ORIGINAL ARTICLE

SEGMENTECTOMIES: 5-YEAR EXPERIENCE OF A CENTER

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Abstract

Introduction: *Segmental anatomical resections have been a subject of debate in recent years. There is increasing evidence that these procedures may offer some advantages in the treatment of early-stage lung cancer, with overall survival (OS) and disease-free survival (DFS) similar to those seen in lobar anatomical resections.*

Materials and Methods: *We conducted a retrospective analysis of patients who underwent segmentectomy at Santa Marta Hospital (HSM) between January 2018 and September 2022. Patients undergoing trauma-related segmentectomy or as a secondary procedure were excluded.*

Results: *37 segmentectomies were performed, of which 34 were included in this analysis. 29 (85.3%) were performed for malignancies, 5 (14.7%) for benign conditions. Of the malignancies, 24 (82.8%) were primary lung cancer (PLC): 18 (75%) adenocarcinomas (ADC), 2 (8.3%) squamous cell carcinomas (SCC), 4 (16.7%) typical carcinoids (TC); 5 (17.2%) were colorectal-origin metastases. Among the benign cases: 3 (60%) were aspergillomas.*

Mean age of PLC patients was 71 years (min=56;max=88), with 9 (37.5%) females and 15 (62.5%) males. In 11 (45.8%), FEV1 or DLCO was <60%. 18 (75%) were smokers. Lesions were mostly solid nodules (N=12;50%). Others included subsolid lesions (N=11;45%) and 1 (4.2%) cystic formation.

At surgery, only 3 (12.5%) patients had a pre-operative histological diagnosis (ADC=2; SCC=1). 21 (87.5%) were stage IA, 2 (8.33%) patients were stage IB and 1 (8.33%) patient was stage IIA.

Procedures were performed via VATS (N=17;70.8%), via thoracotomy (N=5;20.8%) and via RATS (N=2;8.3%). 23 (95.8%) were R0 resections.

Postoperatively: 19 (79.2%) were stage IA; 3 (12.5%) IB; ,1 (4.2%) IIB, and 1 (4.2%) IIIA. 3 (12.5%) had upstaging.

2 (8.3%) patients underwent adjuvant chemotherapy, 1 (4.2%) had completion lobectomy. 2 (8.3%) experienced recurrence. DFS was 100% at 3, 6, and 12 months, and at 3 and 5 years, was 88.9% and 66.7% respectively. OS was 100% at 3, 6, and 12 months and 95% at 3 and 5 years.

Median follow up time was 29 months (IQR: 18 – 44).

Conclusion: *This study reinforces the idea that segmental resections should be considered a viable option for patients with early-stage lung cancer. Although this analysis has some limitations, such as a limited number of preoperative histological diagnoses and postoperative upstaging, our results demonstrate promising OS and DFS, in accordance with recent literature.*

Keywords: *Segmentectomy; Primary Lung Cancer; Surgery*

INTRODUCTION

Thoracic surgery has developed massively in recent years. Not only did the incisions become smaller, but also the type of lung resections, aiming, at first, to spare lung parenchyma in patients with poor pulmonary function.[1,2]

Lobectomy has been considered the gold standard for treatment of early-stage non-small cell lung cancer (NSCLC). Results from 1995 defined the surgical approach in T1N0M0 NSCLC, concluding that patients who underwent sublobar resections had worse prognosis when compared to those who were submitted to lobectomies.[3]

With screening programs being implemented, an increasing number of early-stage lung cancers are detected, particularly subsolid and pure ground-glass-opacities (GGO) lesions.[4-6]

Over the years, several studies from different centers have reported good results after sublobar resection for pure

GGO, tumors that usually represent non-invasive or less invasive lepidic dominant adenocarcinomas (ADC).(4) Other studies have also shown benefits even in solid ADC tumors inferior to 2cm.[7]

Unfortunately, these studies show some flaws, regarding their methods, such as the type of sublobar resection (wedge resection or segmentectomy), and also regarding the results, for example in nodal upstaging.[8,9]

Because of such controversies, there is an urgent need for randomized studies. New developments have been made on segmentectomies for lung cancer, with some evidence showing non-inferiority disease-free-survival and overall survival when compared to lobectomies, for peripheric non-small cell lung tumors with size inferior to 2cm. [10,11]

Therefore, the role of segmentectomies in thoracic surgery is a current topic of most importance.

