Review Article

Lobectomy or sublobar resection?—Comparative analysis of the techniques in the surgical treatment of non-small cell lung cancer: a narrative review

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Objective: The aim of the study is to compare two techniques in the surgical treatment of resectable non-small cell lung cancer (NSCLC).

Background: Minimally invasive surgery is the gold standard in the treatment of lung cancer in the early stage. This strategy is not only related to the reduced surgical access but also to the amount of parenchyma that must be saved, compatibly with the oncological radicality. The purpose of the study is to evaluate if sublobar resection can be a valid alternative to lobectomy, based on results.

Methods: We carried out a systematic analysis of the studies conducted in literature in the last 6 years (from 2015 to 2021), comparing the outcomes of lobectomies and sublobar resections (segmentectomy or wedge). The parameters considered were as follows: complications, relapse rate and overall survival. Lobectomy showed a slightly higher risk of developing complications than sublobar resection, especially in octogenarian or in a high index of comorbidity (0–48% *vs.* 0–46.6%, respectively). Conversely, the relapse rate (2.3–32% *vs.* 2.9–53.4%) and overall survival (45.9–93.8% *vs.* 33.8–100%) were more favorable in patients treated with lobectomy although sublobar resection showed an increasing survival rate over the years.

Conclusions: From the review of literature, lobectomy is still the safest oncologically method to treat the bronchogenic carcinoma. Regarding sublobar resections, there is no clear and distinct classification of results between anatomical segmentectomy and wedge resection. More multicenter randomized studies would be needed in order to compare the three techniques separately.

Keywords: Lung cancer; surgical treatment; outcomes; analytic review

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Introduction

In recent years we have witnessed a continuous technological evolution and the constant development of genetic research, in order to offer targeted medical therapy (1-3) in non-small cell lung cancer (NSCLC). However, the most effective treatment still remains the surgical approach. If the aim of lung cancer surgery is to achieve the oncological radicality, an adequate resection of parenchyma is mandatory to obtain expected results. This decision must also consider

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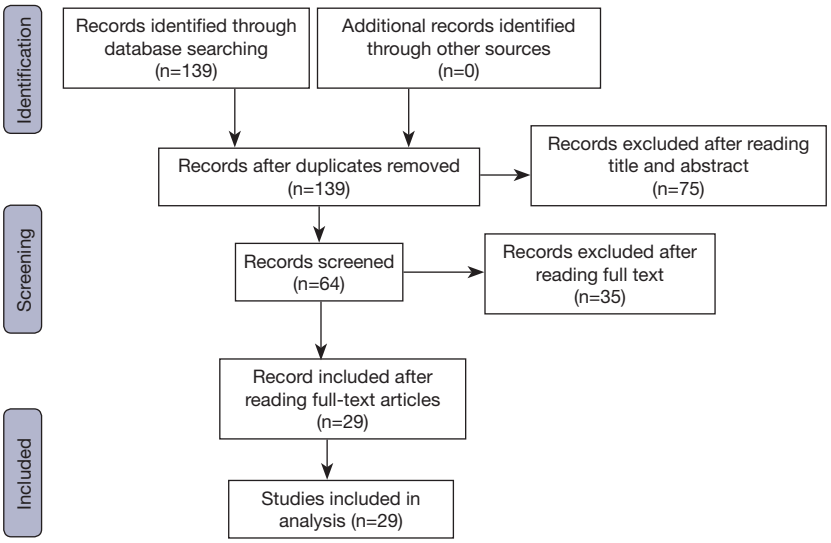

Figure 1 Flow chart of included studies.

the lengthening of average overall survival (4) due to the improvement of the lifestyle and the state of well-being. In fact, comorbidities and other risk factors are evaluated in patients over a hundred years old (5). Limited resections have been proposed in patients whose clinical condition did not allow for major resection (6,7). However, the fundamental question is whether major resections are the right choice in the treatment of early-stage lung cancer regardless to age, comorbidities or general health of the patients (8-10). The study, starting from the evaluation of the results, tries to quantify the risks and benefits of sublobar resections compared to lobectomies (11,12). The analysis was carried out on literature data, in order to understand if parenchyma saving is the way forward. We present the following article in accordance with the Narrative Review reporting checklist (available at https://dx.doi.org/10.21037/asj-21-31).

