Long-term survival and recurrence in patients with resected non–small cell lung cancer 1 cm or less in size

Paul C. Lee, MD, Robert J. Korst, MD, Jeffrey L. Port, MD, Yaniv Kerem, BA, Amanda L. Kansler, MPH, and Nasser K. Altorki, MD

Objective: With the widespread use of computed tomography and the emergence of screening programs, non–small cell lung cancer is increasingly detected in sizes 1 cm or less. We sought to examine the long-term survival and recurrence patterns after resection of these tumors.

Methods: We conducted a retrospective review over a 15-year period to identify patients with surgically resected non–small cell lung cancer measuring 1 cm or less. Medical records were reviewed, and survival data were analyzed by the Kaplan-Meier method.

Results: There were 83 patients (26 men, 57 women) with a median age of 67 years (range 43-88 years). Median tumor size was 0.90 cm. Lobectomy was performed in 71 patients, bilobectomy in 1, pneumonectomy in 1, segmentectomy in 5, and wedge resection in 5. Postoperative stage was IA in 67 patients, IB in 4, IIA in 1, IIB in 4, IIIA in 2, and IIIB in 5. Median follow-up was 31 months. There was 1 operative death (1.2%). In 5 (31.3%) of the 16 patients with non-IA disease, recurrent cancer developed after resection. No recurrences were observed in the 67 patients with stage IA disease. The 5- and 10-year overall survivals for the entire cohort were 86% and 72%, respectively, and the disease-specific survival was 91% at both time points. For patients with stage IA disease, 5- and 10-year survivals were 94% and 75%, respectively, and the disease-specific survival was 100% at both time points.

Conclusion: Eighty-one percent of patients with resected non–small cell lung cancer measuring 1 cm or less had stage IA disease. After surgical resection, recurrence is rare and long-term survival is excellent.

From the Department of Cardiothoracic Surgery, Weill-Cornell Medical Center, New York, NY.

Read at the Eighty-sixth Annual Meeting of The American Association for Thoracic Surgery, Philadelphia, Pa, April 29-May 3, 2006.

Received for publication April 17, 2006; revisions received Aug 16, 2006; accepted for publication Aug 31, 2006.

Address for reprints: Nasser K. Altorki, MD, Department of Cardiothoracic Surgery, Suite M404, New York Presbyterian Hospital—Weill Medical College of Cornell University, 525 East 68th St, New York, NY 10021 (E-mail: nkaltork@med.cornell.edu).

J Thorac Cardiovasc Surg 2006;132:1382-9

0022-5223/$32.00

doi:10.1016/j.jtcvs.2006.08.053

Lung cancer is the leading cause of cancer deaths in the United States. In 2005, an estimated 173,000 Americans were diagnosed with lung cancer, and 164,000 of them will die of their disease.[1] The majority of patients with non–small cell lung cancer (NSCLC) have metastatic or locally advanced disease at presentation, whereas less than 15% present with stage I disease, in which surgical resection results in a 5-year survival of 60% to 80%. The improved survival after surgical resection seen in patients with stage I disease has led to renewed interest in screening programs for lung cancer with the promise of detecting smaller and potentially more curable tumors. With the increased prevalence of screening programs as well as the widespread use of high-resolution computed tomography (CT), NSCLC is more frequently detected in sizes 1 cm or less. However, it is still uncertain whether detection of smaller tumors translates into improved long-term survival. Very few studies have reported the long-term survival and recurrence patterns after resection of these small lesions. There is also controversy regarding the optimal surgical approach for these small tumors. In this study, we reviewed our experience in patients with resected NSCLC measuring 1 cm or less in size to

Abbreviations and Acronyms
CI = confidence interval
CT = computed tomography
ELCAP = Early Lung Cancer Action Program
NSCLC = non–small cell lung cancer
PET = positron emission tomography

determine the overall and disease-specific survival as well as tumor recurrence after surgical resection.

Patients and Methods

Patients

We conducted a retrospective review of all patients with NSCLC in a prospective database to identify patients with pathologic NSCLC measuring 1 cm or less that was surgically resected at our institution from January 1991 to December 2005. Patients who had neoadjuvant therapies before resection were excluded. A total of 83 patients were identified. Hospital and office records of each patient were reviewed for demographic and clinical data including age, gender, smoking status, preoperative pulmonary functional assessment, preoperative radiologic assessment, associated comorbidities, and clinical stage. Records were also reviewed for perioperative and pathologic data, including surgical approach, extent of resection, 30-day operative mortality (defined as death during the same hospitalization or within 30 days after the operation), complications, length of stay, tumor size, histologic type, pathologic stage, and use of adjuvant therapy. Staging was done according to the TNM classification of the American Joint Committee for Cancer Staging and Revised International System for Staging Lung Cancer.[2] Follow-up was obtained through office visits and telephone interviews.