Our study goal was to perform a descriptive analysis of the patients submitted to segmentectomy for PLC and, as primary outcomes, we aimed to evaluate overall (OS) survival and disease-free survival (DFS).

MATERIALS AND METHODS

We conducted a retrospective analysis of patients who underwent segmentectomy at Santa Marta Hospital (HSM), between January 2018 and September 2022.

Patients undergoing trauma-related segmentectomy or as a secondary procedure were excluded from our sample.

We began by conducting a descriptive analysis of all 34 included patients.

Patient-related variables included: age, gender, smoking habits, pre-operative percentage of forced vital capacity at 1 second (FEV1) and diffusing capacity for lung carbon monoxide (DLCO) and comorbidities. Diagnosis and staging variables included: known pre-operative diagnosis, method of diagnosis, radiological findings, invasive mediastinal staging and used method. Procedure-related variables included: type of segmentectomy performed, number of segments removed and surgical approach. Immediate post-operative variables included: drainage time, length of stay (LOS) and 30 days complications. Surgical-specimen related variables included: tumor histology, pathological staging and resection margins; post-operative variables included: use of adjuvant therapy, need for re-intervention, date and site of disease relapse and last known survival.

Segmentectomy was considered when a sublobar resection of 1 or more segments where anatomically removed (dissection and independent section of, at least, artery and bronchus for the respective segment).

All patients were submitted to ipsilateral mediastinal lymph node dissection in the same operative time of segmentectomy.

All specimens removed where analyzed by our center's pathologists. Resection margins and pathological staging were defined according to 8th TNM classification.[12]

OS was a primary goal and was defined as the time interval between date of operation and date of patient's death or date of last appointment. DSF was defined as the period between surgery and evidence of disease relapse.

Categorical data were expressed as absolute value and percentage. Continuous variables were expressed as median and interquartile range (IQR) and, when statistically relevant, minimum and maximum. Survival outcomes were analyzed with the Kaplan Meyer method. Statistical analysis was performed using IBM SPSS® v28 software.

RESULTS

37 segmentectomies were performed, of which 34 were included in this analysis.

Considering these 34 patients: 21 (61.7%) were males. Median age was 68 years (IQR: 62 - 77).

29 segmentectomies (85.3%) were performed for malignancies and 5 (14.7%) for benign conditions. Of the malignancies, 24 (82.8%) were PLC: 18 (75%) adenocarcinomas (ADC), 2 (8.3%) squamous cell carcinomas (SCC), 4 (16.7%) typical carcinoids (TC); 5 (17.2%) were metastases from colorectal origin. Among the benign cases: 3 (60%) were aspergillomas, 1 (20%) was an emphysema bullae and 1 (20%) was a non-infectious inflammatory process. (Table 1.)

Regarding only PLC patients: Median age was 68 (IQR: 63-79) years. 15 (62.5%) were males. 18 (75%) patients were smokers, with a median pack-years of 50 (IQR: 36-83). In 11 (45.8%), FEV1 or DLCO was <60%. All patients presented different comorbidities such as: chronic obstructive pulmonary disease (COPD), hypertension, diabetes mellitus, dyslipidemia, obesity, asthma, other cancers (mainly prostatic, colorectal and breast), but none was prevalent. 12 lesions (50%) were solid nodules, 6 (25%) were part-solid lesions, 5 (20.8%) were pure GGO and 1 (4.2%) was a cystic lesion. (Table 2). Median lesion size was 17mm (IQR: 12 - 23). 21 (87.5%) did not have a pre-operative diagnosis and 3 (12.5%) patients had a pre-operative diagnosis, done by transthoracic needle biopsy; of these 3, 2 (66%) patients had histology compatible with adenocarcinoma and 1 (33%) with squamous cell carcinoma.

21 (87.5%) patients were clinical stage IA: 14 (58.3%) were cT1bN0M0 and 7 (29.2%) were cT1cN0M0. 2 (8.33%) patients were clinical stage IB: cT2aN0M0. 1 (4.2%) patient was clinical stage IIA (cT2bN0M0). (Table 2.)

