Relationship between margin distance and local recurrence among patients undergoing wedge resection for small (≤2 cm) non–small cell lung cancer

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Objective: Successful pulmonary wedge resection for early-stage non–small cell lung cancer requires a pathologically confirmed negative margin. To date, however, no clear evidence is available regarding whether an optimal margin distance, defined as the distance from the primary tumor to the closest resection margin, exists. Toward addressing this gap, we investigated the relationship between the margin distance and local recurrence risk.

Methods: We reviewed all adult patients who had undergone wedge resection for small (≤2 cm) non–small cell lung cancer from January 2001 to August 2011, with follow-up through to December 31, 2011. The exclusion criteria included other active noncutaneous malignancies, bronchoalveolar carcinomas, lymph node or distant metastases at diagnosis, large cell cancer, adenosquamous cancer, multiple, multifocal, and/or metastatic disease, and previous chemotherapy or radiotherapy. Using Cox regression analysis, we examined the relationship between the margin distance and interval to local recurrence, adjusting for chronic obstructive pulmonary disease, forced expiratory volume in 1 second, smoking, diabetes, tumor size, tumor location, surgeon, open versus video-assisted thoracoscopic surgery, and whether the lymph nodes were sampled.

Results: Of 557 consecutive adult patients, 479 met our inclusion criteria. The overall, unadjusted 1- and 2-year local recurrences rate was 5.7% and 11.0%, respectively. From the adjusted analyses, an increased margin distance was significantly associated with a lower risk of local recurrence ($P = .033$). Patients with a 10-mm margin distance had a 45% lower local recurrence risk than those with a 5-mm distance (hazard ratio, 0.55; 95% confidence interval, 0.35-0.86). Beyond 15 mm, no evidence of additional benefit was associated with an increased margin distance.

Conclusions: In wedge resection for small non–small cell lung cancer, increasing the margin distance ≤15 mm significantly decreased the local recurrence risk, with no evidence of additional benefit beyond 15 mm. (J Thorac Cardiovasc Surg 2014;147:1169-77)

Lung cancer now represents the leading cause of cancer deaths for men and women.[1] Currently, complete surgical resection is the ideal treatment modality for patients with early-stage non–small cell lung cancer (NSCLC). Among the different surgical options, wedge resection has been the most common limited resection technique used to remove NSCLC,[2-6] although lobectomy and lymph node dissection are currently the standard treatment for small peripheral resectable NSCLC.[7] Similarly, many studies on the changing histopathologic patterns of lung cancer have been reported. It has been stated that adenocarcinoma has replaced squamous cell carcinoma as the most frequent histologic subtype for both genders and all races. Recent data have also suggested that the rate of lung cancer incidence is greater in women than in men.[8] For wedge resection, the status of the margin and the distance of the tumor from the resection margin have been major concerns regarding local recurrence.[9-15] In an ongoing phase III randomized trial of lobectomy versus sublobar resection for small peripheral NSCLC (Cancer and Leukemia Group B trial 140503), it has been strongly recommended to confirm the absence of disease in the wedge margin using histologic or cytologic frozen section analysis. When performing lung excision for lung cancer, it is mandatory that malignant cells not be left in the residual pulmonary parenchyma. However, several other factors during lung cancer surgery will be important in determining the survival and recurrence outcomes. These have included

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Abbreviations and Acronyms
CI = confidence interval
HR = hazard ratio
NSCLC = non–small cell lung cancer
VATS = video-assisted thoracoscopic surgery

GTS

the degree of histologic differentiation, tumor size, nodal involvement, and visceral pleural invasion.[9,16,17] Within this framework, however, a paucity of published information is available on the association between margin distance and the risk of local recurrence and what constitutes an optimal margin distance, if such exists, in pulmonary wedge resection. Specifically, no clear guidelines are available in the current data regarding the margin distance from the primary tumor to the closest margin for wedge resection for small, localized tumors. The present study, therefore, aimed to characterize the association between the margin distance in patients who had undergone wedge resection for small (≤2 cm) NSCLC and the local recurrence risk. To address this gap, we analyzed detailed follow-up data from a cohort of patients who had undergone successful pulmonary wedge resection for early-stage NSCLC.

METHODS

Study Population

With institutional review board approval, we reviewed the records for all adult patients who had undergone elective surgical resection for NSCLC tumors ≤2 cm at the Brigham and Women's Hospital (Boston, Mass) from January 2001 to August 2011. For the present study, we restricted our attention to pulmonary wedge resections only. All such surgeries were considered, regardless of whether they had been performed by way of thoracotomy or video-assisted thoracoscopic surgery (VATS). To focus our attention on patients with primary NSCLC tumors, we applied the following exclusion criteria: previous major lung resection, distant previous thoracic radiotherapy, neoadjuvant therapy before resection, other active noncutaneous malignancies, pure bronchoalveolar carcinomas, lymph node or distant metastases at diagnosis, multicentric cancers, large cell, adenosquamous, and multiple, multifocal, and/or metastatic cancer, and previous chemotherapy and/or radiotherapy. Figure 1 provides an overview of the study population selection and the effect of the various exclusion criteria.