Methods

The purpose of the study is to analytically establish the safety of the lung resection techniques in NSCLC, comparing the literature data.

The search was carried out using a combination of words, relevant MeSH terms and appropriate filters; the strategy was developed in MEDLINE (via PubMed) from 2015 to 2021. A specific software was used for the management of the records identified with the selected search criteria. As search terms we used: "non-small cell lung cancer AND lobectomy AND/OR sublobar resection AND outcomes". Based on the eligibility criteria, the studies were evaluated by two independent authors who also analyzed the literature and assessed the dissimilarities; any biases were discussed and resolved. A flow chart was created with the included and excluded items. The experiences that contained overlapping data were discussed. Any discrepancies they were resolved by consensus after extensive discussion. The following elements were extracted from each study, if available: first author surname, year of publication, surgical strategy, relapse, complications, 5-year overall survival.

The comparative analysis of the values relating to the different parameters provide an evaluation index of the safety of the methods. Finally, the data were graphically reported with Microsoft Excel in order to make the results evaluable and more easily analyzed.

Results

One hundred and forty-two results were obtained and, after removing the duplicates and non-English articles, 139 articles were identified. After reading the abstract, 75 studies out of 139 were excluded because not relevant. Of the remaining 64 articles, only 29 were considered relevant after evaluating the content of the full text and included in the data analysis (*Figure 1*); 9 are the most recent articles, published from 2019 to 2021 [(13-21), *Table 1*] and 20 published in the 3-year period 2015–2018 [(22-41), *Table 2*]. Information on 48,365 patients treated for resectable NSCLC (stage I–II)

were collected. Of these, 29,789 patients underwent lobectomy and 18,576 underwent sublobar resection (wedge or anatomic segmentectomy). We divided the patients according to the year of publication of the studies and then we classified the three parameters separately according to the procedure performed. The parameters considered were as follows: complications, relapse and overall survival. Comparing sublobar resections and lobectomies, the noted outcomes are the following (*Tables 1*,*2*): (I) incidence of complication ranged from 0% and 46.6% *vs.* 0% and 48%, respectively; (II) incidence of relapses ranged from 2.9% and 53.4% *vs.* from 2.3% and 32%, respectively; (III) 5-year overall survival ranged from 33.8% to 100% *vs.* from 45.9% to 93.8%, respectively. Therefore, sublobar resections are characterized by a reduced complication rate but showed a greater risk of developing relapses with a reduction in overall survival compared to lobectomies. Then, we used Microsoft Excel to analyze these values as a function of time. We obtained the curves of survival comparing the outcomes related to patients undergoing lobectomy (*Figure 2*) and to patients undergoing sublobar resection (*Figure 3*). Analyzing the two curves in a system we notice that the disadvantage of sublobar resections in terms of survival decreasing as a function of time (*Figure 4*). The data are interpreted in a critical sense, not being able to perform a meta-analysis. There are no major differences between the techniques but the data still show a trend that can lead the choice based on the experience of different centers.

Discussion

In the surgical treatment (42) of early stages NSCLC, pulmonary lobectomy has always considered the gold standard (43,44). However, the debate about the role of sublobar resections in these patients is particularly heated in recent years (45). Sparing of pulmonary parenchyma is widely accepted in the treatment of subsolid malignant nodules, but the effectiveness remains controversial in consideration of several factors (46-48). One of these is the tumor spread through air spaces (STAS); the role of STAS in the prognosis of patients undergoing sublobar resections was studied by Zhang *et al.* (17). They have studied 108 patients of whom 58 underwent lobectomy and 50 sublobar resection. Patients showed nodules ≤2 cm and one of the following characteristics: (I) adenocarcinoma *in situ*; (II) ground glass opacity with solid component >50%; (III) doubling time >400 days. The authors highlighted that the differences between the two groups concerned only drainage time, hospital stay and costs. On the other hand, they found no significant differences in terms of efficacy on the basis of the following parameters: (I) STAS; (II) lymph node, vascular or pleural involvement; (III) short-term complications. According to what has been described, the techniques would be equally effective but long-term data such as relapse rate and overall survival are not reported by authors. We disagree with those conclusions as we think that STAS is associated with possible long term relapse.