17 (70.8%) procedures were performed by video-assisted thoracoscopy (VATS), 5 (20.8%) by thoracotomy and 2 (8.3%) by Robotic-Assisted Thoracic Surgery (RATS).

There were 9 (37.5%) segmentectomies performed on the right lung: 1 (11.1%) in apical segment of superior lobe, 1 (11.1%) in posterior segment of superior lobe, 3 (33.3%) in anterior segment of superior lobe and 4 (44.4%) in the apical segment of inferior lobe.

15 (62.5%) segmentectomies were performed on the left lung: 1 (6.7%) in apical segment of superior lobe, 4 (26.7%) in apical segment of inferior lobe, 2 (13.3%) in apico-posterior segment, 7 (46.7%) in the culmen, and 1 (6.7%) in the lingula. (Table 4.)

Table 1 **Histological subtypes of lesions n=34**

Histological Subtypes	n (%)
Malignant disease	**29 (85.3)**
Primary lung cancer	24 (82.8)
Adenocarcinoma	18 (75)
Squamous cell cancer	2 (8.3)
Typical carcinoid tumor	4 (16.7)
Colorectal cancer metastasis	5 (17.2)
Benign disease	**5 (14.7)**
Aspergilloma	3 (60)
Emphysema bullae	1 (20)
Non infectious inflamatory process	1 (20)

Table 2 **Types of imagiological presentation on CT scan of PLC patients lesions n=24**

Imagiological presentation	n (%)
Solid lesions	12 (50)
Part-solid lesions	6 (25)
Pure ground grass opacity	5 (20.8)
Cystic lesions	1 (4.2)

Median drainage time was 3.5 days (IQR: 2 - 5), median LOS time was 4.5 days (IQR: 3 – 8). Postoperative complications were present in 7 (29%) patients, which included: 3 (42.9%) prolonged air leak; 1 (14.3%) pneumonia; 2 (28.6%) atrial fibrillation and 1 (14.3%) pneumothorax after drainage removal. (Table 5.)

Definitive post-operative staging showed that 19 (79.2%) of the removed specimens were stage IA: 2 (4.2%) pT1aN0M0, 12 (50%) pT1bN0M0, and 5 (20.8%) pT1cN0M0. 3 (12.5%) were stage IB: pT2aN0M0; 1 (4.2%) was stage IIB: pT1bN1M0; and 1 (4.2%) was stage IIIA: pT1aN2M0. (Table 6.)

Pathologic examination also revealed that a complete surgical resection (R0) was achieved in 23 (95.8%) cases and 1 (4.2%) surgical specimen had microscopic invasion of surgical margins (R1).

Adjuvant chemotherapy was done in 2 (8.3%) patients and 1 (4.2%) patient had completion lobectomy.

2 patients (8.3%) experienced histologically confirmed recurrence: 1 (4.2%) in mediastinal lymph nodes and 1 (4.2%) in the remaining lobe confirmed by biopsy.

Considering all 24 patients, DFS was 100% at 3, 6, and 12 months, 88,9% at 3 years and 66.7% at 5 years. (Figure 1.) OS was 100% at 3, 6, and 12 months and 95% at 3 and 5 years. (Figure 2.)

Follow up-time was 1-5years. Median follow up time 29 months (IQR: 18 – 44). Follow up was complete for all patients.

When selecting patients with tumors <2cm (n=14), OS and DSF are 100% at 3, 6 and 12 months, and 100% in 3 and 5 years.

Table 3 **Clinical staging of PLC patients n=24**

Clinical staging	n (%)
Stage IA	21 (87.5)
Stage IA2 cT1bN0M0	14 (58.3)
Stage IA3 cT1cN0M0	7 (29.2)
Stage IB cT2aN0M0	2 (8.3)
Stage IIA cT2bN0M0	1 (4.2)

DISCUSSION

The debate over segmentectomies has been going on for decades. As explained earlier, in 1995, the Lung Cancer Study Group defined lobectomy as the best treatment for NSCLC T1N0M0. By then, tumors were detected by radiography and staging of these tumors was precarious. Advances in medicine have been made, not only in the ability to detect smaller tumors with chest-CT, but also in methods of staging, providing more accurate information about the tumor and its stage.[7]