Data Sources

The demographic, clinical, medical and surgical history, and surgical, pathologic, and intra- and postoperative complication data for all patients were abstracted from the hospital clinical records. Using the institutional guidelines, the patients were followed up every 4 months for the first 2 years, every 6 months for years 2 to 5, and annually thereafter. At abstraction, all variables were comprehensively audited. The original imaging (chest radiography and computed tomography) studies were reviewed by a chest radiologist for designation of the location within the hemithorax and the proximity to any major vessels. Vital status as of December 31, 2011 was determined from the hospital records and through the Social Security Death Index.

Local Recurrence

The primary outcome of interest for the present study was local recurrence. In accordance with Martini and Melamed,[18] local recurrence was defined as a tumor of the same histologic type occurring within the same lobe (or draining hilum and/or mediastinum) or a tumor of the same histologic type in a different lobe or lung with carcinoma in the lymphatics common to both, and/or extrapulmonary metastases. Disease recurrence was evaluated by clinical follow-up examination, including chest computed tomography, with the date of the first local recurrence documented. Patients alive on December 31, 2011 who had not experienced local recurrence were administratively censored.

Margin Distance

The margin distance was defined as the distance from the primary tumor to the closest stapled resection margin. The distance was measured by the pathologist, according to a totally deflated lung, and recorded on the final pathology report. Because our interest was in the association between the margin distance and the local recurrence risk, we restricted our analyses to those patients with a confirmed negative margin. Patients with a positive malignant margin were excluded from the analyses, just as were patients with margin distances of <1 mm and those with missing margin data (Figure 1).

Statistical Analysis

The primary outcome for the present study was the interval to local recurrence, with the margin distance the primary exposure of interest. The distributions of the key covariates were calculated and summarized, stratified by the margin distance (1-5, 6-10, 11-15, and 16-30 mm). Continuous covariates (eg, margin distance, age, and percentage of forced expiratory volume in 1 second) were categorized for the purposes of description but were left in their continuous form for modeling.

Multivariable Cox regression analysis was used to model the interval to local recurrence. We adjusted for covariates that were thought, a priori, to be strong candidates as potential confounders of the association between the margin distance and the interval to local recurrence. These included chronic obstructive pulmonary disease, preoperative percentage of forced expiratory volume in 1 second, smoking status, diabetes, tumor size, tumor lobe location, location with the hemithorax (inner vs outer half), surgery type (thoracotomy vs VATS), and whether the lymph nodes had been sampled. The proximity to a major vessel was not included, because it correlated highly with the location in the hemithorax. All Cox models were adjusted for surgeon by stratification of the baseline hazard function. To ensure a stable estimation of these effects, we restricted attention to operations performed by 8 surgeons who had ≥10 observations in our data set; this resulted in the exclusion of 11 surgeries performed by low-volume surgeons (Figure 1). For our analyses, the follow-up period was restricted in the analysis to ≤3 years after surgery owing to the scarceness of data after that point, possibly invalidating the proportional hazards assumption of the Cox model. Finally, despite this restriction, a number of patients died during the follow-up period. To investigate the effect of death on our results, we repeated all our modeling using a composite outcome of local recurrence-free survival, in which we considered the interval to the first of death or local recurrence.

In the absence of an a priori hypothesis regarding the form of the margin distance and interval to local recurrence association, we modeled the association using regression splines to allow for a nonlinear association.[19] For the latter, a single knot was used and set to be the midpoint of the observed margin distance distribution. To evaluate the statistical significance of the overall association between the margin distance and local recurrence risk, we used an omnibus Wald test that jointly evaluated all parameters in the spline specification. All analyses were performed using R, version 2.15 (R Foundation for Statistical Computing, Vienna, Austria).[20] All reported *P* values are 2-sided.

