ORIGINAL ARTICLE

HOT TOPIC IN THORACIC SURGERY: CAN SUBLOBAR ANATOMICAL RESECTIONS BE NON-INFERIOR TO LOBECTOMIES FOR SMALL, PERIPHERAL NON-SMALL-CELL LUNG CANCER (NSCLC)? – 9-YEAR EXPERIENCE IN A SINGLE CENTER

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Abstract

Background: *Technological advances and widely spread screening programs enabled the discovery of ever smaller lesions. As such, in the last years, the tendency has shifted towards lung-sparing procedures. The role of limited surgical excision for small peripheral nodules is currently a topic of heated debate.*

Aim: In our work, we try to answer whether the segmentectomy could adequately treat the peripheral NSCLC staged as Tis/1a-bN0M0.

Materials and methods: *Our analysis is a single-center retrospective study based on the 8-year experience of our department. We identified 73 lobectomy patients and 16 segmentectomy patients. However, the lack of similarity between the two groups made it inadequate to draw satisfactory conclusions, therefore we reduced the lobectomy group and selected only those patients who could be paired with corresponding patients in the segmentectomy group. The established parameters of similarity were age (weighted at 15%), size of the lesion (50%), and follow-up (35%), and the input values were normalized. With this method, we could compare two samples of the most similar patients. 32 cases were included in the final analysis. The inclusion criteria were: NSCLC histology, size up to 2 cm, no visceral pleura invasion, N0 disease, and performed segmentectomy or lobectomy between Jan/2015 and Dec/2022. We analyzed the disease-free time and relapse rate.*

Results: *Data refers to a total of 32 patients distributed in two groups: group A with 16 segmentectomies (S6, S1+2 or S1) and group B with 16 lobectomies. The mean time of follow-up was 30 months (1-85) for group A and 32 months (1-91) for group B. The disease-free survival was 27 months for group A and 31 months for group B. The relapse rate was 19% for segmentectomies and 12.5% for lobectomies.*

Conclusions: *In conclusion, while this article presents our center's experience with segmentectomy, we believe further studies with larger sample sizes are needed to establish its non-inferiority. Nevertheless, our experience indicates that segmentectomy offers significant benefits, including lung preservation and the potential for future resections.*

Keywords: *segmentectomy, lung-sparing surgery, T1N0M0, peripheral lung nodule*

INTRODUCTION

Technological advances and widespread screening programs have enabled the detection of increasingly smaller lesions in the lungs. As a result, there has been a shift towards lung-sparing procedures in recent years. There is currently a heated discussion surrounding the limitation of surgical excision for the treatment of small peripheral Non-small-cell lung Cancer (NSCLC) nodules in patients with adequate cardio-pulmonary function. With the release of recent clinical trial results, it has become evident that anatomical sublobar resections should be considered the standard of care for highly selected patients with T1a-T1b N0M0 staging. This treatment approach can provide satisfactory oncological outcomes.

OBJECTIVE

We conducted a retrospective study at a single center based on our department´s 8-year experience with patients who underwent either lobectomy or segmentectomy for

peripheral NSCLC staged as T1a-bN0M0. The primary endpoints of the study were the disease-free survival time, which was defined as the period between surgery and: the last follow-up, the identification of relapse, or death from any cause, and the relapse rate. The secondary endpoint was overall mortality regardless of the cause.

MATERIAL AND METHODS

We identified 73 lobectomy patients and 16 segmentectomy patients. We were aware of a substantial difference in sample sizes between the two procedures, as we were comparing well-established lobectomies with sublobar resections, which gained trust only recently. This disproportion would be evidently a factor bringing biases to the equation, especially in terms of the number of analyzed cases, the shorter follow-up time and consequently, the disease-free survival for the segmentectomy group.

Since the lack of similarity between the two groups made it inadequate to draw satisfactory conclusions, we reduced the lobectomy group. We selected only those patients who could be paired with corresponding patients in the segmentectomy group. To achieve this, we used a weighted Euclidean distance approach after applying min-max normalization to the input values, scaling them to a range of [0,1]. The established similarity parameters were age (weighted at 15%), lesion size (50%), and follow-up duration (35%). This method allowed us to select the most comparable patients from both groups, ensuring a more balanced comparison.

We identified 32 patients from our database with peripheral NSCLC staged as Tis/T1a-bN0M0 (Tis corresponded to one case) and resected between January 2015 and December 2022. These cases were distributed into group A, which consisted of 16 segmentectomies (S6, S1+2 or S1), and group B, which consisted of 16 lobectomies (including four lobes, without the middle lobe).

The inclusion criteria for the study were as follows: NSCLC histology, tumor size not exceeding 2 cm, no invasion of the visceral pleura, performance of either segmentectomy or lobectomy, confirmed N0 disease, and R0 surgical excision performed between January 2015 and December 2022.

