Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non–Small Cell Lung Cancer

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Background. It has been reported that limited resection (segment or wedge) is equivalent to lobectomy in the management of early stage (T1–2 N0) non–small cell lung cancer.

Methods. A prospective, multiinstitutional randomized trial was instituted comparing limited resection with lobectomy for patients with peripheral T1 N0 non–small cell lung cancer documented at operation. Analysis included locoregional and distant recurrence rates, 5-year survival rates, perioperative morbidity and mortality, and late pulmonary function assessment.

Results. There were 276 patients randomized, with 247 patients eligible for analysis. There were no significant differences for all stratification variables, selected prognostic factors, perioperative morbidity, mortality, or late pulmonary function. In patients undergoing limited resection, there was an observed 75% increase in recurrence rates ($p = 0.02$, one-sided) attributable to an observed tripling of the local recurrence rate ($p = 0.008$ two-sided), an observed 30% increase in overall death rate ($p = 0.08$, one-sided), and an observed 50% increase in death with cancer rate ($p = 0.09$, one-sided) compared to patients undergoing lobectomy ($p = 0.10$, one-sided was the predefined threshold for statistical significance for this equivalency study).

Conclusions. Compared with lobectomy, limited pulmonary resection does not confer improved perioperative morbidity, mortality, or late postoperative pulmonary function. Because of the higher death rate and locoregional recurrence rate associated with limited resection, lobectomy still must be considered the surgical procedure of choice for patients with peripheral T1 N0 non–small cell lung cancer.

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Non–small cell lung cancer (NSCLC) affects more than 140,000 people in the United States annually. An estimated 14% of these patients will be cured of their disease, most curable patients presenting with early stage (I or II) disease [1]. For the past 40 years, the standard surgical treatment for early stage lung cancer has been lobectomy whenever possible [2]. After lobectomy, patients with T1 N0 NSCLC experience up to an 80% 5-year cancer-free survival [3]. In an attempt to preserve pulmonary function, in 1973 Jensik and colleagues [4] were the first to suggest that a lesser resection (segmentectomy) might be an adequate operation for this stage of disease. Many other investigators have subsequently reported results using lesser resections (wedge or segmental resection) for stage I disease, but these were viewed by most surgeons as a "compromise" procedure for patients having limited pulmonary function [5–9]. However, recently some centers have advocated lesser resections as appropriate treatment for patients with T1 N0 NSCLC [10–12]. The theoretical advantages of such a procedure include preservation of pulmonary function, decreased perioperative mortality and morbidity, and the ability of the patient to undergo further resections in the future if a second primary lung cancer should develop [13, 14]. The theoretical disadvantage would be the potential for an increased local recurrence rate and, ultimately, a poorer cure rate for this deadly disease.

In 1982, the North American Lung Cancer Study Group initiated a prospective, randomized trial comparing limited resection (segmentectomy or adequate wedge resection) with lobectomy for the treatment of patients with T1 N0 NSCLC. Accrual to the study was concluded in November, 1988. After a minimum follow-up of 4.5 years, we report the results of this trial.

Material and Methods

Patient Eligibility

All patients had suspected lung cancer discovered on chest roentgenogram. Patients were screened preoperatively and "registered" for entry into the study if they had a clinical T1 N0 peripheral tumor (3 cm or less in all dimensions on posteroanterior and lateral chest roentgenogram), suspected or proven to be a lung cancer that was not visible on flexible bronchoscopy. All patients were able to tolerate a lobectomy as assessed by cardiopulmonary function. Patients were ineligible if they had a history of previously treated cancer other than basal or squamous cell carcinoma of the skin. In addition, before registration, there had to be no evidence of metastatic disease as determined by history, physical examination, and blood chemistry analysis including a normal alkaline phosphatase and serum glutamic-oxaloacetic transaminase. Abnormalities in any of these parameters required a metastatic survey including computed tomography or

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ultrasonography of the liver and a radionuclide bone scan. Routine computed tomographic examination of the brain, lung, liver, and adrenal glands to detect occult metastases was not required.