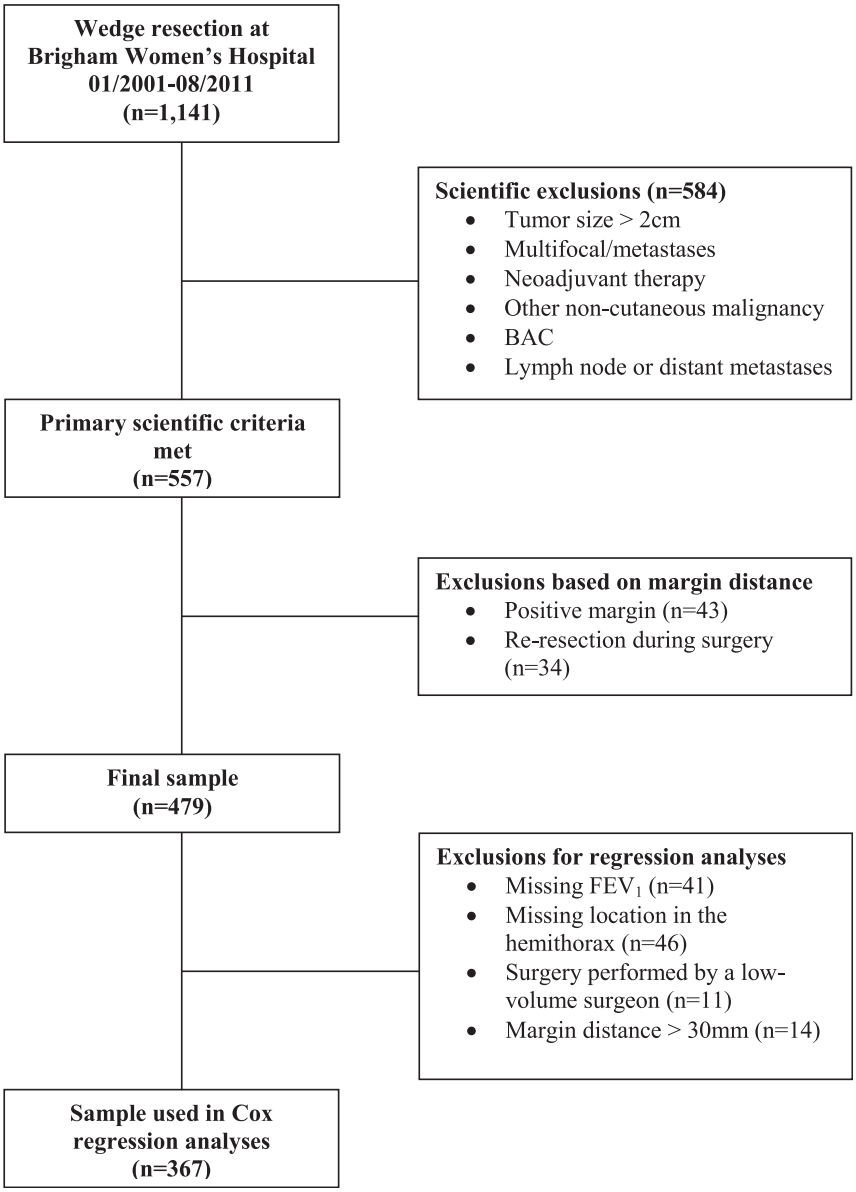

FIGURE 1. Consolidated Standards of Reporting Trials-style diagram illustrating the selection of patients included in the data analysis. *NSCLC*, Non–small cell lung cancer.

RESULTS

Of 557 consecutive patients, 479 met our primary scientific inclusion and exclusion criteria (Figure 1). The demographic, clinical, and pathologic information for these patients are listed in Table 1. Although not included in Table 1, 41 patients (8.6%) experienced ≥1 major complication; only 1 patient (0.2%) died perioperatively.

Kaplan-Meier Analyses

Figure 2 shows the Kaplan-Meier plots for local recurrence and local recurrence-free survival during the 3 years of postoperative follow-up, stratified by margin distance. The observed overall 1-year local recurrence rate, adjusted for censoring, was 5.7% (95% confidence interval [CI], 3.1-8.1). The observed overall 2- and 3-year local recurrence rate was 11.0% (95% CI, 7.4-14.5) and 16.4% (95% CI, 11.8-20.9), respectively.

Adjusted Models

Of the 479 patients in our sample, 367 had complete data and were used as the basis for the adjusted analyses. Of the 112 patients not included in the adjusted analyses, 41 had missing data on the forced expiratory volume in 1 second (Table 1), 46 had missing chest computed tomography

TABLE 1. Demographic, clinical, and surgical characteristics

Characteristic	n (%)
Total	479
Gender	
Female	307 (64.1)
Male	1172 (35.9)
Age (y)	
≤50	15 (3.1)
51-60	80 (16.7)
61-70	172 (35.9)
71-80	164 (34.2)
>80	48 (10.0)
FEV_1%	
≤50	66 (13.8)
51-100	279 (58.2)
>100	93 (19.4)
Missing	41 (8.6)
Tumor location	
LLL	56 (11.7)
LUL	141 (29.4)
RLL	86 (18.0)
RML	26 (5.4)
RUL	170 (35.5)
Tumor size (mm)	
1-5	14 (2.9)
6-10	104 (21.7)
11-15	226 (47.2)
15-20	135 (28.3)
Margin distance (mm)	
1-5	169 (35.3)
6-10	123 (25.7)
11-20	138 (28.8)
>20	49 (10.2)
Histologic type	
Adenocarcinoma	367 (76.6)
Squamous cell	91 (19.0)
Other NSCLC*	21 (4.4)
Surgery type	
Open	202 (42.4)
VATS	274 (57.6)
Lymph nodes sampled	
No	324 (67.6)
Yes	155 (32.4)