We analyzed the disease-free time and relapse rate as primary outcomes. However, due to the small size of our patient cohort, statistical significance was not achieved. Therefore, we decided to analyze the results using descriptive analysis as a tool.

RESULTS

Our study included a total of 32 patients, divided into two groups: group A with 16 segmentectomies (S6, S1+2 or S1) and group B with 16 lobectomies. The patients' characteristics for each group are presented in Table I for group A and Table II for group B. The average follow-up time was 30 months (ranging from 1 to 85 months) for group A and 32 months (ranging from 1 to 91 months) for group B. The disease-free survival was 27 months for group A and 31 months for group B. The relapse rate was 19% for segmentectomies and 12.5% for lobectomies. The overall mortality rate was similar in both groups, with 6% in group A and 12.5% in group B.

We also assessed the surgical margins in the 5 cases that experienced a relapse (Table III). In group A, 66% (2 cases) of the patients had a short surgical margin, defined as a distance less than 1 cm between the suture and the nodule: the one with 0.6 cm and the other with 0.1 cm. In group B, only one patient had an insufficient margin of 0.5 cm (50% of the cases). The characteristics of the cases with recurrence are presented in Table IV.

DISCUSSION

The first pneumectomy for the surgical treatment of lung cancer was performed in 1933[1], and for a long time, it was strongly believed that only the radical removal of an affected organ in its entirety could be an appropriate treatment for lung carcinoma[2]. This paradigm changed only after Shimkin et al reported in 1982 that lobectomy and pneumectomy patients operated for limited lung cancer had equivalent survival rates[3]. Sublobar resections were even more challenging to be recognized as an adequate treatment. Although commonly accepted for the management of benign diseases like bronchiectasis it was never believed to ensure a desired oncologic result in malignant diseases. In these cases, sublobar resection was treated as an option for patients who were not candidates for major resections due to limited cardiopulmonary reserve.

The first and, until recently, the only randomized controlled trial (LCSG821) reported by the Lung Cancer Study Group in 1995 has compared lobectomy with sublobar resection for patients with peripheral T1 N0 NSCLC. However, it failed to show any advantage in perioperative morbidity, mortality, or late postoperative pulmonary function. Additionally, it detected a 75% increase in the recurrence rate. The main weakness of the study was including both segmentectomies and wedge resections in the limited resection group. Therefore, the study erroneously recommended lobectomy as the gold standard based on its lower death rate and locoregional recurrence ratio compared to limited resection[4].

In the following years, technological advances and widely spread screening programs have enabled the discovery of ever smaller and more initial lesions. As such, in the last years, the tendency has shifted towards lung-sparing procedures. The work by Okada et al.[5] published in 2001 in The Annals of Thoracic Surgery, concluded that extended segmentectomy should be considered as an alternative for patients with cT1N0M0 NSCLC of 2 cm or smaller. In the following years, more studies emerged with similar results favoring segmentectomies. In 2018 Landreneau et al.[6] enthusiastically stated that the segmentectomy is the future of cT1N0M0 NSCLC treatment. For these small peripheral lesions, anatomic segmentectomy appears to offer comparable local control and the opportunity for

Table 1 **Patients caracteristics - group A (segmentectomy)**

	n=16 (100%)
Gender	
Women	7 (44%)
Men	9 (56%)
Mean age of surgery	67.3 years old (range 48-82)
Pleural invasion	
Yes	0 (0%)
No	16 (100%)
Segment removed	
S6	13 (81%)
S1	1 (6%)
S1+2	2 (13%)
Pathologic results	
ADC papilar (80%) e acinar (20%)	9 (56%)
ADC acinar	3 (19%)
ADC papillar	1 (6%)
ADC MI	1 (6%)
Lepidic + acinar	1 (6%)
ADC invasive	1 (6%)
Mean size (cm)	1.5 (range 1.1-2.0 days)
Pathologic stage	
pT1bN0 M0– IA2	15 (94%)
pT1bNxM0	1 (6%)
Mean follow-up	30 months (1-85 months)
Recurrence-free survival time	27 months (1-85 months)
Recurrence	3 (19%)
Death	1 (6%)

Table 2 **Patients caracteristics - group B (lobectomy)**

	n = 73 (100 %)
Gender	
Women	28 (38.4%)
Men	45 (61.6%)
Mean age of surgery	64.6 years old (range 33-80)
Visceral pleural invasion	
Yes	0 (0%)
No	73 (100%)
Lobe removed	
Right Superior Lobectomy	32 (44%)
Left Superior Lobectomy	21 (29%)
Right Inferior Lobectomy	14 (19%)
Left Inferior Lobectomy	4 (5%)
Middle Lobectomy	2 (3%)
Pathologic results	
ADC predominatly acinar	33 (45%)
ADC predominatly lepidic	1 (1.5%)
ADC predominatly solid	6 (8%)
ADC in situ	1 (1.5%)
ADC pavement cell	5 (7%)
ADC not caracterised otherwise	27 (37%)
The mean size (cm)	1.5 (range 0.7-2.0 cm)
Patologic stage	
pT1aN0 – IA	11 (15.0%)
pT1bN0 – IA	61 (83.6%)
pTisN0 - 0	1 (1.4%)
The mean follow-up	37 months (1-91 months)
Recurrence-free survival time	37 months (1-91 months)
Recurrence	2 (3%)
Death	4 (5%)