For this reason, in our analysis, we considered a 5-year overall survival. Another justification for choosing sublobar resection seems to be the subsolid nature of nodules.

Im *et al.* (13) carried out a prospective multicenter observational study on 173 patients with stage IA lung adenocarcinoma. Patients were selected from 250 with radiological evidence of ground glass opacity (part solid nodules and pure ground glass). Of these, 63 underwent pulmonary lobectomy and 110 sublobar resection. The goal was to assess the relapse rate in the two groups which proved to be overlapping (2.3% *vs.* 2.6%) over a follow-up of 5 years on average. However, the same authors admit the existence of biases in the study: (I) firstly, the recurrence rate was too low; (II) secondly, patients were not assigned uniformly in the groups; (III) thirdly, in 24 patients underwent sublobar resection no lymph node dissection was performed. We opine that the radiological characteristics of the nodules alone cannot justify a sublobar resection. Furthermore, the recurrence of disease can be linked to lymph node micrometastases not radiologically identified. Then, it is also important to perform a systematic nodal dissection in patients undergoing sublobar resection.

Wald *et al.* (14) studied 162 T1N0 NSCLC patients, from 2008 to 2018, of which 107 underwent lobectomy and 55 segmentectomy or wedge resection. Lymph node dissection was performed in all lobectomies and in 85% of sublobar resections. Sublobar resection compared to lobectomy showed a slightly higher 5-year survival rate (75.9% *vs.* 71.8%); Authors suggested that, in selected patients, the effectiveness of this technique is comparable to lobectomy. The most frequently detected complications were: (I) airway infections or pneumonia; (II) changes in heart rhythm (atrial fibrillation); (III) alteration of white blood cells, platelets or hemoglobin; (IV) limited bleeding; (V) prolonged air leaks. Other types of complications found less frequently: (I) chylothorax; (II) kidney failure; (III) bleeding requiring reintervention; (IV) respiratory failure requiring re-intubation; (V) acute coronary syndrome; (VI) pulmonary embolism (32,39,40). In our study we noted

Table 1 Selected papers (13-21) from 2019 to 2021 for the comparison between lobectomy and sublobar resection

Author	Number of patients/ procedures	Type of resection	Complications	Incidence of recurrence	Overall survival
Im *et al.* 2021	173	63 lobectomy; 110 sublobar	–	2.3%; 2.9%	–
Wald *et al.* 2021	162	107 lobectomy; 55 sublobar	–	–	71.8%; 75.9%
Dong *et al.* 2020	121	Sublobar	22%	–	82.8%
Baig *et al.* 2020	4,332	3,977 lobectomy; 355 sublobar	–	–	45.9%; 33.8%
Zhang *et al.* 2020	108	58 lobectomy; 50 sublobar	Tot. 15 (13.9%); P=0.473		
Chang *et al.* 2019	364	Segmentectomy	4.1–8.5%	4.1%	-
Amiraliev *et al.* 2019	200	148 lobectomy; 52 segmentectomy	–	–	82%; 86%
Kamigaichi *et al.* 2019	166	Segmentectomy	–	3.6% [6]	93.5%
Stiles *et al.* 2019	4,582	3,890 lobectomy; 692 sublobar	–	–	60.9%; 54.4%

Table 2 Selected papers (22-41) from 2015 to 2018 for the comparison between lobectomy and sublobar resection