Statistical Analysis

Statistical analysis was performed with SPSS statistical software (SPSS Inc, Chicago, Ill). Overall and disease-specific survival of the entire cohort and for two subgroups (stage IA group and stage non-IA group) was analyzed by the Kaplan-Meier method. In this study, overall survival is defined as the percentage of patients who have survived for a defined period of time after surgical resection. Disease-specific survival is defined as the percentage of patients who have survived lung cancer for a defined period of time after surgical resection. In calculating this percentage, we counted only deaths from lung cancer, excluding patients who died of other causes. The log-rank test was used to determine significance of survival distributions among groups. Independent *t* tests were used for two-group comparisons of continuous variables. Categorical data in cross-tabulation tables were compared by the Fisher exact test or the Pearson χ^2 test. Nonparametric data were analyzed with the Mann-Whitney *U* test. This study was approved by the Institutional Review Board of the Weill Medical College of Cornell University.

Results

Clinical Findings

During the 15-year study period from January 1991 to December 2005, 83 patients were identified (26 men, 57 women) with a median age of 67 years (range 43-88 years). The number of NSCLCs 1 cm or less in size increased steadily over the study period. The numbers of resected tumors were 8, 21, and 54 over the 3 consecutive 5-year periods. These represented 3.8%, 5.8%, and 7.0% of the total number of surgical resections for NSCLC over the same time periods. Seventy-eight patients were smokers and 5 were never-smokers. Of the smokers, 17 were current and 61 were former smokers. Median pack-years of all smokers was 40. Seventeen patients had respiratory symptoms at presentation, which included cough, shortness of breath, and fever. The majority of the tumors were discovered incidentally by CT or chest radiograph. Tissue diagnoses were obtained by CT-guided fine needle aspiration in 48 patients and flexible bronchoscopy in 1 patient. In the remaining 34 patients, the diagnosis was suggested by a positive result on positron emission tomography (PET) scanning (n = 13) or suspicious findings on CT scanning (n = 21). Twenty-one patients were enrolled in the Early Lung Cancer Action Project (ELCAP) screening program and had their tumors detected by low-dose CT. Pulmonary function tests were performed in 70 patients. Mean forced expiratory volume in 1 second was 83% of predicted (range 36%-100%). Mean forced vital capacity was 87% of predicted (range 53%-100%). Mean diffusing capacity was 76% of predicted (range 31%-100%).

PET Scanning

PET scanning was obtained preoperatively in 37 patients in whom a standard uptake value was reported. Twenty-two patients had a positive finding. The median standard uptake value for a positive result was 2.7 g/mL. The histologic characteristics for the 22 PET-positive tumors were as follows: adenocarcinoma in 17 (mixed subtype of adenocarcinoma with bronchoalveolar features in 3, bronchoalveolar carcinoma subtype in 2), squamous cell carcinoma in 2, and large cell carcinoma in 3. Of 4 patients with pathologic N1 disease, only 1 patient's nodal disease was PET positive preoperatively. One of 2 patients with pathologically confirmed N2 disease had a preoperative PET scan that showed no uptake in the mediastinum. Of the 5 patients with intralobar satellite lesions (T4), 3 patients had a preoperative PET scan. In all 3 patients the PET scan failed to identify the satellite lesions.

Surgical Approach and Extent of Resection

All surgical procedures are listed in Table 1. Eighteen patients underwent mediastinoscopy. The indications for mediastinoscopy were lymphadenopathy (>1.5 cm on CT) in 3 patients, central tumor in 2, positive mediastinal uptake on PET in 2, associated medical comorbidities in 3, and surgeon preferences in 8. One patient was found to have N2 disease by mediastinoscopy. Lobectomy was the most com-