FEV_1%, Percentage of forced expiratory volume in 1 second; *LLL*, left lower lobe; *LUL*, left upper lobe; *RLL*, right lower lobe; *RML*, right mid-lobe; *RUL*, right upper lobe; *NSCLC*, non–small cell lung cancer; *VATS*, video-assisted thoracic surgery. *Cases in which the pathologist was sure the tumor was not small cell but could not differentiate between adenocarcinoma and squamous cell cancer.

information, 11 had undergone surgery by 1 of 3 low-volume surgeons, and 14 had a margin distance > 30 mm (Figure 1; see also, the "Statistical Analysis" section). A detailed graphic representation of the spline-based nonlinear trend in the smooth hazard ratio (HR) association between the margin distance and the local recurrence risk, along with the pointwise 95% CIs, is presented in Figure 3. Overall, an increased margin distance was significantly associated with a lower risk of local recurrence ($P = .033$; Figure 3, *top*), with evidence of diminished additional benefit beyond a margin distance of approximately 15 mm. Specifically, beyond 15 mm, the downward trend flattened out, indicating diminished benefits of increasing the margin distance. In contrast, beyond a margin distance of 20 mm, the trend appeared to increase, although, because the pointwise 95% CI was so wide (owing to the small number of observed events among the patients with large margin distances), this should be interpreted with caution.

Numeric estimates of the HRs, taken from Figure 3, comparing the risk of local recurrence among patients with a 5-mm margin distance and patients with varying margin distances are listed in Table 2. After adjustment for potential confounding (Table 2, left), the patients with a margin distance of 2 mm were estimated to have a 54% greater risk (HR, 1.54; 95% CI, 1.11-2.14) of local recurrence than patients with a margin distance of 5 mm. Among patients with a 10-mm margin distance, the local recurrence risk was estimated to be 45% lower than that in patients with a 5-mm margin distance (HR, 0.55; 95% CI, 0.35-0.86). As the margin distance increased by another 5 mm, additional benefits were found, although they were diminished. The estimated risk of recurrence among patients with a 15-mm margin distance was 59% lower than the risk among patients with a 5-mm margin distance (HR, 0.41; 95% CI, 0.21-0.81).

Finally, Table 2, *right*, and Figure 3, *bottom*, provide results from the adjusted models of the association between the margin distance and local recurrence-free survival. The results were consistent with those for local recurrence, in that an increasing margin distance conferred a lower risk of local recurrence, with no evidence of additional benefit beyond 15 mm.

DISCUSSION

In the present study, we found that in wedge resection for small (≤2 cm) NSCLC, increasing the resection margin distance significantly decreased the risk of local recurrence. The patients who underwent pulmonary wedge excision for small tumors (≤2 cm) with a 15-mm distance had a 113% lower risk of local recurrence than patients with a margin distance of 2 mm. Our findings were consistent with our hypothesis. These results indicate that such a finding is a significant prognostic factor in wedge resection, a surgical option for small NSCLC.[15,21] The accurate diagnosis of the wedge resection margins status, the margin distance, and efficacy to prevent local recurrence are matters of great concern. It has generally been accepted that limited lung resection is safe and effective in a selected group of patients. However, great concern exists regarding local recurrences. In the published data, the local recurrence rate for wedge resection has varied from 2.7% to 30.0% for NSCLC stage I.[2-7] What is unknown is the safe limit of a wedge resection margin