Randomization Procedure

After preoperative registration, at the time of thoracotomy and before randomization, if not previously proven, the tumor was confirmed by the pathologist to be a NSCLC, and by the surgeon to be T1 by intraoperative assessment of size. Frozen section analysis of sampled segmental, lobar, hilar, and mediastinal lymph nodes from the drainage area of the tumor confirmed the N0 status. A minimum sample of one node from each area was required. As well, an assessment was made by the surgeon as to the appropriateness of a limited resection for curative treatment and whether the intended limited procedure would be an adequate large wedge or a segmental resection. Middle lobe tumors were excluded because of the small size of the lobe involved. At this point, randomization occurred intraoperatively by telephone communication to the Operations Office (Information Management Services, Rockville, MD). Eligible patients were randomly assigned to one of two treatment groups, lobectomy or limited resection, and stratified according to age, pulmonary function, and whether the intended limited resection would be a wedge or a segment.

The study design and informed consent procedures were reviewed and approved by the Institutional Review Board for the protection of human subjects at each participating North American Lung Cancer Study Group institution. Each patient, before registration and operation, gave written informed consent.

Surgical Technique

The technique of segmental resection required isolation, division, and suture of the appropriate segmental bronchus, artery, and vein. In this protocol, portions of up to two adjacent segments could be removed as part of a limited resection. Surgeons were allowed latitude of technique in methods of division of pulmonary tissue. This included segmental stripping, "cut-and-sew" technique, or the use of surgical staplers.

Large adequate wedge resections could also be used as a limited resection treatment when considered appropriate. At least 2 cm of normal lung tissue was required to be resected beyond the tumor. As with segmental resection, surgeons were allowed latitude in surgical technique for division of pulmonary tissue.

After completion of the resection, the surgeon had to confirm that clinically the tumor had been completely resected and all required lymph node stations had been sampled and, by frozen section analysis, confirmed to be negative for metastatic disease. If resection was incomplete or the tumor was found to be greater than T1 or N0 by immediate pathologic analysis, the protocol specified that the surgeon complete the lobectomy.

Postoperatively, the surgeon was required to complete a detailed surgical form to ensure standardized surgical quality control.

Pathologic Assessment

At the time of operation, frozen section analysis was required of all bronchopulmonary, hilar, and mediastinal lymph nodes submitted by the surgeon. Once the tumor was resected, the pathologist was required to measure immediately the tumor and assess the lack of pleural invasion to confirm its T1 status, perform a frozen section analysis of the primary tumor to confirm its non–small cell carcinoma status, and ensure that all resection margins including pulmonary tissue margins indicated a complete resection. The pathologist was required to inform the surgeon if any of these variables did not conform with the study intent of a T1 N0 NSCLC completely resected.

Patient Follow-up

Postoperatively, all minor and major postoperative complications, mortality, and length of hospital stay were recorded. Patients were then followed at 3-month intervals for the first 2 years, and 6-month intervals for the subsequent 3 years, and yearly thereafter. Follow-up evaluation included history and physical examination, routine hematologic and biochemical analysis, and chest roentgenograms were monitored for evidence of recurrent disease. Pulmonary function tests were administered preoperatively, and at 6-month intervals postoperatively for the first 18 months. These included 1 second forced expiratory volume, forced volume capacity, maximum midexpiratory flow rate, and maximum voluntary ventilation.

Statistical Methods

Trial size and duration was originally determined by the number of patients and follow-up necessary for approximately 80 deaths and 70 recurrences (exclusive of second primaries) to occur, which yields a power of 0.9 to detect a 1.8-fold difference in median survival or a 1.85-fold difference in median time to recurrence, both treatment effects in favor of lobectomy, with a one-sided log rank test of size 0.10. This original design (in particular, the use of $\alpha = 0.10$, one-sided) had as its purpose to maximize the power of this equivalency study to detect a medically significant advantage for lobectomy, should it exist, given the practical constraints on accrual time and subsequent follow-up time. In conformance with this original design, we report the one-sided p values associated with the log rank tests of potential over-all survival and recurrence advantage differences in favor of lobectomy, and we declare as statistically significant those that are less than 0.10. Analyses of potential survival and recurrence differences within subgroups, and analyses of potential prognostic factors, are reported with two-sided p values and for these comparisons, 0.05 is the threshold for statistical significance.