TABLE 1. Operative procedures

Procedure type	No. of patients	Percent
Lobectomy	71	85.5
Open	58	69.9
Thoracoscopic	13	15.7
Bilobectomy	1	1.2
Pneumonectomy	1	1.2
Segmentectomy	5	6.0
Wedge	5	6.0
Open	3	3.6
Thoracoscopic	2	2.4
R0 resection	83	100
Mediastinoscopy	18	21.7
Negative	17	20.5
Positive	1	1.2
Mediastinal lymph node dissection	74	89.2

monly performed resection. Bilobectomy was done in 1 patient because of an endobronchial tumor at the bifurcation of the middle and lower lobe bronchus. In another patient, a pneumonectomy was performed because of a centrally located tumor involving the bifurcation of the left upper and lower lobe bronchus. Limited resections were done in 10 patients (5 segmentectomies, 5 wedge resections). The reasons for limited resection included compromised pulmonary reserve in 6 patients, prior lobectomy in 1, associated comorbidities in 1, and incorrect initial frozen-section diagnosis in 2. As presented in Table 2, the group with limited resection had significantly compromised preoperative pulmonary reserve compared with patients with anatomic resections. Seventy-four (89%) patients had mediastinal lymph node dissection. All patients had curative R0 resections.

Perioperative Course

There was 1 operative death, with an operative mortality of 1.2%. This patient died at home of a myocardial infarction on postoperative day 13. Major complications occurred in 8 patients, with minor complications in 18 patients (Table 3). The median length of stay in the hospital for the entire group was 5 days (range 2-14 days). The median length of stay in the hospital for the open lobectomy group was 5 days (range 2-14 days) compared with 4 days (range 2-12 days) in the thoracoscopic lobectomy group ($P = .003$ by the Mann-Whitney test).

TABLE 2. Mean preoperative pulmonary function tests in patients with limited and anatomic resection

	Limited resection	Anatomic resection	*P* value
% FEV_1	65	86	.015
% FVC	76	89	.007
% DLCO	57	80	.001

FEV_1, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *DLCO*, diffusing capacity for carbon monoxide.

TABLE 3. Postoperative complications

Complications	No. of patients
Major	
Reintubation	1
Pneumonia	3
Pulmonary embolism	3
Empyema	1
Minor	
Arrhythmia	6
Prolonged air leak	10
Urinary tract infection	1
Wound infection	1

Pathologic Findings

Histopathologic characteristics of all 83 patients with resected NSCLC measuring 1 cm or less in size are presented in Table 4. Forty-six percent of tumors were 1 cm in size, with 54% smaller than 1 cm in size. Adenocarcinoma was the predominant histologic type. Of the 21 patients who had

TABLE 4. Histopathologic characteristics of all 83 patients with resected ≤1 cm NSCLC

Characteristic	n
Tumor size (cm)	
Median	0.90
Range	0.20-1.00
<1 cm	45
1 cm	38
Histology	
Adenocarcinoma	68
Mixed adenoca/bronchoalveolar subtype	25
Bronchoalveolar carcinoma subtype	9
Squamous cell carcinoma	9
Large cell carcinoma	6
Pathologic stage	
T1 N0—IA	67
T2 N0—IB*	4
T1 N1—IIA	1
T2 N1—IIB	3
T3 N0—IIB	1
T1 N2—IIIA	2
T4 N0—IIIB†	5
Pathologic stage of ELCAP patients	
T1 N0—IA	16
T2 N0—IB	2
T1 N2—IIIA	1
T4 N0—IIIB	2

NSCLC, non–small cell lung cancer; *ELCAP*, Early Lung Cancer Action Project. *All patients had visceral pleura invasion. †All patients had satellite tumors.

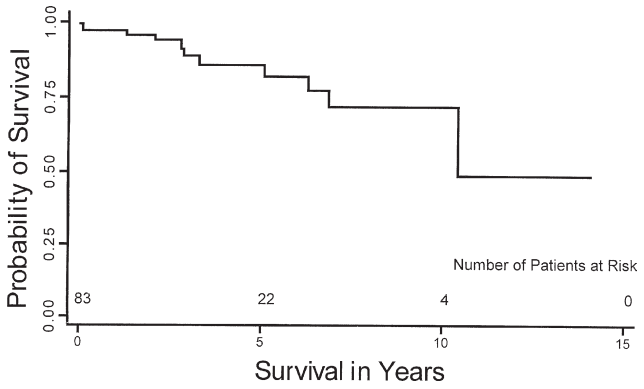

Figure 1. Overall survival of 83 patients with NSCLC measuring 1 cm or less after resection. *NSCLC*, non–small cell lung cancer.