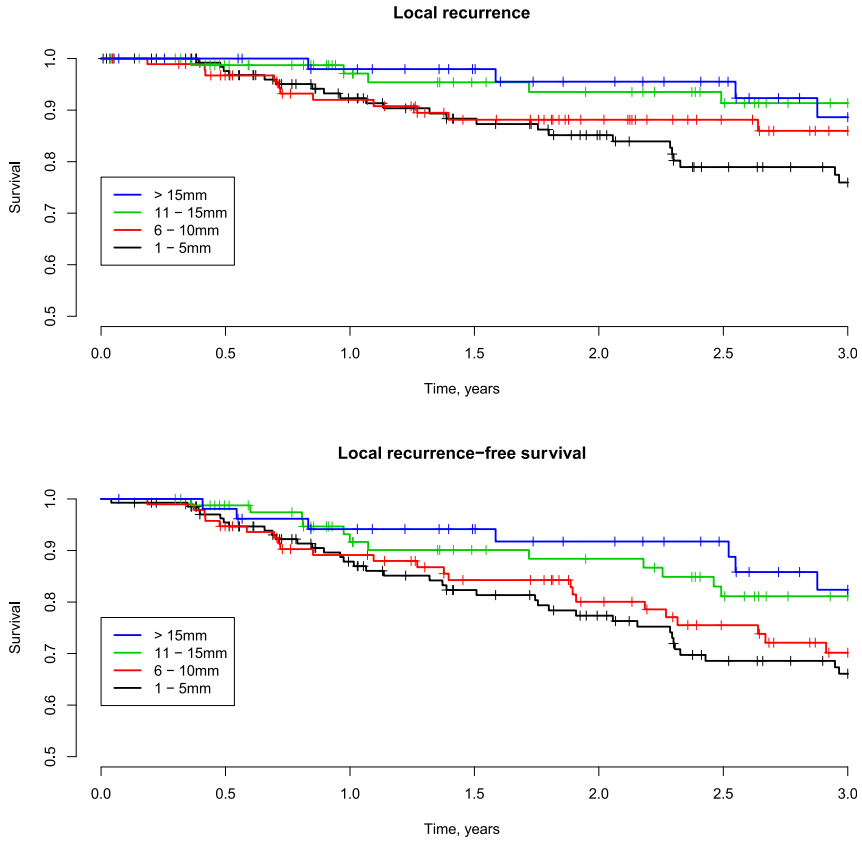

FIGURE 2. Kaplan-Meier plots for local recurrence and local recurrence-free survival during 3 years of postoperative follow-up, stratified by margin length.

distance for a small size lung cancer and how the technique of wedge resection affects the extent of this margin and the ability to perform facile, prompt, and accurate pathologic assessments. Furthermore, in the published data, no clear guidelines are available regarding the margin distance for small tumors.

The treatment of choice for early-stage, node-negative NSCLC has been surgical resection, preferably with an anatomic lobar procedure. In cases in which lobar resection is not possible because of poor lung function or other major comorbidity, a segmentectomy or wedge resection can be accomplished.[22] With a limited resection for NSCLC, the risk of margin relapse can be high. Complete surgical resection with a negative margin provides the best chance of cure. A more recent, albeit, single-institution, retrospective review, found no difference in locoregional recurrence or disease-free survival between the 2 resection strategies when the tumor was <2 cm.[23] Postoperative radiotherapy is indicated in the setting of a close or positive margin; however, in the absence of these criteria, the postoperative radiotherapy meta-analysis indicated a fairly clear potential for harm in patients with early-stage NSCLC.[24] The risk of local recurrence after segmentectomy is lower than that after wedge resection, because with the former, a greater volume of tissue is removed and has a lower potential of leaving residual tumor cells at the surgical margin, which could lead to a lower risk of local recurrence. In general, the larger the margin, the better. El-Sherif and colleagues[25] postulated that a large proportion of local recurrence will be related to an inadequate resection margin and reported that the margin is an important consideration in surgical resection for NSCLC. Wedge resection has frequently been associated with a margin <1 cm and a high risk of local recurrence. Sawabata and colleagues,[26] in a multicenter prospective study, suggested that when the margin distance was greater than the maximum tumor diameter, the chances for margin relapse were low. Sawabata and colleagues,[27] in another study, suggested that pulmonary wedge resection for peripheral tumors should result in negative malignant margins, which could be obtained from a sufficient tumor margin ratio of ≥1. Our results correlate with those from El-Sherif and colleagues[25] that a margin distance of >1 cm is associated with a lower risk of local recurrence. Additionally, we found that as the margin distance increased, the risk of local recurrence decreased, which correlated with the findings from Sawabata and colleagues.[26,27]

Our study had a number of important strengths arising from the rigorous and detailed data collection of a broad