With the detection of smaller tumors, questions emerged about making smaller resections, in order to preserve lung parenchyma and lung function.[1,2] Moreover, with the implementation of screening programs, there is an earlier detection of these cancers, having more young patients diagnosed. Therefore, preserving lung parenchyma might be crucial for the event of new primary lung cancers that could appear.[7]

Segmentectomies are now becoming a usual practice for NSCLC amongst most centers. New studies about this topic are emerging. These studies evaluated patients with tumors under 2cm submitted do segmentectomy, with intra-operative histologic examination of surgical margins and N1 lymph nodes. If surgical margins are clear and lymph nodes are negative for cancer, segmentectomy shows non-inferior results when comparing to lobectomy.[10,11]

This retrospective study only included 24 patients with PLC because, in our center, segmentectomies were performed according to state knowledge during the study period, based on international guidelines: patients with poor pulmonary function precluding lobectomy; when, without a pre-operative diagnosis, a wedge resection was technically non-feasible (deep nodules); and lesions hard to identify at palpation (e.g. GGO) to guarantee excision with adequate margins. Most of our patients were necessity segmentectomies, according to these criteria, and only few were segmentectomies with curative intent, regarding specific cases of <2cm pure GGO lesions without pre-operative diagnosis and in whom frozen section was difficult due to small size of the lesions.

Pre-operative histological diagnosis was lacking in most patients due to nodule characteristics (subsolid lesions, small lesions) or location in lung parenchyma, making biopsies

Table 4 **Types of segmentectomies n=24**

Lung segments ressected	n (%)
Right lung	**9 (37.5)**
Right upper lobe	
Apical	1 (11.1)
Posterior	1 (11.1)
Anterior	3 (33.3)
Right lower lobe	
Superior	4 (44.4)
Left lung	**15 (62.5)**
Left upper lobe	
Apical	1 (6.7)
Apico-posterior	2 (13.3)
Culmen	7 (46.7)
Lingula	1 (6.7)
Left lower lobe	
Superior	4 (26.7)

Table 5 **Post operative complications stratified according to Clavien-Dindo classification (1) n=7**

Post operative complications	n (%)
Clavien-Dindo grade I complications	3 (42.9)
Prolonged air leak	3 (42.9)
Clavien-Dindo grade II complications	3 (42.9)
Atrial fibrillation	2 (28.6)
Pneumonia	1 (28.6)
Clavien-Dindo grade IIIa complications	1 (14.3)
Post chest tube removal pneumothorax	1 (14.3)

Table 6 **Pathological staging of PLC patients n=24**

Pathological staging	n (%)
Stage IA	19 (79.2)
Stage IA1 pT1aN0M0	2 (4.2)
Stage IA2 pT1bN0M0	12 (50)
Stage IA3 cT1cN0M0	5 (20.8)
Stage IB pT2aN0M0	3 (12.5)
Stage IIB pT1bN1M0	1 (4.2)
Stage IIIA pT1aN2M0	1 (4.2)

unfeasible by available techniques. However, histological specimens were acquired in 3 patients. 2 patients had ADC histology and 1 had SCC histology, with 32, 42 and 11mm in size, and poor pulmonary function. In the first and second cases, a segmentectomy was preferred over local therapy for the advantage of having a complete lymph node dissection that would allow more appropriate staging to define adjuvant treatment. In the third case, segmentectomy was preferred over stereotactic body radio therapy (SBRT), not only because of what was described for the first and second cases, but also because SBRT is not always timely assured in our center.

Considering nodal status, 2 patients had nodal upstaging. These patients did not have indication for invasive mediastinal staging and had unforeseen N1 and N2 disease. Post-operatively, they underwent chemotherapy. In cases where there was no indication for invasive mediastinal staging, some studies showed low rates of unforeseen N1 and N2 disease, ranging from 3.7% to 10%.[13–15] This means that a small percentage of patients with these characteristics will have unforeseen N1 and N2 disease, as in these two cases. This data reinforces the key point of importance of lymph node dissection when selecting patients for treatment, favoring surgery when compared with non-surgical alternatives.