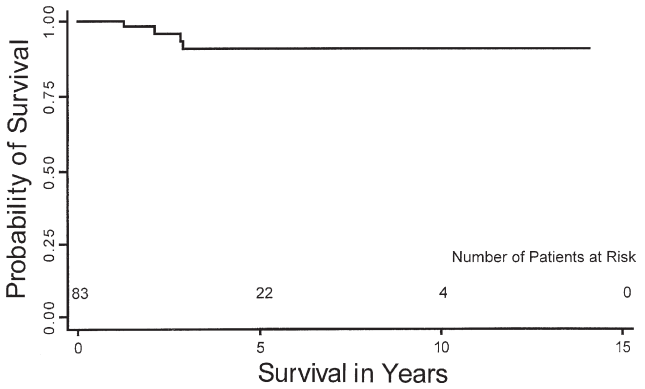

Figure 3. Disease-specific survival of 83 patients with NSCLC measuring 1 cm or less after resection. *NSCLC*, non–small cell lung cancer.

their tumors detected by ELCAP low-dose screening CT, 86% had stage I disease.

Adjuvant Therapies

One patient was found to have N2 disease by mediastinoscopy. This patient subsequently underwent resection followed by adjuvant chemotherapy and radiotherapy. Four other patients were selected to receive adjuvant chemotherapy for postoperative pathologic stages of IB, IIA, IIB, and IIIA. One patient received adjuvant radiotherapy as the sole modality after resection of NSCLC with N1 metastasis.

Overall and Disease-specific Survival

Median follow-up of all patients was 31 months. Nineteen percent of patients (n = 16) with resected NSCLC measuring 1 cm or less in size had greater than stage IA disease. Recurrent cancer developed after resection in 5 (31.3%) of the 16 patients with non-IA disease. Sites of recurrence were mediastinum, contralateral lung, brain, spine, and both spine and mediastinum in 1 patient each. The single patient with isolated mediastinal recurrence underwent surgical resection of the recurrence followed by adjuvant radiotherapy and is currently alive without disease recurrence 12 months after treatment. No recurrences were observed in the 67 patients with stage IA disease during the follow-up period. Five- and 10-year overall survival for the entire cohort was 86% (95% confidence interval [CI] 72%-93%) and 72% (95% CI 51%-85%), respectively (Figure 1). Patients were separated into stage IA and non-IA groups for survival comparison (Figure 2). For patients in stage IA, 5- and 10-year overall survivals were 94% (95% CI 79%-98%) and 75% (95% CI 48%-89%), respectively. For those with non-IA disease, 5- and 10-year overall survival was significantly decreased to 48% (95% CI 12%-77%) ($P = .014$).

Lung cancer disease-specific survival was calculated for the entire cohort. Five- and 10-year disease-specific survival was 91% (95% CI 78%-97%) at both time points (Figure 3). For patients with stage IA disease, 5- and 10-year disease-specific survival was 100% at both time points (Figure 4). For those with non-IA disease, 5- and 10-year disease-specific survival was significantly decreased to 48% (95% CI 12%-77%) ($P < .001$).

When overall 5- and 10-year survival was compared between patients with limited resection (n = 10) and anatomic resection (n = 73), there was no significant difference in survival between the two groups ($P = .828$). Over the past 4 years, lobectomies were mainly done by thoracoscopic approaches. When the thoracoscopic (n = 13) and the open (n = 58) groups were compared, there was no significant difference in overall survival ($P = .478$).

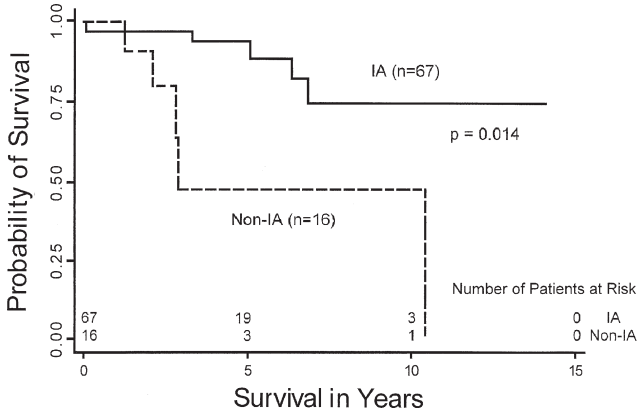

Figure 2. Overall survival of patients with NSCLC measuring 1 cm or less after resection, subdividing into pathologic IA and non-IA stage. *NSCLC*, non–small cell lung cancer.