Table 3 **Surgical margin in relapse cases**

Resection tipe	Segmentectomy n=3	Lobectomy n=2
Relapse rate	3 (19%)	2 (3%)
Short margin	2 (66 %)	1 (50%)

Table 4 **Patients characteristics in relapse cases**

Ressection tipe	Segmentectomy n=3	Lobectomy n=2
Surgical margin (cm)	0.6/2/0.1	0.5/ >1
Nodule size (cm)	1.5/1.5/1.2	1.5/1
Relapse	local	local
Segment/lobe	S6	Left Superior Lobectomy
Histopathology	Acinar/acinar/papillar	Pavimentocellular/acinar

prolonged disease-free and overall survival that is not statistically different when compared with lobectomy.

Last year, however, brought probably the most important and game-changing results. A multicenter, noninferiority, phase 3 trial (CALGB 140503) proved that sublobar resection was not inferior to lobectomy concerning disease-free survival. The most recent and exciting research (JCOG0802/WJOG4607L) - a multicenter, open-label, phase 3, randomized, controlled, non-inferiority trial - also confirmed that segmentectomy should be the standard surgical procedure, rather than lobectomy, for patients with small-sized (≤2 cm), peripheral NSCLC with a consolidation-to-tumour ratio >0,5, even though the expected evidence of superiority in postoperative respiratory function in the segmentectomy group was not found[8].

Based on the most recent results, our conviction strongly favored sublobar resections in strictly selected patients. Our results support this view, showing very similar outcomes: a relapse rate of 19% in the segmentectomy group compared to 12.5% in the lobectomy group.

We considered further analyzing the surgical margin as the probable cause of the slight difference in relapse rates. To the best of the authors' knowledge, this parameter was not included in the analyses of the CALGB 140503[7] study whereas in the JCOG0802/WJOG4607L[8] research, the inclusion criteria encompassed an adequate surgical margin.

All of our cases of recurrence were classified as R0, but some of them had a short surgical margin, defined as a distance between the suture and the nodule less than 1 cm. In group A, this fraction was higher than in group B: 66% (2 cases, 0.6 cm and 0.1 cm) in group A compared to only 50% of the relapsed patients in group B (1 case, margin of 0.5 cm). If we removed these outliers from the comparison, we would be able to compare only the extent of resection as a determining factor. Hence, it turns out that we have only 1 relapsed case in each group. We should emphasize the importance of intraoperatory margin evaluation, which failed in our center. After analysis, it should be performed to ensure the best oncological results.

Wedge resections were permitted in the CALGB 140503 and were grouped together with anatomical resections, which was explained as a more "real life" setting, as wedge resections constitute the majority of surgeries performed in Europe and the United States of America[7]. The JCOG0802/WJOG4607L[8] research included only anatomical resections, which is more consistent with our trial. Building on these recent studies, we strongly believe that segmentectomy with an adequate surgical margin and proper lymph node assessment is the only alternative to lobectomy in oncologic surgeries with curative intent.

CONCLUSIONS

The results of our review need to be interpreted with a certain degree of caution. Our study is a retrospective analysis and our cohort is small, making it challenging to draw significant conclusions and impossible to obtain adequate statistical data. Additionally, we are comparing well-established lobectomies with sublobar resections, which have gained trust only recently. As a result, the two groups vary in follow-up time which affects the duration of the disease-free survival.

Since we observe a much higher recurrence rate in cases with a short surgical margin, it is crucial to prioritize a satisfactory clean resection area. Even in early, small, and peripheral lesions, we should ensure that the nodules are resected with an adequate perimeter. Without this factor, we cannot guarantee curative, oncologic outcomes, and all the benefits of lung tissue-sparing surgery diminish, leading to an elevated risk of relapse.

We would like to emphasize that this article is primarily focused on describing our clinical experience with segmentectomy at our center, rather than presenting definitive conclusions on its non-inferiority. While we acknowledge that a larger sample size and more robust statistical analysis would be required to draw firm conclusions, our experience suggests that segmentectomy offers several notable advantages. Specifically, it is a less invasive, lung-sparing procedure that helps preserve respiratory function, which is particularly important for patients with limited lung capacity. Additionally, segmentectomy leaves more viable lung tissue, providing a potential benefit for future resections in cases of second primary lung tumors.

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