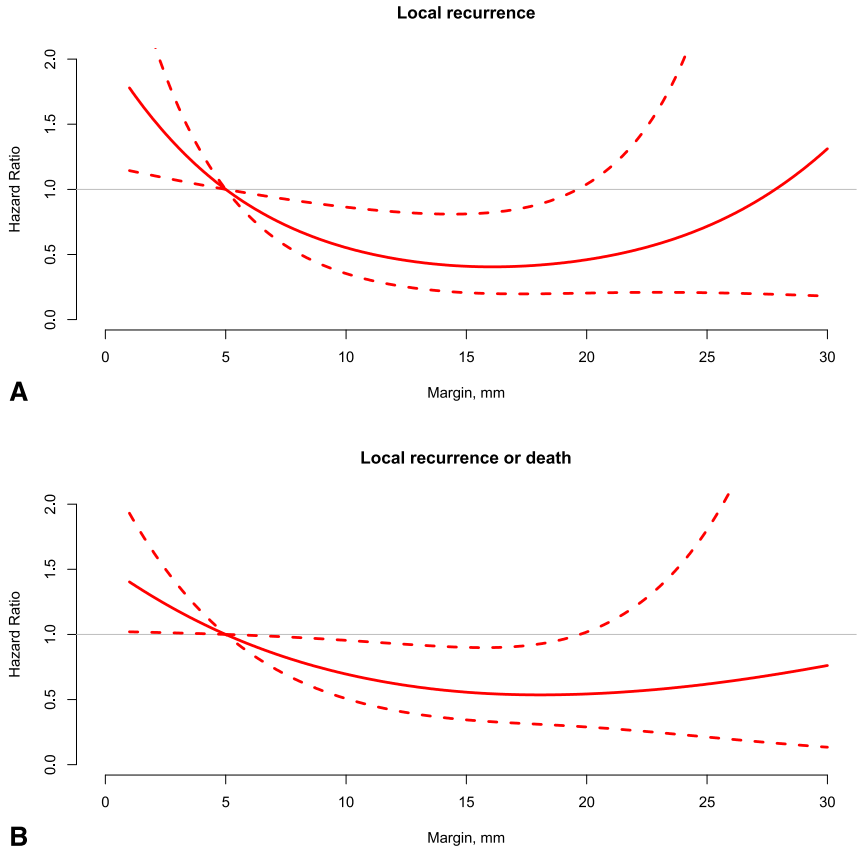

FIGURE 3. Adjusted hazard ratios from Cox regression model for the association between margin length and risk of (A) local recurrence and (B) local recurrence or death. The *solid line* represents the ratio of the hazard for the given outcome for the corresponding margin distance to the hazard for the outcome for a referent margin distance of 5 mm, holding adjustment covariates constant. *Dashed lines* represent pointwise 95% confidence intervals.

range of factors, including comprehensive long-term follow-up, for a large cohort of patients with early-stage NSCLC. Methodologically, the control for a broad range of potential confounders and the adjustment for missing data, using multiple imputations, mitigated bias and, we believe, strengthened our results and conclusions. Several limitations of our study also merit discussion. First, this was a retrospective analysis of the results for surgery performed by a variety of surgeons with variable technique used, including a mixture of VATS and open surgery and variable pathologic nodal staging in the form of preoperative mediastinoscopy or intraoperative lymph node sampling. In many cases, the resection was performed for both diagnostic and therapeutic intervention. Second, just as with all observational studies, our results could have suffered from unobserved residual confounding. Nevertheless, our analyses were comprehensive in that we used our extensive administrative databases to perform a rich adjustment for confounding, including the adjustment for patient- and surgeon-specific effects. Given the strength of the observed association between the margin distance and the risk of local recurrence, we do not believe that sufficient residual confounding were present to reverse our conclusions. Third, we did not investigate the difference between the VATS and open approaches in regard to the margin distance and/or local recurrence. The final limitation was the potential for selection bias that results from analyzing the data collected after a rigorous pathologic review with the study inclusion criteria in which patients with positive margins, repeat

TABLE 2. Adjusted hazard ratios from Cox models of association between margin distance and local recurrence risk and risk of local recurrence or death

	HR* (95% CI)	
Margin distance (mm)	Local recurrence†	Local recurrence or death‡
2	1.54 (1.11-2.14)	1.29 (1.02-1.64)
5	Referent	Referent
10	0.55 (0.35-0.86)	0.70 (0.51-0.95)
15	0.41 (0.21-0.81)	0.56 (0.34-0.90)
20	0.46 (0.20-1.04)	0.54 (0.29-1.02)

HR, Hazard ratio; *CI*, confidence interval. *Adjusted for chronic obstructive pulmonary disease, forced expiratory volume in 1 second, smoking, diabetes, tumor size, tumor lobe location, location within the hemithorax, surgeon, open versus video-assisted thoracic surgery, and whether lymph nodes were sampled. †$P = .033$, omnibus Wald-based P value for overall association. ‡$P = .058$, omnibus Wald-based P value for overall association.

resection, multifocal disease, induction therapy, distant metastases, large cell cancer, and adenosquamous cancer were all excluded. Although this limited the generalizability of these results, it has enhanced the validity by reducing the heterogeneity in the study population.