Discussion

The diagnosis of bronchogenic carcinoma carries a dismal prognosis for the majority of patients. The stage of carci-

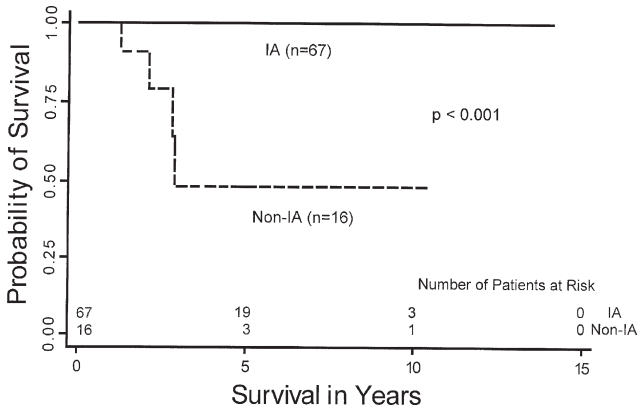

Figure 4. Disease-specific survival of patients with NSCLC measuring 1 cm or less after resection, subdividing into pathologic IA and non-IA stage. *NSCLC,* non–small cell lung cancer.

GTS

noma at diagnosis remains one of the most important determinants of survival in NSCLC, with earlier-stage patients having a better chance of long-term survival.[2] For patients with resectable stage I disease, 5-year survival can be as high as 80%.[3] Unfortunately, less than 15% of patients present with stage I disease. The improved survival in patients with stage I disease led to renewed interest in lung cancer screening programs with detection of smaller and possibly more curable tumors. The ultimate goal of lung cancer screening programs is to shift the stage distribution of tumors at the time of diagnosis to earlier stages, thus improving the overall curability of lung cancer. Indeed, screening studies have demonstrated a consistent stage shift with stage IA reported in as many as 80% of participants.[4]

Yet controversy still exits regarding the relationship between tumor size and survival within stage IA tumors. We[5] and others[6,7] have shown improved survival for stage I tumors measuring less than 2 cm, whereas others investigators have not.[8,9] This issue has important implications for lung cancer screening with CT scanning. If there is no difference in survival between subcentimeter tumors and their larger counterparts, then the rationale for using CT scanning (as opposed to chest radiographs) in detecting small lesions is less compelling.

In the current study, 81% of patients with resected NSCLC measuring 1 cm or less had stage IA disease and had a 100% lung cancer–specific survival at 5 and 10 years. No recurrence was noted during our study period for patients with stage 1A disease. Other investigators have demonstrated this superior survival as well. Martini and associates[10] noted in their review of 598 patients with resected stage I NSCLC that 35 patients had tumors measuring less than 1 cm with 5- and 10-year survivals of 97% and 93%. Miller and colleagues[11] reported on 100 patients with resected NSCLC measuring 1 cm or less, of whom 93 had stage I disease with a 5-year lung cancer–specific survival of 87%. Our finding supports the concept that size *does* have a strong impact on survival. If CT screening does indeed detect subcentimeter tumors and thus shifts the size and stage distribution of tumors at diagnosis, then the impact on lung cancer survival may be considerable. In the current series, 21 patients had their tumors discovered through the ELCAP screening program with low-dose CT. Eighteen patients (86%) had stage I disease and only 1 patient had N2 disease.

However, it appears that a subset of small tumors may have aggressive biologic behavior. Ohta and coworkers[12] have shown that nodal micrometastases were found in 20% of patients with adenocarcinoma measuring 1.1 to 2.0 cm in size and in 4 of 11 patients with tumor measuring 1.0 cm or less in size. In the current report of 83 patients, 16 patients had greater than stage IA disease, including N1 nodal metastasis in 4 patients and N2 metastasis in 2 patients. In addition, 5 patients had pleural invasion (T2 in 4, T3 in 1) and 5 patients had intralobar satellite lesions (T4). The survival in this non-IA group was significantly diminished compared with the IA group, mainly because of tumor recurrences.