To overcome this problem, most of the studies regarding sublobar resections refer intra-operative pathologic examination of N1 disease.[4,10,11,16] Also, some studies refer that SUVmax value of primary tumor, and the combination of TC and PET-CT can give more information about the tumor invasiveness and aid in the selection of patients for segmentectomy.[4,8,14]

Regarding surgical margins, 1 patient had microscopic invasion (R1). Unfortunately, frozen section of the margins and lesion was not available. He had an ADC diagnosed post-operatively and due to his good pulmonary function, he was referred to completion lobectomy. This raises the question of the necessity of a better planning of the surgical resection margins. The nodule location should be correctly identified in a segmental area and that can be achieved not only with a better collaboration with the radiology department, but also with the use of different techniques or software, such as, the use of indocyanine green or inflation-deflation method of lung parenchyma after segmental bronchus clamping.[17]

As far as recurrences are concerned, our study showed that 1 patient had recurrence in the staple line and 1 in mediastinal lymph nodes (N2). The first patient had a 42mm solid ADC with a R0 resection. He had recurrence in staple line 36 months after surgery and was treated with SBRT. The second patient had a post-operative diagnosis of ADC, with positive N1 disease. 54 months later, he had recurrence in N2 lymph node (ADC in station 4R confirmed by mediastinoscopy). He is now under chemoradiotherapy with sequential immunotherapy.

Finally, our survival curves show that only one patient died 15months after surgery, by other cause of death rather than disease progression. When considering only patients with tumors <2cm, our survival results (100% OS) are

