurrences. Patients with recurrence and/or distant metastasis underwent additional treatments according to standard clinical practice.

Statistical analysis

The summary statistics of patients’ characteristics were tabulated either as mean ± standard deviation (SD) for continuous variables or as number of patients and percentages for categorical variables. Student’s t-test and chi-square test were used to compare different variables, as appropriate. Overall survival (OS) was defined as the interval between the time of surgery and date of death or censoring. OS was calculated with the kaplan-meier method, and intergroup
differences were evaluated by log-rank test. Univariable analysis used the following variables: age (≤70 year-old vs. >70 year-old); gender (male vs. female); histology (adenocarcinoma vs. others); fissure integrity (T-ALI-A vs. T-ALI-D); type of resection (pneumonectomy/bilobectomy vs. lobectomy associated with sublobar resection), surgical margin of resection (<2 cm vs. ≥2 cm), lymph node involvement (pN0 vs. pN1/pN2). Variables having P-value <0.05 at univariable analysis were included in multivariable analysis (Cox proportional hazard model), and prognostic factors were considered significant if P-value was <0.05. MedCalc statistical software (Version 12.3, Broekstraat 52; 9030 Mariakerke; Belgium) was used.

**Results**

In the study period, 2245 patients underwent surgical resection for lung cancer. Of these, 146 (6.5%) presented T-ALI, but 11 were excluded from the analysis as three had chest wall invasion, five presented a histological diagnosis different from NSCLC (two SCLC, three atypical carcinoid), and three had concurrent malignant disease. Thus, our study population contained 135 patients summarized in Table 1.

The mean age of population was 68 ± 3.5-year-old with 72% being male patients. Pneumonectomy was performed in 23 patients (17%), bilobectomy in 42 (31%), and lobectomy with sublobar resection of the adjacent lobe in 70 patients, including 45 (33%) wedge resections, and 25 (18%) segmentectomies. Squamous cell carcinoma was observed in 71 patients (53%) and adenocarcinoma in 53 cases (39%). Stages pN0 included 96 (71%) patients undergoing pneumonectomy (n = 2; 2%); bilobectomy (n = 35; 36%); lobectomy plus segmentectomy (n = 20; 21%); lobectomy plus wedge resection (n = 39; 43%); Stage pN1 included 15 (11%) patients undergoing pneumonectomy (n = 10; 67%); bilobectomy

| Variable                  | All     | T-ALI-A | T-ALI-D | P-value |
|---------------------------|---------|---------|---------|---------|
| Number of patients (%)    | 135     | 98 (72%)| 37 (38%)| —       |
| Age (year-old)            | 68 ± 3.5| 67 ± 1.8| 68 ± 2.8| 0.67    |
| Sex (male)                | 97 (72%)| 70 (71%)| 27 (73%)| 0.85    |
| Type of resection         |         |         |         |         |
| Pneumonectomy             | 23 (17%)| 18 (18%)| 5 (13%) | 0.27    |
| Bilobectomy               | 42 (31%)| 32 (33%)| 10 (27%)|         |
| Lobectomy + wedge         | 45 (33%)| 35 (36%)| 10 (27%)|         |
| Lobectomy + segmentectomy | 25 (18%)| 13 (13%)| 12 (33%)|         |
| Histology                 |         |         |         | 0.54    |
| Squamous cell carcinoma   | 71 (53%)| 50 (51%)| 21 (56%)|         |
| Adenocarcinoma            | 53 (39%)| 40 (41%)| 13 (35%)|         |
| Large cell carcinoma      | 11 (8%) | 8 (8%)  | 3 (9%)  |         |
| Main location + ALI       |         |         |         | 0.77    |
| RUL + RML                 | 47 (35%)| 35 (36%)| 12 (32%)|         |
| RML + RLL                 | 20 (15%)| 13 (13%)| 7 (19%)  |         |
| RUL + RLL                 | 29 (21%)| 21 (21%)| 8 (22%)  |         |
| LUL + LLL                 | 39 (29%)| 29 (30%)| 10 (27%)|         |
| pTumor size               | 4.8 ± 1.3| 4.7 ± 1.9| 4.8 ± 1.1| 0.49    |
| pT1 (≤3 cm)               | 25 (18%)| 19 (19%)| 6 (16%)  |         |
| pT2 (>3 to 5 cm)          | 44 (33%)| 32 (33%)| 12 (32%)|         |
| pT3 (>5 to 7 cm)          | 52 (39%)| 38 (39%)| 14 (39%)|         |
| pT4 (>7 cm)               | 14 (10%)| 9 (9%)  | 5 (13%)  |         |
| pN status                 |         |         |         | 0.004   |
| pN0                       | 96 (71%)| 63 (64%)| 33 (90%)|         |
| pN1                       | 15 (11%)| 13 (13%)| 2 (5%)  |         |
| pN2                       | 24 (18%)| 22 (23%)| 2 (5%)  |         |
| Surgical margin           |         |         |         | 0.76    |
| ≤20 mm                    | 26 ± 5.9| 26 ± 1.3| 26 ± 4.9|         |
| >20 mm                    | 12 (10%)| 8 (8%)  | 4 (11%)  |         |