In the analysis of the data, sites of relapse were categorized as "local only" (ipsilateral lung or mediastinum) versus "nonlocal" (distant sites as well as simulta-

neous local and distant sites). The Pearson χ^2 test was used for contingency table analyses, with Yates continuity correction in the case of two-by-two tables [15]. Survival curves were estimated as in the Kaplan-Meier method [16], and significance tests were based on log rank statistics as given by Mantel but without continuity correction [17]. Adjusted survival analyses for stratification variables and for other important covariates were obtained from the Cox model [18] or from a stratified log rank score statistic. Variables were screened for prognostic value for death with a score statistic based on the proportional hazards model with stratification for treatment.

A number of definitions were used for the end points of the study. Disease-free interval was the number of days from randomization to proven detection of recurrence or metastases (locoregional, distant, or second primary). Recurrent disease was defined as the discovery of any new lesion considered to be recurrence of the original lung cancer and required pathologic proof. Locoregional recurrence included recurrence at or near the primary site or in lymphatic drainage areas, either bronchopulmonary or mediastinal. Second primary tumors in the lung were considered only if the lesion met accepted criteria [19]. Survival time was the number of days from randomization to death. All randomized patients were followed until death or study termination, unless lost to follow-up.

Results

Patient Population

The study was activated in February 1982 and was closed in November 1988 when 276 patients had been entered. An additional 495 patients were "registered" and appeared to eligible for the study before operation, but for various reasons were found to be ineligible at operation. Approximately 40% of these were found to have benign disease, 25% (because of tumor location or configuration) required more than a limited resection for adequate treatment, and 25% had greater than T1 N0 tumors or other than non–small cell histologies (Table 1).

Of the 276 randomized patients, 29 had major protocol violations; 8 patients had ineligible cell types, 8 patients did not have T1 N0 disease, 8 patients had benign disease, 1 patient had a middle lobe tumor, 2 patients had metastases appear within 1 week of randomization, 1 patient had a previous malignancy, and 1 patient had a primary that was nonpulmonary. This leaves 247 patients (89%) ultimately considered as eligible, 122 receiving a limited resection and 125 lobectomy. Eight additional patients were unable to receive the assigned form of operation as a result of complications during the operation. Eleven of the 139 "limited resection" patients required a completion lobectomy because of either disease greater than T1 N0 or incomplete resections.

Stratification and Prognostic Variables

There were no significant differences between the lobectomy patients and the limited resection patients for all stratification variables and selected prognostic factors (Table 2).

Table 1. Reasons for Not Randomizing 495 of 771 Registered Patients

Reason Not Randomized	No. of Patients
Benign disease	189
Limited resection not feasible (because of tumor location or configuration)	129
Not T1 N0	122
>T1	46
>N0	67
M1	9
Not non–small cell lung cancer	17
Middle lobe tumor	12
Patient refusal	11
Other	15
Total	495

Postoperative Morbidity and Mortality

There was no significant difference in the type or number of postoperative complications or postoperative mortality except that in the lobectomy group, 6 patients developed respiratory failure requiring postoperative ventilation for more than 24 hours. No patient in the limited resection group required postoperative ventilatory assistance. There were three postoperative deaths among the 276

Table 2. Stratification and Selected Prognostic Factors Variables for the 247 Eligible Patients in LCSG 821, Demonstrating No Significant Differences in Allocation

	Surgical Approaches			
	Limited Resection		Lobectomy	
Variables	No. of Patients	%	No. of Patients	%
Total no. of Patients	122		125	
Intended limited resection				
Wedge	40	32.8	40	32.0
Segmental	82	67.2	85	68.0
Performance status = 10	68	55.7	73	58.9
Preop $FEV_1 \geq 50\%$ predicted	114	93.4	116	92.8
Previous wt loss <10%	111	91.0	113	91.1
Nonsquamous histology	92	77.3	92	73.6
Previous cardiac disease	27	22.1	26	21.0
Preop WBC >9,100/μL	34	27.9	35	28.0
Age				
<60 y	45	37.0	38	30.0
≥60 y	77	63.0	86	69.0
Unknown	...		1	1.0

FEV_1 = 1 second forced expiratory volume; Preop = preoperative; WBC = white blood cell count.