CONCLUSIONS

The focus of the present study was on the distance from the primary tumor to the closest margin in wedge resection. Crucially, we could not report on the differential effect that the margin distance might have for tumors of different sizes because we did not have enough power to detect the effect. However, we did not restrict the results to a specific postulated margin-to-tumor size ratio but, rather, quantified the effect of the margin distance, in general, on the risk of recurrence. We found that an increasing margin distance yielded decreased local recurrence rates for a margin distance of $\leq$15 mm, regardless of the tumor size when the tumors were $\leq$2 cm. Thus, we can decrease the risk of local recurrence during wedge resection of small NSCLC if we can achieve an adequate ($\leq$15 mm) margin distance. Although we believe our results speak to the potential benefits associated with a resection margin of $\leq$15 mm, they cannot specify the ideal margin distance for small tumor size. Our results suggest that an important avenue for future work will be to gather more data from patients from other institutes and to further determine the optimal margin distance for small tumors. This association should be investigated in future studies that explicitly consider the relationship between the margin distance and local recurrence.

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Discussion

Dr Joshua R. Sonett *(New York, NY).* Thank you for your excellent presentation and for the rather significant effort and energy to collect, analyze, and study this large cohort of patients. Having pathologic data with long-term follow-up of patients who underwent wedge resection for this is important, because our treatment options for early-stage lung cancer are continually debated, not only by surgeons. As our less invasive options for treating lung cancer are introduced, we need to ensure we do not diminish our cure rates at the heels of ease, expediency, and minimalism.

Your results build on the results from El-Sherif in that $\geq$1-cm margins are important, and you conclude that >1.5 cm might be the point of diminishing return. I, similar to probably half this audience, do not understand spline statistics, but I had a very competent statistician look at it for me. They thought your data were done

very well in terms of the statistics, although the >1.5-cm population was a little bit low in the number of patients you had, those with margins >1.5 cm.

I have several questions, more about the philosophy for wedge resection and how you responded to the results. By the age of your patients when I read your report, the pulmonary function, which was pretty reasonable in a large population, and the tumor location, which was predominantly right upper lobe, left upper lobe, and middle lobe, it appears to me that these patients would have easily tolerated much larger resections. So, how do you presently decide, short of the currently randomized Cancer and Leukemia Group B (CALGB) trial, in which patients with <2-cm tumors receive a wedge resection?

Dr Mohiuddin. Thank you very much.

We presently decide according to patient age, tumor size, tumor location, percentage of forced expiratory volume in 1 second (FEV_1), distant metastasis, and patient comorbidities. Those are our criteria.

Dr Sonett. In your data, 60% of your patients had <1-cm margins and 67% had no lymph nodes sampled. Again, this was by very competent thoracic surgeons. So, what is your current practice for lymph node sampling in these patients? Do you think it is relevant in this cohort to sample the lymph nodes, and how can you advocate for surgical resection instead of, say, stereotactic body radiotherapy (SBRT) if we are not going to sample the nodes and achieve >1-cm margins?

Dr Mohiuddin. Our current practice is to take the lymph nodes, and we strongly think it is relevant to sample the lymph nodes. How we advocate surgical resection over SBRT, we believe surgical resection has more advantages and benefits, such as sampling the lymph nodes. With SBRT, we cannot sample the lymph nodes. No long-term data are yet available on the effect of radiation on the lungs.

Dr Sonett. Much of the published data, and I would say including the last report and Dr Faber's discussion, have shown improved results with segmental resection. Now, it is not clear whether the benefit of segmental resection results from actually removing the anatomic segment and lymphatics versus just attaining a good, safe margin. Given your data presented, do you measure the distance of your margin in the operating room and consider performing either a larger resection or segmentectomy if the margin is not adequate as you had defined?

Dr Mohiuddin. We ensure that the surgical resection margin is negative in the operating room, and we do measure the distance, and we do consider performing a larger resection or a segmentectomy or lobectomy if the patient has an adequate percentage of FEV_1.

Dr Sonett. So, as opposed to the historical data, now that you have shown these data, if you were to perform a wedge resection right now with a <1-cm margin, what would be your course of events?

Dr Mohiuddin. Sorry, can you repeat the question?

Dr Sonett. If you were to perform a wedge tomorrow for a lesion and, pathologically, on frozen section analysis, the margin was <1 cm, what would be your answer in the operating room?

Dr Mohiuddin. We have 2 options. It all depends on the FEV_1 for determining whether we can go back and resect at the same time.

Dr Scott J. Swanson *(Boston, Mass).* I can maybe answer that. Kamran is a fellow, and I think he is not going to really make that decision. I think our philosophy based on the learning from this database would be to perform a more aggressive resection, whether segmentectomy or lobectomy, with nodal dissection, and I think this has been pretty informative for us. The points you brought up are pretty revealing. So, we are taking this forward to do a more aggressive resection. But, is 15 mm the right number? I do not think we know that. However, if we believe that we are not at least over the tumor diameter ratio, I think most of us would do a larger resection.