ALI, adjacent lobe invasion; LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.
lobectomy plus segmentectomy (n = 2; 13%); lobectomy plus wedge resection (n = 1; 7%); and Stage II included 24 (18%) patients undergoing pneumonectomy (n = 11; 46%); bilobectomy (n = 5; 21%); lobectomy plus segmentectomy (n = 3; 12%); and lobectomy plus wedge resection (n = 5; 21%). The mean surgical margin was 2.6 ± 5.9 mm.

Recurrence

Data are summarized in Table 2. The mean follow-up was 38 ± 17 months (range: 6–83 months). There were a total of 48 recurrences in this study, representing 35% of the patient population. Loco-regional recurrence was seen in 10 patients (7% of the entire population) undergoing pneumonectomy (n = 2; 13%); lobectomy plus segmentectomy (n = 2; 13%); lobectomy plus wedge resection (n = 1; 7%); and Stage II included 24 (18%) patients undergoing pneumonectomy (n = 11; 46%); bilobectomy (n = 5; 21%); lobectomy plus segmentectomy (n = 3; 12%); and lobectomy plus wedge resection (n = 5; 21%). The mean surgical margin was 2.6 ± 5.9 mm.

Recurrence

Data are summarized in Table 2. The mean follow-up was 38 ± 17 months (range: 6–83 months). There were a total of 48 recurrences in this study, representing 35% of the patient population. Loco-regional recurrence was seen in 10 patients (7% of the entire population) undergoing pneumonectomy (n = 2; 13%); lobectomy plus segmentectomy (n = 2; 13%); lobectomy plus wedge resection (n = 1; 7%); and Stage II included 24 (18%) patients undergoing pneumonectomy (n = 11; 46%); bilobectomy (n = 5; 21%); lobectomy plus segmentectomy (n = 3; 12%); and lobectomy plus wedge resection (n = 5; 21%). The mean surgical margin was 2.6 ± 5.9 mm.

Survival related to fissure status

The mean overall survival was 53 ± 3.3 months; three-year survival rate (YSR) and five-YSR were 62% and 43%, respectively (Fig 3a). Among all patient (n = 135), 98 (72%) were included into T-ALI-A group, and 37 (38%) into T-ALI-D group. As reported in Table 1, no significant intergroup differences were found regarding type of resection (P = 0.27), histology (P = 0.54), tumor location (P = 0.77), tumor size (P = 0.49) and suture margin (P = 0.76). T-ALI-A compared to T-ALI-D was associated with higher lymph node involvement rates (35% vs. 4%; P = 0.004), and higher recurrence rates (43% vs. 16%; P = 0.01). The survival of T-ALI-D patients was 63.9 ± 7.0 months; the three-YSR, and five-YSR were 62% and 43%, respectively. The survival of T-ALI-A patients was 48.9 ± 3.9 months; three-YSR and five-YSR were 54% and 37%, respectively. T-ALI-D showed a better survival than T-ALI-A (HR: 2.13; 95% CI:1.1–4.11; P = 0.01, Fig 3b).