Table 3. Recurrence and Death Rates for the 247 Eligible Patients on LCSG 821[a]

Event	Limited Resection		Lobectomy		
	No. of Patients	Rate (per person/y)	No. of Patients	Rate (per person/y)	*p* Value
Recurrence (excluding second primary)	38	0.101	23	0.057	0.02[b]
Recurrence (including second primary)	42	0.112	32	0.079	0.079[b]
Locoregional recurrence[d]	21	0.060	8	0.020	0.008[c]
Nonlocal recurrence[d]	17	0.048	15	0.037	0.672 (NS)[c]
Death (with cancer)	30	0.073	21	0.049	0.094[b]
Death (all causes)	48	0.117	38	0.089	0.088[b]

[a] Note locoregional recurrence rates and death rates are significantly increased after limited resection. [b] One-sided (refer to text); [c] two-sided (refer to text); [d] for definition of recurrences, refer to text.

NS = not significant.

patients undergoing resection, two in the lobectomy and one in the limited resection group.

Survival Differences

A total of 86 patients have died among the 247 eligible patients, 38 in the lobectomy group and 48 in the limited resection group. Of these 86 patients, 51 died with cancer at the time of death (21 in the lobectomy group and 30 in the limited resection group) and 35 died cancer-free. Both the death rates and the death with cancer rates were lower after lobectomy than after limited resection, although the observed differences were of borderline statistical significance (Table 3 and Fig 1). Limited resection was associated with a 30% increase in the overall death rate and a 50% increase in the observed death with cancer rate. These observed survival differences are reduced when the entire population of 276 patients is considered (to approximately 20% and 30%, respectively) and lose statistical significance.

The death rates from any cause for groups defined by initial prognostic variables among the eligible patients demonstrated no significant differences other than by age and by performance status (Table 4). There were statistically significant ($p = 0.02$ two-sided) increases in the death rates of patients older than 60 years and in patients with Karnofsky performance status less than 10 (hazard ratios equal to 1.8 and 1.6, respectively).

Recurrence Differences

Among the 247 eligible patients, there was an observed 75% increase in the recurrence rate (0.101 versus 0.057), exclusive of second primaries ($p = 0.02$, one-sided) associated with the limited resection arm (Table 3 and Fig 2). This observed increase in recurrence rate is 50% when the entire population of 276 randomized patients is considered but it maintains statistical significance ($p = 0.06$, one-sided). The approximate doubling of the recurrence rate, among eligible patients, associated with the limited resection arm appears to apply regardless of whether the intended resection was wedge or segmental ($p < 0.10$ more than two-sided, with or without inclusion of second primaries).

When the recurrences are segregated by site, the increased recurrence associated with the limited resection is seen to be attributable to an observed tripling of the locoregional recurrence rate ($p = 0.008$, two-sided), whereas the distant recurrence rate is unaffected by treatment (Table 3). This effect appears to apply regardless of whether the histology was squamous or nonsquamous or whether the intended resection was wedge or segmental. The locoregional recurrence rate per person/year was 0.022 for lobectomy, 0.044 for segmental resection, and 0.086 for wedge resection.

Preservation of Pulmonary Function

Pulmonary function testing was performed preoperatively and postoperatively, but pulmonary function follow-up and reporting was judged to be not totally reliable after funding for the Lung Cancer Study Group was terminated in 1989. We report the results of the pulmonary function testing that were available as of July 1989. Of the eligible patients with at least 9 months follow-up at that time, only 60% received a 6-month pulmonary function examination. Compliance on the 12- to 18-month examination was only 66%. On the 6-month examination, the changes from baseline for all pulmonary function tests except the maximum midexpiratory flow rate are significantly better for patients receiving limited resection, but these treatment differences decrease and (excepting 1 second forced expiratory volume) lose statistical significance when we compare the 12- to 18-month pulmonary function tests (Table 5).