There is ongoing controversy as to the extent of resection necessary for stage I NSCLC. The Lung Cancer Study Group showed that for stage IA NSCLC, patients who underwent a limited resection (segmentectomy or wedge) had a higher recurrence rate and lower survival than did those treated by lobectomy.[13] Miller and associates[11] demonstrated that for NSCLC measuring 1 cm or less, patients who underwent lobectomy had significantly improved survival and fewer recurrences than did those having limited resection. However, other authors have suggested that limited resections are adequate treatment for early-stage disease.[14-16] In our study, only 10 patients (12%) had limited resection, mainly because of poor pulmonary reserve and/or associated comorbidities. There was no significant difference in overall survival between patients with limited resection and those with anatomic resection. In the 67 patients with stage IA tumors, 8 patients had limited resection. No recurrence was noted in either the limited resection or the anatomic resection group during the follow-up period. Two limited resections were performed in the non-IA group for T2 N0 tumors with visceral pleural involvement. One patient had mediastinal recurrence that was treated with surgical resection and radiotherapy and is currently alive at 12 months without disease. Although the survival of patients with limited resection in this series suggests that limited resection for 1 cm or less tumors may have equivalent results to lobectomy, the small sample size examined precludes any definitive conclusions. Furthermore, we were unable to distinguish clinically, either by CT or PET scanning, patients who had nodal metastasis or intralobar me-

tastasis before resection. Of the 4 patients with N1 nodal metastasis and 5 patients with intralobar metastasis on final pathologic examination, only 1 patient was staged clinically as having more advanced than IA disease before resection. Clearly, a large prospective randomized trial comparing limited resection with lobectomy is mandatory before firm recommendations are made favoring limited resections over lobectomy for these small tumors.

PET scanning was performed in 37 patients preoperatively and 15 patients had a negative result, with a false negative rate of 41%. Among the 5 patients with pathologic nodal disease (N1 or N2) who had preoperative PET scanning, PET was positive in only 1 patient's nodal station. The false negative rates in detection of the primary tumor as well as nodal metastasis are unacceptably high. Indeed, we[17] have previously reported our results of PET scanning in 64 patients with NSCLC measuring 2 cm or less. Forty-five percent of tumors had negative PET results, and the PET sensitivity and specificity for nodal metastases were only 45% and 89%. Even though PET scanning has recently become a routine tool in preoperative evaluations of patients with NSCLC, our findings suggest that PET scanning has a very limited role in diagnosis and staging of tumors measuring 1 cm or less.

In the current series, mediastinal lymph node dissection was performed in 74 patients, 89% of the cohort. The incidence of N2 nodal metastasis was 2.4%. It is doubtful that this low incidence of upstaging by mediastinal nodal dissection will translate into a meaningful survival benefit in this population of patients. The Z0030 trial sponsored by the American College of Surgeons Oncology Group was designed to determine the survival benefits of mediastinal lymph node sampling versus complete nodal dissection at the time of resection for NSCLC. Ideally, the results of this trial (unpublished data) will clarify the role of mediastinal lymph node dissection.

In this current study, no significant difference in overall survival was observed between the open and the thoracoscopic lobectomy groups. The median length of stay in the hospital for the thoracoscopic group was 4 days compared with 5 days in the open lobectomy group. Although there is no published large randomized prospective series to compare the two approaches, various investigators have shown that thoracoscopic lobectomy can be done safely[18] and with uncompromised survival.[19-21] For patients with subcentimeter tumors, thoracoscopic lobectomy might be an attractive approach.

There are several limitations in this study. This is a surgical series of resected NSCLC with a pathologic size of 1 cm or less. Our survival results should not be extrapolated to all NSCLC tumors measuring 1 cm or less in size at the time of diagnosis, because patients with obvious mediastinal or distant metastases might not have been referred for surgical evaluation. Patients who received neoadjuvant therapies were also excluded in this study because the pathologic size at resection might reflect treatment effects and not the true pathologic tumor size at the time of diagnosis. The sample size in our series is also too small to make any definitive recommendations on the roles of limited resection and mediastinal lymph node dissection in the management of NSCLC measuring 1 cm or less in size. Large prospective randomized studies are necessary to address these issues.

In summary, the number of NSCLC tumors measuring 1 cm or less that are detected is increasing because of the widespread use of CT and the emergence of screening programs. Even though the majority of tumors at resection are in stage IA, some of these tumors may have intralobar satellites or lymph node metastases. After surgical resection of NSCLC tumors measuring 1 cm or less, recurrence is rare and long-term survival is excellent.