Survival related to extent of resection

Survival of patients undergoing pneumonectomy, bilobectomy, lobectomy with segmentectomy, and lobectomy with wedge resection was 39.8 ± 7.0; 53.9 ± 8.2; 54.3 ± 6.6; and 59.8 ± 4.8 respectively (Fig 4). The comparison of survival showed no

| Recurrence | All (n = 135) | T-ALI-A (n = 98) | T-ALI-D (n = 37) |
|------------|---------------|-----------------|-----------------|
| Total      | 48 (35%)      | 42 (43%)        | 6 (16%)         |
| Loco-regional |             |                 |                 |
| - Lung     | 10 (7%)       | 8 (8%)          | 2 (5%)          |
| - Pleura with malignant effusion | 2 (1.5%) | 2 (2%) | 0 |
| - Lymph node/mediastinum | 6 (4%) | 5 (5%) | 1 (2.5%) |
| Distant    | 38 (28%)      | 34 (35%)        | 4 (11%)         |
| - Contralateral lung | 4 (3%) | 3 (3%) | 1 (3%) |
| - Contralateral chest wall | 1 (2%) | 1 (1%) | 0 |
| - Brain    | 3 (2%)        | 2 (2%)          | 1 (3%)          |
| - Adrenal gland | 4 (3%) | 3 (3%) | 1 (3%) |
| - Liver    | 5 (4%)        | 4 (4%)          | 1 (3%)          |
| - Bone     | 3 (2%)        | 3 (3%)          | 0               |
| - Kidney   | 4 (3%)        | 4 (4%)          | 0               |
| - Multiple sites | 3 (2%) | 3 (3%) | 0 |
| - Distant  | 11 (6%)       | 11 (12%)        | 0               |

(n = 2; 13%); lobectomy plus segmentectomy (n = 2; 13%); lobectomy plus wedge resection (n = 1; 7%); and Stage II included 24 (18%) patients undergoing pneumonectomy (n = 11; 46%); bilobectomy (n = 5; 21%); lobectomy plus segmentectomy (n = 3; 12%); and lobectomy plus wedge resection (n = 5; 21%). The mean surgical margin was 2.6 ± 5.9 mm.

Patients with recurrence underwent radiotherapy, chemotherapy, or combined chemotherapy and radiotherapy based on location of recurrence and their clinical condition. At the end of the time interval investigated, there were 37 deaths, while 10 patients were alive with NSCLC recurrence.

Survival related to extent of resection

Survival of patients undergoing pneumonectomy, bilobectomy, lobectomy with segmentectomy, and lobectomy with wedge resection was 39.8 ± 7.0; 53.9 ± 8.2; 54.3 ± 6.6; and 59.8 ± 4.8 respectively (Fig 4). The comparison of survival showed no
difference ($P = 0.09$). Lobectomy with sublobar resections group compared to pneumonectomy/bilobectomy group was associated with higher rates of pN0 patients (61% vs. 38%; $P = 0.024$) and of pT $\leq 5$ cm patients (88% vs. 11%; $P < 0.0001$), while pneumonectomy/bilobectomy group was associated with higher rate of pN1/pN2 patients (72% vs. 28%; $P = 0.006$) and of pT $>5$ cm patients (13% vs. 87%; $P < 0.0001$). No significant difference regarding the rate of pneumonectomy/bilobectomy compared to that of lobectomy with sublobar resections was found in patients with a surgical margin $\leq 2$ cm, and in those with a surgical margin $>2$ cm (Table 3).

No significant survival difference was observed between patients undergoing lobectomy with sublobar resections compared to those undergoing pneumonectomy/bilobectomy in relation to pN0 (61.8 ± 4.7 month vs. 63.4 ± 8.2; $P = 0.52$;...
HR: 0.6; 95% CI: 0.23–2.25; Fig 5a), to pN1/pN2 (31.8 ± 2.3 months vs. 35.6 ± 2.6, respectively; \( P = 0.83; \) HR: 0.9; 95% CI: 0.23–2.25; Fig 5b), to pT ≤5 cm (47 ± 17 months vs. 53 ± 3.6 months, respectively; \( P = 0.40; \) HR: 0.4; 95% CI: 0.06–2.98, Fig 5c), and to pT >5 cm (43.8 ± 5.3 months and 43.5 ± 7.9 months, respectively; \( P = 0.93; \) HR: 0.96; 95% CI: 0.40–2.28; Fig 5d).

**Univariable and multivariable analysis for overall survival**

The results are summarized in Table 4. On the univariable analysis T-ALI-D (HR: 2.13; \( P = 0.01 \)), pN0 stage (HR: 3.75; \( P = 0.0004 \)), pT ≤5 cm (HR: 3.87; \( P = 0.0001 \)), and margin resection >2 cm (HR: 1.03; \( P = 0.04 \)) were associated with a better survival. On the multivariable analysis T-ALI-D (HR: 2.54; \( P = 0.01 \)), pN0 stage (HR: 3.85; \( P = 0.0002 \)), pT ≤5 cm (HR: 3.91; \( P = 0.0001 \)) were associated with a better survival.