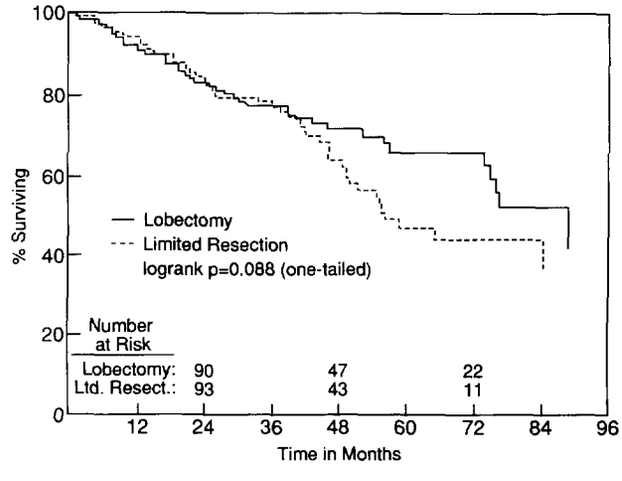

Fig 1. Time to death (from any cause) by treatment for 247 eligible patients.

Table 4. Death Rates for Groups Defined by Initial Prognostic Variables Among Eligible Patients

Variable	No. of Patients at Risk	No. of Deaths	Death Rate (per person/y)	Significance Level[a]
Eligibility histology				
Squamous	60	19	0.100	NS
Nonsquamous	184	64	0.100	
Performance status				
1–9	105	43	0.134	$p = 0.018$
10	141	43	0.084	
Percent weight loss				
<10%	224	74	0.098	NS
≥10%	22	12	0.152	
Preoperative WBC (cells/μL)				
≤9,100	178	60	0.098	NS
>9,100	69	26	0.118	
Age at randomization				
<60	83	20	0.068	$p = 0.020$
≥60	163	66	0.122	
Smoking status at randomization				
Never	12	3	0.068	NS
Former	88	29	0.102	NS, trend
Current	146	54	0.107	
Sex				
Male	149	57	0.110	NS
Female	97	29	0.093	
Alkaline phosphatase (U/L)				
Normal	213	76	0.106	NS
Abnormal	31	10	0.098	
Calcium (mg/dL)				
<9.3	86	31	0.106	NS
9.3–9.7	79	28	0.120	($p = 0.085$)
>9.7	54	14	0.066	NS, trend
Side of operation				
Left	127	45	0.099	NS
Right	120	41	0.108	
Tumor location				
Upper lobe	189	66	0.104	NS
Lower lobe	50	16	0.098	
Tumor volume				
0–3,000 mm^3	59	20	0.102	NS
3,001–8,000 mm^3	67	23	0.096	NS, trend
8,001–27,000 mm^3	52	17	0.091	

[a] Significance level is computed from the log rank test. The trend test and two-group comparisons are two-sided.

NS = not significant; WBC = white blood cell count.

Effect of Tumor Size

There was no difference observed in locoregional recurrence or cancer death rates among tumors less than 3, 9, or 27 cm^3 (Table 4).

Second Primary Cancer

Second primary cancers developed in 13 of the 247 eligible patients, a rate of 0.017 per person/year. Among these second primary tumors, nine occurred in the lobectomy group and four in the limited resection group. There were five second pulmonary malignancies (four in the lobectomy group and one in the limited resection group) and eight new primary malignancies in other sites.

Comment

Although this trial was designed to prove that a lesser resection would afford a similar chance of cancer-free survival and a no greater chance of local recurrence, unfortunately, the study proves that limited resection carries a significantly increased risk of local recurrence and a lesser chance of overall survival and disease-free survival. It should be noted, however, that the observed treatment differences for survival (time to death and time to death with cancer) are of borderline statistical significance for the analysis of eligible patients ($p = 0.09$, one-sided for both comparisons). Because this trial was an equivalency study, we were particularly concerned about failing to detect a potential benefit for lobectomy. In trials that involve testing a conservative experimental therapy against a more aggressive standard therapy, one is more concerned about failing to detect a potential benefit associated with the more aggressive therapy than if that therapy were the experimental therapy. To maximize the power of detecting a potential benefit for lobectomy, we set the significance level at 0.10, one-sided, in accord with common statistical practice reflected by the statement by Makruch and Simon [20] that in equivalency trials "it will often be necessary to use a significance level of 0.10 or 0.20 rather than the usual 0.05 to avoid the more dangerous false negative conclusion." In contrast with the observed treatment differences for survival, the observed treatment difference for recur-