References

1. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, et al. Cancer statistics, 2005. *CA Cancer J Clin.* 2005;55:10-30.
2. Mountain CF. Revisions in the International System for Staging Lung Cancer. *Chest.* 1997;111:1710-7.
3. Nesbitt JC, Putnam JB Jr, Walsh GL, Roth JA, Mountain CF. Survival in early-stage non–small cell lung cancer. *Ann Thorac Surg.* 1995;60:466-72.
4. Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet.* 1999;354:99-105.
5. Port JL, Kent MS, Korst RJ. Tumor size predicts survival within stage IA non–small cell lung cancer. *Chest.* 2003;124:1828-33.
6. Birim O, Kappetein P, Takkenberg JJM, van Klaveren RJ, Bogers AJ. Survival after pathological stage IA nonsmall cell lung cancer: tumor size matters. *Ann Thorac Surg.* 2005;79:1137-41.
7. Koike T, Terashima M, Takizawa T, Watanabe T, Kurita Y, Yokoyama A. Clinical analysis of small-sized peripheral lung cancer. *J Thorac Cardiovasc Surg.* 1998;115:1015-20.
8. Yanagi S, Sugiura H, Morikawa T, Kaji M, Okushiba S, Kondo S, et al. Tumor size does not have prognostic significance in stage Ia NSCLC. *Anticancer Res.* 2000;20:1155-8.
9. Patz EF Jr, Rossi S, Harpole DH Jr, Herndon JE, Goodman PC. Correlation of tumor size and survival in patients with stage IA non–small cell lung cancer. *Chest.* 2000;117:1568-71.
10. Martini N, Bains MS, Burt ME, Zakowski MF, McCormack P, Rusch VW, et al. Incidence of local recurrence and second primary tumors in resected stage I lung cancer. *J Thorac Cardiovasc Surg.* 1995;109:120-9.
11. Miller DL, Rowland CM, Deschamps C, Allen MS, Trastek VF, Pairolero PC. Surgical treatment of non–small cell lung cancer 1 cm or less in diameter. *Ann Thorac Surg.* 2002;73:1545-51.
12. Ohta Y, Oda M, Wu J, Tsunezuka Y, Hiroshi M, Nonomura A, et al. Can tumor size be a guide for limited surgical intervention in patients with peripheral non–small cell lung cancer? Assessment from the point of view of nodal micrometastasis. *J Thorac Cardiovasc Surg.* 2001;122:900-6.
13. Ginsberg RJ, Rubstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non–small cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg.* 1995;60:615-22.
14. Erret LE, Wilson J, Chiu RJ, Munro DD. Wedge resection as an alternative procedure for peripheral bronchogenic carcinoma in poor-risk patients. *J Thorac Cardiovasc Surg.* 1985;90:656-61.
15. Pastorino U, Valente M, Bedini V, Infante M, Tavecchio L, Ravasi G. Limited resection of stage I lung cancer. *Eur J Surg Oncol.* 1991;17:42-6.

16. Okada M, Yoshikawa K, Hatta T. Is segmentectomy with lymph node assessment an alternative to lobectomy for non–small cell lung cancer of 2 cm or smaller? *Ann Thorac Surg.* 2001;71:956-61.
17. Port JL, Andrade RS, Levin MA, Korst RJ, Lee PC, Becker DE, et al. Positron emission tomographic scanning in the diagnosis and staging of non–small cell lung cancer 2 cm in size or less. *J Thorac Cardiovasc Surg.* 2005;130:1611-5.
18. McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. *Ann Thorac Surg.* 2006;81: 421-6.
19. Kaseda S, Aoki T. Video-assisted thoracic surgical lobectomy in conjunction with lymphadenectomy for lung cancer *J Jpn Surg Soc.* 2002;103:717-21.
20. Lewis RJ, Caccavale RJ. Video-assisted thoracic surgical non–rib spreading simultaneously stapled lobectomy (VATS(n)SSL) *Semin Thorac Cardiovasc Surg.* 1998;10:332.
21. McKenna RJ Jr, Fischel RJ, Wolf R, Wurnig P. Is VATS lobectomy an adequate cancer operation? *Ann Thorac Surg.* 1998;66:1903-8.

Discussion

Dr Daniel L. Miller *(Atlanta, Ga).* Dr Lee, I congratulate you and your colleagues at Cornell for your continued refinement in CT screening and treatment of early-stage lung cancer.