**Discussion**

T-ALI is an uncommon condition with its incidence ranging from 5.5% to 17.1%.\(^6\) In this setting, prognosis is still debated; some authors\(^6\)–\(^13\) observed a survival rate similar to T2 NSCLC while others\(^8\)–\(^13\) reported a prognosis similar to...
Controversy also exists concerning the type of resection; Yang et al.\textsuperscript{11} found that lobectomy of the adjacent lobe provided a better survival while other authors\textsuperscript{7–9} found that sublobar resection of the adjacent lobe was associated with a better survival. Different inclusion criteria, lymph node status and type of resection may explain these controversial results. T-ALI was defined as T2 in the seventh TNM classification proposed by IASLC, and no further modification was considered in the eighth classification.\textsuperscript{3} However, previous TNM staging editions, including the eighth, do not consider the fissure status in the definition of T-ALI, and only few reports observed T-ALI outcome concerning this variable. Another limitation of previous studies was that T-ALI was only suspected on the basis of CT images and operative findings, but then it was pathologically confirmed to be a simple interlobar fissure adhesion in most cases.

In our report, T-ALI account for 6.8% of all tumors. In agreement with the findings of Nonaka et al.\textsuperscript{6} and Dziedzic et al.\textsuperscript{12} the incidence of squamous cell carcinoma was higher than adenocarcinoma. A possible explanation is that squamous cell carcinomas are more often central tumors, and could preferentially be closer to the fissure or require pneumonectomy or broncho-vascular sleeve resections.\textsuperscript{14–16}

Most of the patients presented with a complete fissure (T-ALI-A), while only 30% had an incomplete one (T-ALI-D), especially on the right side. T-ALI-D had a better survival than T-ALI-A, in line with previous experiences. Ohtaki et al.\textsuperscript{2} found that T-ALI-A patients had a worse outcome than T-ALI-D (52% vs. 85.7%; \(P = 0.01\)) and therefore should be upstaged to T2b while T-ALI-D tumors had outcomes similar to T1 tumors. Similarly, Dziedzic et al.\textsuperscript{12} found a better three-YSR in T-ALI-D patients than in T-ALI-A patients (67% vs. 58% \(P = 0.003\)). In theory, T-ALI-A presented with an aggressive biology as it invaded twice the pleural space with more chance of invading blood vessels and lymphatic ducts, of which the subpleural space is rich.\textsuperscript{17} Conversely, T-ALI-D
Table 4 Cox regression analysis (dependent variable: overall survival)

| Covariates                          | Univariable                      | Multivariable                      |
|-------------------------------------|----------------------------------|-----------------------------------|
|                                     | Coefficient | HR  | 95% CI | P-value | Coefficient | HR  | 95% CI | P-value |
| **Age**                             |            |     |        |         |            |     |        |         |
| ≤70 vs. >70                         | 0.42        | 1.52 | 0.52–1.34 | 0.19    | —           | —   | —      | —       |
| **Gender**                          |            |     |        |         |            |     |        |         |
| Male vs. female                     | 0.46        | 1.19 | 0.89–1.78 | 0.65    | —           | —   | —      | —       |
| **Histology**                       |            |     |        |         |            |     |        |         |
| Adenocarcinoma vs. others           | 0.76        | 0.45 | 0.75–1.87 | 0.69    | —           | —   | —      | —       |
| **Resection**                       |            |     |        |         |            |     |        |         |
| Pneumonectomy/bilobectomy vs. lobectomy with sublobar resection | −0.13      | 0.86 | 0.64–1.56 | 0.75    | —           | —   | —      | —       |
| **pN stage**                        |            |     |        |         |            |     |        |         |
| pN0 vs. pN1/pN2                     | 1.29        | 3.75 | 1.59–3.45 | 0.0004  | 1.49        | 3.85 | 1.74–3.21 | 0.0002  |
| **pT stage**                        |            |     |        |         |            |     |        |         |
| ≤5 cm vs. >5 cm                     | 1.86        | 3.87 | 1.68–2.87 | 0.0001  | 1.86        | 3.91 | 1.68–2.87 | 0.0001  |
| **Margin resection**                |            |     |        |         |            |     |        |         |
| ≤2 cm vs. >2 cm                     | 0.48        | 0.51 | 0.59–1.35 | 0.37    | —           | —   | —      | —       |