Author	Number of patients/ procedures	Type of resection	Complications	Incidence of recurrence	Overall survival
Yang *et al.* 2018	4,866	Sublobar	–	–	58.5%
Ali *et al.* 2018	242	Segmentectomy	8.26%		100%
Yendamuri *et al.* 2018	3,916	Sublobar	–	–	65.8%
Subramanian *et al.* 2018	1,687	1,354 lobectomy; 333 sublobar	–	–	61.8%; 55.6%
Brandt *et al.* 2018	2,392	Lobectomy	–	13% [115]	–
Moon *et al.* 2018	133	Sublobar	–	–	49.9–100%
Gossot *et al.* 2017	284	Segmentectomy	15.3%	–	–
Tsunezuka *et al.* 2017	62	Sublobar (wedge)	–	53.4%	56.4%
Hattori *et al.* 2017	184	148 lobectomy; 36 sublobar	–	–	69.4%; 78.6%
Koike *et al.* 2016	65	32 lobectomy; 33 sublobar	–	6.2%; 9.1%	93.8%; 90.9%
Echavarria *et al.* 2016	251	208 lobectomy; 43 sublobar	40.4%; 46.6%	–	–
Fiorelli *et al.* 2016	239	149 lobectomy; 90 sublobar		19%; 23%	60.5%; 45%
Gulak *et al.* 2016	5,749	4,424 lobectomy; 1,325 sublobar	0–8.7%; 0–9.5%	–	–
Dai *et al.* 2016	15,760	11,520 lobectomy; 4,240 sublobar	–	–	HR: 1.37/1.83
Kent *et al.* 2016	212	Sublobar	–	–	58.4%
Razi *et al.* 2016	1,640	1,051 lobectomy; 589 sublobar	–	–	50.2%; 38.6–43.8%
Hattori *et al.* 2016	115	Sublobar	–	<27.8%	82.2%
Kim *et al.* 2015	222	181 lobectomy; 41 sublobar	43.1%; 7.3%	–	–
Dell'Amore *et al.* 2015	73	44 lobectomy; 29 sublobar	48%; 31%	32%; 32%	56%; 58%
Ito *et al.* 2015	65	43 lobectomy; 22 sublobar	–	–	78.4%; 48.5%

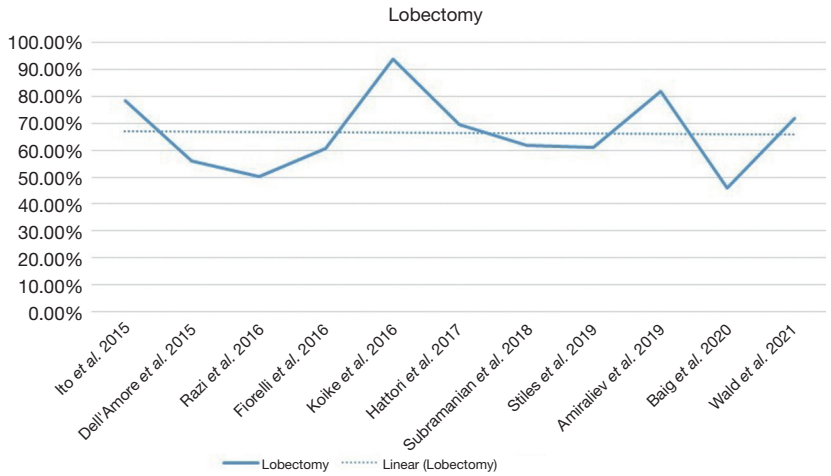

Figure 2 Trend of the survival curve for lobectomies.