Dr Sonett. Well, if you consider Dr Altorki's results, you consider your results, and you consider the prospective trial on radiation seeds that was presented at the Southern, those 3 trials, all by really good, dedicated thoracic surgeons, all had miserable margins. So it would be hard for us to advocate for surgery when we are achieving crappy margins against SBRT. I think we as a group have to either do better segmental resections or perform lobectomies, but we cannot perform a crappy wedge resection with small margins just to try to keep pace with SBRT, because we will not be doing anybody a favor, including ourselves and our patients.

Dr Harvey Pass *(New York, NY).* I would like to follow-up on what Josh said and also to ask the Brigham group. The Brigham group is known, not only for terrific thoracic surgery, but also for terrific radiology imaging. My problem as an old surgeon is where is the lesion? There are easy wedges, and there are deep wedges that are not very easy. You have a study that considered the margins and you also have imaging studies for all these patients. Is not this the perfect study to also correlate the image findings preoperatively of where the lesion is and whether you could actually document beforehand whether you could perform an adequate resection? The deeper lesions will be the ones that, yes, you find you cannot resect and achieve a 1-cm margin, but you cannot do another resection; you must use segmentectomy. As I get older, I like to plan and know what I will have to do beforehand. I think that your imaging data at the cross-sectional diameter, where this is, and the distance from the hilum as a uniform point, or from the visceral pleura, could be very enlightening regarding whether you approach a case as a wedge or segmentectomy.

Dr Mohiuddin. I agree with you. Thanks.

Dr Daniel L. Miller *(Atlanta, Ga).* We are killing ourselves here. I mean from the point of view of lymph node evaluation, we suck: 67%, nothing in this. The previous study, 44%. We are giving these cases away. That is not acceptable. I am sorry; it is not. We must do a better job at that or we are going to lose this business. SBRT results in a 5-mm margin. We are coming down to their level. We must do better than that. Now, I think it is embarrassing that we have these studies that show that. If the values are not there, we take that out of our analysis. But we must do a better job or we are going to lose this.

My 1 question I have is, did you consider the biohistologic features of the tumor? Was there a difference in the lymphatic invasion, neuroinvasion, and vascular invasion and was there a difference in visceral pleural invasion? I think that considers recurrence and so forth, but we must do better.

Dr Mohiuddin. I agree with you. We did include lymphovascular invasion and pleural invasion, and we adjusted for that in our analysis.

Dr Miller. But, did you have to resect a larger volume for those patients?

Dr Mohiuddin. I agree. We need more patient data. Right now, we cannot comment on that.

Dr Michael I. Ebright *(Boston, Mass).* I am going to follow-up on Dr Pass's point. Previous studies have suggested that tumors within the central one third of the lung, the central tumors, will have up to a 50% rate of lymph node metastases. As one's tumors become more central, it becomes more technically difficult or perhaps not even feasible to perform a sublobar resection with a wedge, and we might need to default to segmentectomy, even if that would not be our initial preferred approach. I would assume that most of the tumors in your studies were peripheral, but I am wondering whether you have any data to suggest whether you are treating the peripheral tumors differently than the central tumors.

Dr Mohiuddin. I agree. In our data we have had more peripheral tumors. That was determined by the radiologic evaluation. The radiologist evaluated within the hemithorax the location, and from our data, you are right.

Dr David C. Rice *(Houston, Tex).* How did you measure your margin? The Sawabata report measured it from the cut edge of the staple line and did smears on that; thus, that little 5-mm bit was included in their margin.

I also want to make a comment. We are shooting ourselves in the foot if we continue to call this local recurrence, because the radiation oncologists, like it or not, are not going to play by our rules. They have termed recurrence at the tumor site "local recurrence." This is really locoregional recurrence if you are including the lymph nodes. I would beg you to include that in your report, at least make it clear, so that an internist will at least be able to compare apples with apples.

Dr Mohiuddin. The resection margin was evaluated by the pathologist, and it was the distance from the tumor to the resection margin, not including the staple line.

I am sorry, can you repeat the second question?

Dr Rice. That is okay. It was just a comment.

Dr Gunda Leschber *(Berlin, Germany).* I would like to come back to this margin and the measurement of the margin. You said the pathologist measured it, but was it with an inflated lung or was it in a formalin-fixed lung? When was it measured? We know that the margin will shrink if we put it in formalin.

Dr Mohiuddin. It was in an inflated lung.

Dr Thomas Rice *(Cleveland, Ohio).* I am curious about your need to create a new term. "Margin length." I expected you to measure the length of the margin. Why did you not call it what we all call it—the distance from the primary tumor to the closest margin. Be precise. Be accurate. You are a surgeon. I would change your term "margin length."

Dr Mohiuddin. Thank you.