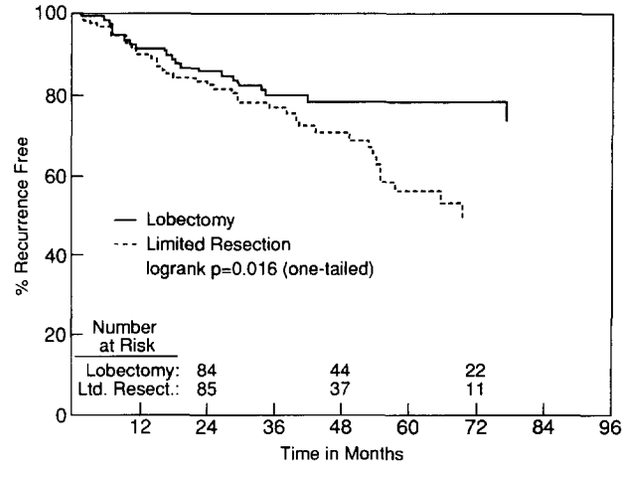

Fig 2. Time to recurrence (excluding second primaries) by treatment for 247 eligible patients.

Table 5. Percent Difference in 6 Months and 12 to 18 Months Pulmonary Function Tests Compared to Initial Preoperative Values

	Limited Resection			Lobectomy			
Test	No. of Patients	Mean % Difference	SD	No. of Patients	Mean % Difference	SD	*p* Value[a]
6 mo							
FEV_1	71	−1.76	(15.3)	67	−9.10	(16.7)	0.008
FVC	71	1.93	(19.4)	67	−5.93	(13.9)	0.007
MMFR	64	4.47	(64.5)	58	−6.66	(61.9)	0.334NS
MVV	50	5.06	(24.6)	47	−7.42	(29.7)	0.026
12–18 mo							
FEV_1	71	−5.18	(16.1)	58	−11.09	(16.3)	0.041
FVC	71	0.52	(22.1)	58	−5.74	(18.3)	0.087NS
MMEFR	60	8.95	(128.6)	55	−9.71	(76.8)	0.352NS
MVV	47	9.72	(75.3)	41	−0.15	(93.9)	0.586NS

[a] Significance level is computed from Student's *t* test and is reported two-sided.

FEV_1 = 1 second forced vital capacity; FVC = forced vital capacity; MMEFR = maximum midexpiratory flow rate; MVV = maximum voluntary ventilation.

rence, excluding second primary, is quite substantial. Longer follow-up would be necessary for a final assessment of survival differences. For the above reasons, we cannot recommend less than a lobectomy for the treatment of even peripheral T1 N0 NSCLC when the patient can tolerate a lobectomy without significantly adverse effects on pulmonary function.

The original reports by Jensik and colleagues [4] from Rush-Presbyterian were extremely optimistic, suggesting that segmental resection was equivalent to lobectomy both in survival and freedom from recurrence for these early stage tumors. However, a recent analysis by the Rush-Presbyterian group, comparing, in a nonrandomized retrospective fashion, their recent results of segmental resection and lobectomy in these early stage patients corroborates our findings in this report of a higher local recurrence rate for patients treated by segmental resection [21].

Other reports have suggested that the addition of postoperative radiotherapy may decrease the local recurrence rate in patients undergoing wedge resection as definitive treatment, especially those with squamous cell carcinoma [8, 9]. Although there is no documented evidence, there is concern that postoperative radiotherapy to the surrounding pulmonary tissue confers at least as much pulmonary function loss as one would expect from a lobectomy. As well, the economic costs related to such additional therapy would be considerable.

This trial has important implications for the standard care of lung cancer patients. In North America of the 14% of patients who ultimately survive their lung cancer each year, it is estimated that at least 75% have stage I NSCLC tumors, about half of whom are T1 N0 [22]. The increased deaths conferred by the use of limited resection (versus lobectomy) would be substantial when one considers the worldwide lung cancer population.

In our study, there were no observed late functional advantages or decreased perioperative morbidity for limited resection. With the very gross methods of pulmonary function assessment performed in this trial, we could not demonstrate a prolonged benefit for limited resection, there being no significant difference in the two groups in ultimate pulmonary function as measured by us in the 12- to 18-month follow-up (except a modest benefit in 1 second forced expiratory volume). Other studies have demonstrated impaired pulmonary function after lobectomy but did not extend measurements beyond 6 months [13, 23, 24]. Our limited assessment suggests no medically significant difference at 12 to 18 months postoperatively. Similarly, the perioperative morbidity and mortality of limited resection was no different than that of lobectomy, save the 5% of patients requiring prolonged ventilation in the lobectomy group.