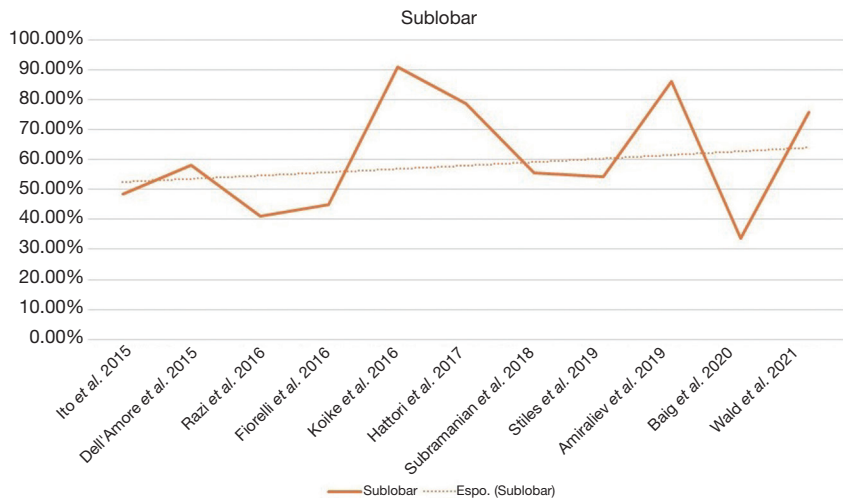

Figure 3 Trend of the survival curve for sublobar resection.

that some authors showed a complication rate <1% while others displayed values >40%. In consideration of these heterogeneous data in the literature, we can state that it is not possible to establish the advantages and disadvantages of a sublobar resection compared to a lobectomy in the treatment of early-stage NSCLC. Often, the outcomes of wedge resections are not clearly distinct from those of anatomical segmentectomies, so it is impossible to define the role and limits of these methods. Cao *et al.* (49) and Zhang *et al.* (50) carried out meta-analysis in order to establish what is the safest and most advisable procedure. We noted that the type of resection was subordinated to the clinical characteristics of patients rather than the oncological effectiveness of method. This is clearly a bias as there is a risk of comparing patients and not techniques. In fact, the different methods should only be evaluated in homogeneous groups of patients in which each technique can be freely and safely used. Starting from these considerations (the non-mandatory nature of the type of procedure) we did not find in literature any data that would allow a correct meta-analysis.

Furthermore, many studies do not provide complete data on the incidence of complications or of relapses relating to the different approaches. All this explains the difficulty of performing statistical analysis and the impossibility of proceeding with a meta-analysis. Based on these

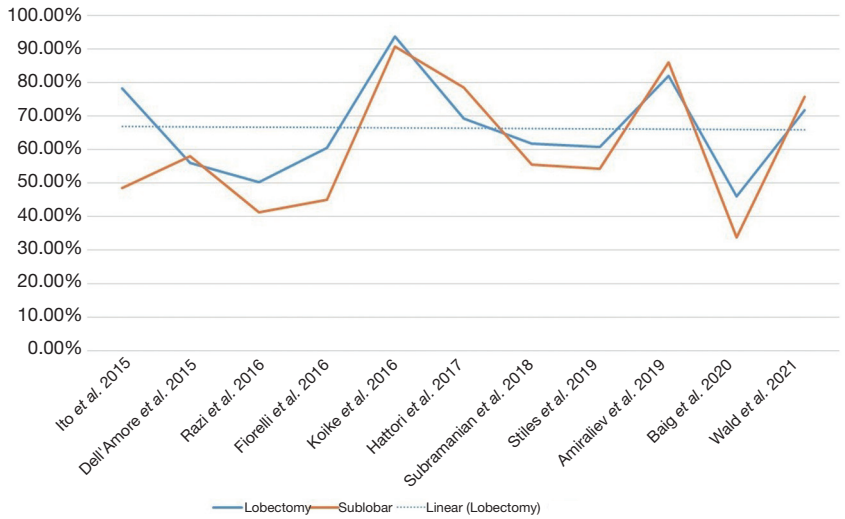

Figure 4 Comparison of the survival curves for lobectomies and sublobar resection.

considerations, we believe that multicentre randomized studies, with clear primary and secondary end points, are necessary in order to acquire homogeneous and comparable data in a large number of patients. This would allow for a meta-analysis on meaningful data in order to define future guidelines about the recommended surgical methods for early-stage NSCLC.

Conclusions

From the evaluation of the literature and from the statistical analysis of the data we believe that lobectomy still represents the oncologically safest and effective technique to treat early-stage NSCLC. Currently, sublobar resection is a valid alternative to lobectomy in selected cases. The increased experience of minimally invasive approaches and of lung resections with parenchymal sparing shows that good results can be achieved in the short-term and medium-term follow-up. The long-term validity of anatomical segmentectomy and/or wedge resection need further specific and comparable randomized control trials.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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