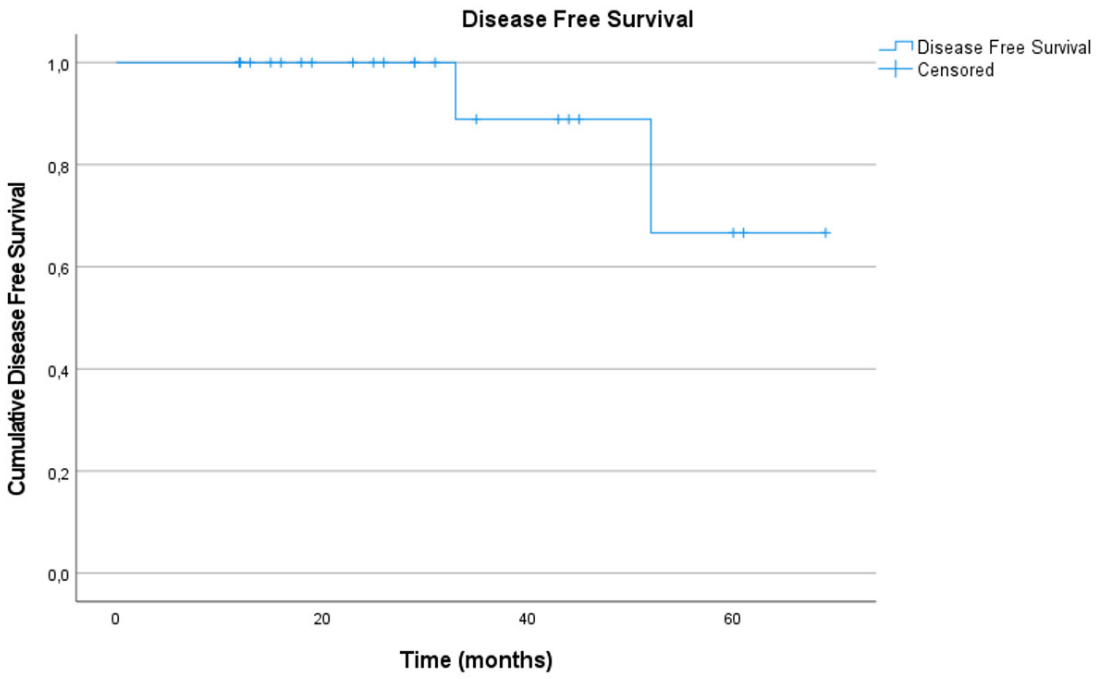

Figure 1 *Disease-Free Survival (n=23)*

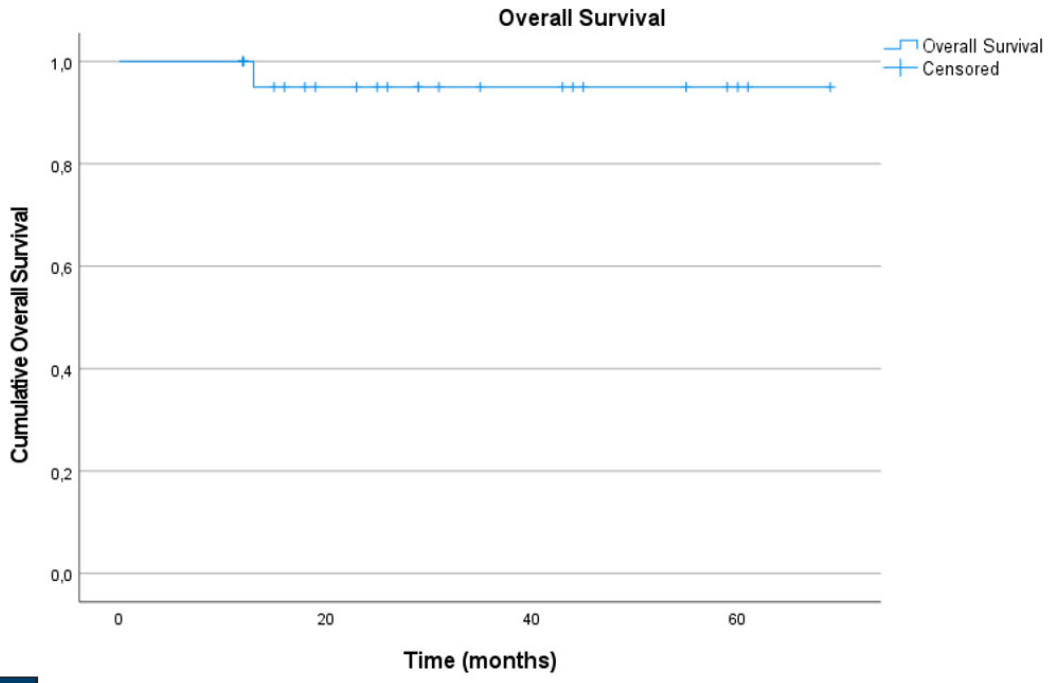

Figure 2 *Overall Survival (n=23)*

compliant to those reported in the literature. [10,11]

Our study has several limitations. It was a retrospective study, with an inherent selection bias.

Most of our patients did not have a pre-operative diagnosis. This study overviewed patients since the year 2018 and, since then, the diagnostic accuracy has improved in our center, providing more information about the lesions. In the beginning of the study period, a diagnosis of an invasive ADC would exclude some patients for segmentectomy, preventing eventual post-operative recurrences and upstaging, particularly in patients with good pulmonary function and in whom lobectomy was an option.

Also, as referred earlier, most of the studies have an intra-operative pathologic analysis of the removed specimen. We believe that having an intra-operative pathologic evaluation of the lesions, the lymph nodes and resection margins would be of benefit for our patients. For logistic reasons, that was impossible to be done in our center at the study period.

CONCLUSION

Much has changed since the first publication of treatment for T1N0M0 tumors. We now have more accurate information about the type of lesions and its staging. Several articles have been developed over the years sustaining that segmentectomy might be a proper approach for T1N0M0 tumors. With the results from recent studies about sublobar resections versus lobectomies for the treatment of early-stage lung cancer, we are now entering an era where the benefits of sublobar resections are clearer.[10,11]

However, caution is advised when interpreting such studies as they were designed to prove non-inferiority. Strict criteria to indicate segmentectomy should remain standard as the lobectomy remains the mainstay of treatment in tumors over 2 cm.

Therefore, it is important to look over our own results regarding the patients submitted to this type of surgery and understand which patients are suitable for this approach, and which are not.

Despite our study limitations, our results demonstrate promising OS and DFS for segmental resections, particularly for patients with tumours <2cm, in accordance with recent literature, reinforcing the idea that this approach can be considered a viable option for patients with early-stage lung cancer.