Many investigators, including proponents of video-assisted thoracoscopic techniques, have suggested the use of wedge resection for the definitive treatment of very small peripheral primary lung tumors [11, 12, 25]. The results of this study suggest that this frequently will not be adequate therapy. This is extremely relevant when using video-assisted techniques in cancer operations where lymph node staging may be less than complete and the temptation to perform a large wedge resection as definitive therapy is greatest. In such circumstances, it would be anticipated that a large number of patients would undergo less than adequate operation, leaving tumor behind at resection margins, in lymphatic channels, and lymph nodes. This would almost certainly result in even higher local recurrences and cancer death rates than in our study because of failure of adequate staging and resections.

The locoregional recurrence rates in this trial demonstrated a threefold increase with wedge resection and 2.4-fold increase with segmental resection compared to lobectomy. Although impossible to assess, it is believed that this increased locoregional recurrence with limited resection is most likely due to two factors: inadequate

resection of the primary tumor or failure to identify and resect intrapulmonary microscopic and lymphatic spread of the tumor [26–32]. Occult intrapulmonary lymphatic and nodal disease almost certainly was present in limited resection patients accounting for the higher locoregional recurrence rate. It would be impossible for any pathologist to identify all microscopic lymphatic spread beyond the tumor but within the lobe.

It has been suggested that tumors less than 1 cm rarely contain lymphatic metastases and have a smaller risk of locoregional recurrence and greater chance of survival [11, 12, 25]. When we assessed this variable by estimating initial tumor volume (less than 3, 9, 27 cm^3) we found no significant difference in locoregional recurrence or cancer death rates per person/year. Treatment of T1 N0 NSCLC, no matter the size, appears to be adversely affected by limited resection.

The importance of accurate intraoperative staging including lymph node sampling is demonstrated by the fact that more than 25% of patients with lung cancer (122 of 427) deemed to be clinically T1 N0 were found to have a higher stage of disease after the intraoperative maneuvers of primary tumor and lymph node assessment (Table 1).

There are certain instances where lobectomy cannot be the procedure of choice for patients with early stage lung cancer including patients with insufficient pulmonary reserve to tolerate a lobectomy, especially those patients where a previous contralateral pneumonectomy has been performed [33]. In such instances, a lesser resection is appropriate treatment with segmental resection affording in lesser risk of locoregional recurrence than wedge resection.

This study has failed to demonstrate the equivalence of wedge or segmental resection to lobectomy for those patients with lung cancer deemed to have a peripheral NSCLC T1 N0 tumor. Lobectomy with systematic hilar and mediastinal lymph node sampling or dissection should remain the standard surgical treatment for such individuals.

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Appendix 1. Participating Institutions

Principal investigators of institutions participating in this study include E. Carmack Holmes (Lung Cancer Study Group Chairman, University of California, Los Angeles, CA); John C. Ruckdeschel (Albany Medical College, Albany, NY); Michael Johnston (University of Colorado, Denver, CO); Paul A. Thomas, Jr (Illinois Cancer Council, Chicago, IL); Jean Deslauriers (Hospital Laval, Quebec, Canada); Frederick L. Grover (University of Texas Health Science Center, San Antonio, TX); Lucius D. Hill (Fred Hutchinson Cancer Research Center, Seattle, WA); Ronald Feld, Robert J. Ginsberg (University of Toronto, Toronto, Ont, Canada); and Clifton F. Mountain (University of Texas Reference Center for Anatomic and Pathologic Classification, Houston, TX). Members of the Lung Cancer Study Group participating in this study included John C. Ruckdeschel, Stanley Dzuiban, Maureen Kiely, Martin F. McKneally, Darroch W. O. 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INVITED COMMENTARY

This article only partially supports its authors' conclusion "compared with lobectomy limited pulmonary resection does not confer improved perioperative mortality or late postoperative pulmonary function."