I have three questions. I was impressed by your cytopathologists and interventional radiologists who achieved a diagnosis by fine-needle aspiration on 58% of your patients with a subcentimeter nodule, but also I was disappointed that 45% of your patients underwent a PET scan for a 1 cm or less nodule that was nondiagnostic 41% of the time. What is your institution's current algorithm for the workup of a subcentimeter pulmonary nodule?

Dr Lee. We do not generally obtain PET scans for subcentimeter nodules. Unfortunately, most of the patients we see in the office have already had a PET scan that was ordered by the referring physician.

In terms of workup for subcentimeter nodules, we are very privileged to have a very good interventional radiologist who can needle a lot of these subcentimeter tumors. That is probably not true in other institutions. Fifty-eight percent of our patients had tissue diagnosis obtained by fine-needle aspiration before resection. As part of our workup, we examine previous x-ray films or CT scans. If the nodule is a new growth, if it has suspicious CT findings of solid lesion and spiculation in someone who is older with a smoking history, then we proceed to fine-needle aspiration. If the nodule is not otherwise suspicious, we are inclined to monitor the patient by CT scan in 6 months or a year. I can tell you from our experience that we do not routinely order PET scans to work these nodules up, again, because of the data indicating high false negative results by PET scan in detecting subcentimeter tumors.

Dr Miller. My second question is in two parts and it concerns the histologic type of your tumors. Eighty-two percent of the tumors are either adenocarcinoma and/or bronchoalveolar carcinoma. In your study was there any difference in survival based on the histologic type? If so, was this difference related to nodal involvement because of the histologic type?

Dr Lee. We did not see any differences in survival among the different cell types. As you mentioned, 82% of the patients had adenocarcinomas, so the number of squamous cell cancers and large cell cancers is small in our study. The only survival difference that we noticed was among different stages, for example, stage IA versus non-IA.

Dr Miller. You had an outstanding 5-year and 10-year survival for your lung cancer deaths only for stage IA. How many of those patients had bronchoalveolar cancer? Such a high survival is very similar to the Japanese data.

Dr Lee. Nine patients had bronchoalveolar cancer in that group.

Dr Miller. And they were all in the IA group?

Dr Lee. Correct.

Dr Miller. Finally, 12% of your patients underwent a limited resection, either a wedge or segmentectomy. You found that there was no difference in survival based on the type of resection, and this is probably related to the small number in that subset. What are your institution's current recommendations for the type of resection and the approach for these subcentimeter lung cancers, and especially in regard to bronchoalveolar cancer?

Dr Lee. Our institution has undergone a shift in terms of doing more and more thoracoscopic lobectomies over the past 3 or 4 years. The gold standard is still a lobectomy among good-risk patients. We need a large prospective randomized study looking at limited resection versus lobectomy to be able to fully answer that question. As it stands right now, if a patient is at good risk with a good performance status, we offer the patient a lobectomy. Now, if the patient has medical comorbidities or limited functional status, I think it is very reasonable to offer a limited resection. Although we had only 2 patients with N2 metastases, we did have 5 patients with intralobar satellites. The disadvantage of a limited resection is that you might miss the intralobar satellite lesions. Until we have the results of a large prospective randomized study, we do not have the full answer yet. As it stands right now, we do perform a lot of thoracoscopic lobectomies, and the only time we perform limited resection is for very small peripheral tumors and in someone who has poor performance status or limited pulmonary functions. There are also some studies suggesting that non-solid or bronchoalveolar cancer lesions might be more amenable to limited resection. We are looking at those questions and others with Dr Altorki.

Dr Darroch W. O. Moores *(Albany, NY).* Do you have any data on second primaries in this long follow-up, and if the patients had secondary primaries, did they have second operations?

Dr Lee. We did not look specifically at second primaries. We noted 5 recurrences overall in the patients with non-IA disease. There were also several patients in our series who had previous lobectomies for lung cancer. They were 6 or 7 years out from the first operation when their current second primary tumors developed.

Dr Jack A. Roth *(Houston, Tex).* Dr Lee, you mentioned that 21 of your patients were in the ELCAP study, so the lesion was picked up with screening, is that correct?

Dr Lee. Correct.

Dr Roth. Presumably the others were all incidental findings. What percent of those 21 patients actually had stage IA disease, and did you see any differences in survival in that group versus the patients who had the lesions picked up incidentally?

Dr Lee. Eighty-six percent of that group of 21 patients had stage I disease. There was only 1 patient in that group with N2 disease. We did not see any differences in survival between that screened group and the remaining group.