CI, confidence interval at 95%; HR, hazards ratio.
higher risk of morbidity and mortality compared to more limited resection. Demir et al.\textsuperscript{3} (66.6\%), Haam et al.\textsuperscript{10} (58.7\%), and Riquet et al.\textsuperscript{18} (55.2\%) reported a higher rate of pneumonectomy compared to other types of resection. Despite pneumonectomy having a lower five-year survival rate when there was less extensive resection, these authors\textsuperscript{10,12,18} highlighted that the prognostic value of pneumonectomy was not related to the type of resection itself, but to the size of the tumor, the high rate of LN metastases, and/or its invasion beyond the visceral pleura, all factors that require extensive resection. Obviously, the choice of performing pneumonectomy, especially if on the right side, requires careful patient selection before surgery and intensive care after surgery and the decision should be made by the balance of obtaining a radical tumor resection, and preserving a good clinical status.\textsuperscript{28}

Several limitations should be considered when interpreting our results. The main limitation is the retrospective nature of the study as the choice of resection was chosen by the surgeon’s preference rather than randomization. The variations in surgical techniques and histological assessment due the multicenter nature are additional factors that may have affected our results. Yet, due to the small number of patients we included in the same group pneumonectomy and bilobectomy, despite the different extent of resection, neither propensity score match analysis was performed to limit the difference among different subgroups.

In conclusion, our data showed that prognosis of T-ALI tumor was significantly associated with fissure integrity, while the extent of the resection did not affect patient survival. In theory, lobectomy with sublobar resections could be the preferred strategy in patients with small T-ALI-D and without lymph node involvement while more extensive resections could be indicated in advanced T-ALI-A in order to obtain a complete resection of the tumor and lymph nodes. Future prospective randomized studies should confirm our results.

**Acknowledgments**

None.

**Disclosure**

The authors declare no conflicts of interest.

**References**

1 Shimizu K, Yoshida J, Nagai K et al. Visceral pleural invasion classification in non-small cell lung cancer: A proposal on the basis of outcome assessment. J Thorac Cardiovasc Surg 2004; 127 (6): 1574–8.

2 Ohtaki Y, Hishida T, Yoshida J et al. The clinical outcome of non-small cell lung cancer patients with adjacent lobe invasion: The optimal classification according to the status of the interlobar pleura at the invasion point. Eur J Cardiothorac Surg 2013; 43 (2): 302–9.

3 Goldstraw P, Chansky K, Crowley J et al. International Association for the Study of Lung Cancer staging and prognostic factors committee, advisory boards, and participating institutions; International Association for the Study of Lung Cancer staging and prognostic factors committee advisory boards and participating institutions. The IASLC lung cancer staging project: Proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 2016; 11 (1): 39–51.

4 Taylor MD, Nagji AS, Bhamidipati CM et al. Tumor recurrence after complete resection for non-small cell lung cancer. Ann Thorac Surg 2012; 93 (6): 1813–20.

5 Xiao Z, Cao C, Mei J, Liao H, Yan T, Liu L. Should tumor with direct adjacent lobe invasion (Tdali) be assigned to T2 or T3 in non-small cell lung cancer: a meta-analysis. J Thorac Dis 2016; 8 (8): 1956–65.

6 Nonaka M, Kataoka D, Yamamoto S et al. Outcome following surgery for primary lung cancer with interlobar pleural invasion. Surg Today 2005; 35 (1): 22–7.

7 Miura H, Taira O, Uchida O, Kato H. Invasion beyond interlobar pleura in non-small cell lung cancer. Chest 1998; 114 (5): 1301–4.

8 Okada M, Tsubota N, Yoshimura M, Miyamoto Y, Matsuoka H. How should interlobar pleural invasion be classified? Prognosis of resected T3 non-small cell lung cancer. Ann Thorac Surg 1999; 68 (6): 2049–52.

9 Demir A, Gunluoglu MZ, Sansar D, Melek H, Dincer SI. Staging and resection of lung cancer with minimal invasion of the adjacent lobe. Eur J Cardiothorac Surg 2007; 32 (6): 855–8.