The late studies of pulmonary function were not completed, and we do not have information about the pulmonary function that most likely would differentiate those with a lesser resection from those with lobectomy—work and activity status combined with maximum oxygen consumption, studies that provide some knowledge of the actual ability of the patient to live comfortably. The recent popularity of pneumectomy for patients with advanced emphysema must make the thoracic surgeon realize the need for dynamic measurements of pulmonary function. No information was given about the tolerance of patients for resection of secondary cancers, one of the major justifications for limiting lung loss with the first operation.

Does a lesion in the lingula do better with a left upper lobectomy than with a lingulectomy? If a patient has a middle lobe lesion should he or she have an upper and middle lobectomy? Do these authors have enough information to say that all 1-cm or 2-cm lesions will fare better with lobectomy than with segmentectomy or adequate wedge resection?

The recurrence rates are higher in the limited resection

group. The survival times when calculated for the groups separately differ, but when using the entire group for the analysis this difference becomes only marginal. This tells us that people with cancer of the lung die of other causes so that marginal increases in survival time from cancer have little overall effect. Does this study face us with the same dilemma that has arisen regarding radical prostatectomy for cancer of the prostate? Statistics can provide many answers and conflicting conclusions, particularly when applied to a multiinstitutional study such as this. There are many variables unaccounted for that suggest caution in interpretation of small differences

These questions raised will not cover all the questions that should or could arise from reading this article. They are my reasons for considering the conclusion stronger than the information presented.

Improvement in case selection, by improving methods for evaluation of extent of tumor, the adequacy of margins, and methods of evaluating gas exchange functional capacity, can provide means to prevent removal of functional lung not involved with cancer. Perhaps the ability to continue physical exercise after a limited resection will prolong life as much as a lower cancer recurrence rate.

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INVITED COMMENTARY

Among 771 registered patients, 495 (64%) did not have randomized choice as to the type of lung resection that was used. There were 276 patients who had lobectomies or limited resections by random choice. After subtraction of patients with major protocol violations, and otherwise ineligible patients, 247 patients met the study criteria. These facts underscore the difficulty of this type of research, and the credit that is due to the LCSG for having carried it out.

The authors acknowledge that the differences in death rates and death with cancer rates between the group that had lobectomies and the group that had lesser resections were of "borderline significance." They state that "these ... survival differences are reduced (and lose statistical significance) when the entire population of 276 patients is considered." There were 30/247 patients (12%) with limited resections who died with cancer and 21/247 (8.5%) with lobectomies who died with cancer. Recurrences, excluding second primary cancers, occurred in 38/247 patients (15%) who had limited resections as compared with 23/247 patients (9.3%) who had lobectomies. Even with the benefit of a cooperative trial, the number of patients was relatively small.

The article includes potentially misleading statements and much opinion. An example of a statement that could mislead is the following: "... limited resection carries a significantly increased risk of local recurrence and a lesser chance of overall survival and disease-free survival...." The facts support the first part of this contention, but the second part remains in doubt. Although the data about lung function after 1989 are acknowledged as insufficient, the authors say that there was "... no observed late functional advantage or decreased perioperative morbidity for limited resection." The authors further stretch from facts to opinion with their comments about video-assisted thoracic surgery. Although their opinions about video-assisted thoracic surgery may be correct, they are irrelevant to this article because LCSG did not examine video-assisted thoracic surgery.

In the Comment section the authors properly state that "Longer follow-up would be necessary for a final assessment of survival differences," and they express their viewpoint that "... [they] cannot recommend less than a lobectomy for the treatment of even peripheral T1 N0 NSCLC...." They summarize their position by saying "this study has failed to demonstrate the equivalence of wedge or segmental resection to lobectomy...." Although their conclusion that lobectomy remains the operation of choice for the treatment of lung cancer may be correct, it could also be wrong. The LCSG data are insufficient to support dogma about the superiority of lobectomy because its main proven advantage over smaller resections is fewer postoperative local recurrences. Local recurrence by itself is not known to be a lethal happening. In short, if the goal of resection is to prevent death due to systemic cancer, the LCSG results could be interpreted as having failed to show that lobectomy is better than limited resection. At least for patients with significantly impaired lung function, and perhaps whenever feasible, segmentectomy or wedge resection remain good treatment options when such resections provide adequate margins of normal parenchyma.

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