REFERENCES

1. Iizasa T, Suzuki M, Yasufuku K, Iyoda A, Otsuji M, Yoshida S, et al. Preoperative pulmonary function as a prognostic factor for stage I non–small cell lung carcinoma. Ann Thorac Surg. 2004 Jun;77(6):1896–902.
2. Shennib H. Sublobar resection for lung cancer*1. European Journal of Cardio-Thoracic Surgery. 1999 Sep;16:S61–3.
3. Randomized Trial of Lobectomy Versus Limited Resection for T1 NO Non-Small Cell Lung Cancer. 1995.
4. Sagawa M, Oizumi H, Suzuki H, Uramoto H, Usuda K, Sakurada A, et al. A prospective 5-year follow-up study after limited resection for lung cancer with ground-glass opacity. European Journal of Cardio-thoracic Surgery. 2018 Apr 1;53(4):849–56.
5. de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. New England Journal of Medicine. 2020 Feb 6;382(6):503–13.
6. Kaneko M, Eguchi K, Ohmatsu H, Kakinuma R, Naruke T, Suemasu K. Peripheral lung cancer: screening and detection with low-dose spiral CT versus radiography. Radiology. 1996;
7. Altorki NK, Yip R, Hanaoka T, Bauer T, Aye R, Kohman L, et al. Sublobar resection is equivalent to lobectomy for clinical stage 1A lung cancer in solid nodules. Journal of Thoracic and Cardiovascular Surgery. 2014 Feb;147(2):754–64.
8. Ghaly G, Rahouma M, Kamel MK, Nasar A, Harrison S, Nguyen AB, et al. Clinical Predictors of Nodal Metastases in Peripherally Clinical T1a N0 Non-Small Cell Lung Cancer. Annals of Thoracic Surgery. 2017 Oct 1;104(4):1153–8.
9. Bedetti B, Bertolaccini L, Rocco R, Schmidt J, Solli P, Scarci M. Segmentectomy versus lobectomy for stage I non-small cell lung cancer: A systematic review and meta-analysis. J Thorac Dis. 2017 Jun 1;9(6):1615–23.
10. Saji H, Okada M, Tsuboi M, Nakajima R, Suzuki K, Aokage K, et al. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial [Internet]. Vol. 399, www.thelancet.com. 2022. Available from: www.thelancet.com
11. Altorki N, Wang X, Kozono D, Watt C, Landrenau R, Wigle D, et al. Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer. New England Journal of Medicine. 2023 Feb 9;388(6):489–98.
12. Ettinger D, Wood D, Chair V, Aisner D, Akerley W. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer NCCN Guidelines. 2022;
13. Cerfolio RJ, Ojha B, Bryant AS, Raghuveer V, Mountz JM, Bartolucci AA. The accuracy of integrated PET-CT compared with dedicated PET alone for the staging of patients with nonsmall cell lung cancer. Annals of Thoracic Surgery. 2004 Sep;78(3):1017–23.
14. Moon Y, Kim KS, Lee KY, Sung SW, Kim YK, Park JK. Clinicopathologic Factors Associated With Occult Lymph Node Metastasis in Patients With Clinically Diagnosed N0 Lung Adenocarcinoma. Annals of Thoracic Surgery. 2016 May 1;101(5):1928–35.
15. Bousema JE, Heineman DJ, Dijkgraaf MGW, Annema JT, van den Broek FJC. Adherence to the mediastinal staging guideline and unforeseen N2 disease in patients with resectable non-small cell lung cancer: Nationwide results from the Dutch Lung Cancer Audit - Surgery. Lung Cancer. 2020 Apr 1;142:51–8.
16. Koike T, Nakamura A, Shimizu Y, Goto T, Sato S, Toyabe S ichi, et al. Characteristics and risk factors of recurrence in clinical stage I non-small cell lung cancer patients undergoing anatomic segmentectomy. Gen Thorac Cardiovasc Surg. 2020;
17. Chen X, Zhang Z, Xu N, Ma D, Li H. Review of Approaches to Developing Intersegmental Plane during Segmentectomy. Thorac Cardiovasc Surg. 2022 Jun 16;70(04):341–5.