10 Haam SJ, Park IK, Paik HC et al. T-stage of non-small cell lung cancer directly invading an adjacent lobe. Eur J Cardiothorac Surg 2012; 42 (5): 807–10.

11 Yang HX, Hou X, Lin P et al. Peripheral direct adjacent lobe invasion non-small cell lung cancer has a similar survival to that of parietal pleural invasion T3 disease. J Thorac Oncol 2009; 4 (11): 1342–6.

12 Dziedzic D, Rudzinski P, Langfort R, Orlofski T. Polish lung cancer study group (PLCSG). Results of surgical treatment and impact on T staging of non-small-cell lung cancer adjacent lobe invasion. Eur J Cardiothorac Surg 2016; 50 (3): 423–7.

13 Joshi V, McShane J, Page R et al. Clinical upstaging of non-small cell lung cancer that extends across the fissure: Implications for non-small cell lung cancer staging. Ann Thorac Surg 2011; 91 (2): 350–3.
14 D’Andrilli A, Maurizi G, Andreetti C et al. Pulmonary artery reconstruction with pulmonary vein conduit for lung cancer: Medium-term results. Ann Thorac Surg 2014; 98 (3): 990–5.
15 Cusumano G, Marra A, Lococo F et al. Is sleeve lobectomy comparable in terms of short- and long-term results with pneumonectomy after induction therapy? A multicenter analysis. Ann Thorac Surg 2014; 98 (3): 975–83.
16 Marulli G, Rea F, Zampieri D et al. Safe resection of the aortic wall infiltrated by lung cancer after placement of an endoluminal prosthesis. Ann Thorac Surg 2015; 99 (5): 1768–73.
17 Fiorelli A, Santini M. In lung cancer patients where a malignant pleural effusion is found at operation could resection ever still be justified? Interact Cardiovasc Thorac Surg 2013; 17 (2): 407–12.
18 Riquet M, Berna P, Arame A et al. Lung cancer invading the fissure to the adjacent lobe: More a question of spreading mode than a staging problem. Eur J Cardiothorac Surg 2012; 41 (5): 1047–51.
19 Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 1995; 60 (3): 615–22.
20 Vansteenkiste J, Crinò L, Dooms C et al. Panel members. 2nd ESMO consensus conference on lung cancer: Early-stage non-small-cell lung cancer consensus on diagnosis, treatment and follow-up. Ann Oncol 2014; 25 (8): 1462–74.
21 Fiorelli A, Caronia FP, Daddi N et al. Sublobar resection versus lobectomy for stage I non-small cell lung cancer: An appropriate choice in elderly patients? Surg Today 2016; 46 (12): 1370–82.
22 El-Sherif A, Fernando HC, Santos R et al. Margin and local recurrence after sublobar resection of non-small cell lung cancer. Ann Surg Oncol 2007; 14 (8): 2400–5.
23 Sawabata N, Ohta M, Matsumura A et al. Thoracic surgery study group of Osaka university. Optimal distance of a malignant negative margin in excision of nonsmall cell lung cancer: A multicenter prospective study. Ann Thorac Surg 2004; 77: 415–20.
24 Maurizi G, D’Andrilli A, Ciccone AM et al. Margin distance does not influence recurrence and survival after wedge resection for lung cancer. Ann Thorac Surg 2015; 100 (3): 918–24.
25 Mohiuddin K, Haneuse S, Sofer T et al. Relationship between margin distance and local recurrence among patients undergoing wedge resection for small (≤2 cm) non-small cell lung cancer. J Thorac Cardiovasc Surg 2014; 147 (4): 1169–75.
26 Wolf AS, Swanson SJ, Yip R et al. The impact of margins on outcomes after wedge resection for stage I non-small cell lung cancer. Ann Thorac Surg 2017; 104 (4): 1171–8.
27 Leuzgi G, Cesario A, Cafarotti S et al. Surgical treatment in patient with non-small-cell lung cancer with fissure involvement: Anatomical versus nonanatomical resection. J Thorac Oncol 2014; 9 (1): 97–108.
28 Fiorelli A, Sagan D, Mackiewicz L et al. Incidence, risk factors, and analysis of survival of unexpected N2 disease in stage I non-small cell lung cancer. Thorac Cardiovasc Surg 2015; 63 (7): 558–67.