Review Article on Early Stage Lung Cancer: Sublobar Resections are a Choice?

Lobectomy versus sublobar resection in patients with non-small cell lung cancer: a systematic review

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Abstract: Surgery is the gold standard treatment of lung cancer. The minimally invasive technique does not only concern access to the chest but also the limits of parenchymal resection. The study debates on the safety and oncological adequacy of sublobar resections in bronchogenic carcinoma patients. A systematic analysis of the data in the literature was carried out, comparing the outcomes of patients with resectable non-small lung cancer (NSCLC) who underwent lobectomy or sublobar resection. These last interventions include both segmentectomies and wedge resections taking into consideration the following parameters: complications, relapse rate and overall survival. The complication rate is higher in patients underwent lobectomy compared to sublobar resection, especially in presence of high comorbidity index or octogenarian patients (overall values respectively between 0 and 48% and 0 and 46.6%). Contrarily, the relapse rate (6.2% to 32% *vs.* 3.6% to 53.4%) and overall survival (50.2% to 93.8% *vs.* 38.6% to 100%) are more favorable in patients undergoing lobectomy. Sublobar resections are particularly indicated in elderly patients and in patients with high comorbidity index or reduced respiratory functional reserve. However, pulmonary lobectomy still remains the safest and oncologically correct method in patients with good performance status or higher risk of recurrence.

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

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Introduction

In recent years, thoracic surgery showed a significant boost technological evolution in the treatment of non-small cell lung cancer (NSCLC) associated with the development of genetic research for a targeted medical therapy (1-3). Currently, the wide resection is mandatory in order to obtain an oncologically adequate lung cancer (NSCLC) treatment; in fact, limited resection can be performed only if the general condition of patient is not particularly compliant (4,5). However, general well-being and lifestyle habits increased the average overall survival (6) to such that risk factors and comorbidities have been studied in over 100 years older age human (7). Older people benefit most from less invasive surgical approach also with the saving of lung parenchyma. However, regardless of the age and general status of the patients it is questionable whether major resection is still justified in early-stage NSCLC (8-10). Moreover, it is imperative to define risks and benefits of sublobar resections compared to the classic lobectomies not only in relation to the perspective survival (11,12). The purpose of the study was to evaluate the data in the literature regarding lobectomies and limited resections, in order to establish the correct indications for one or the other technique.

Methods

A search strategy using a combination of free-text words, relevant MeSH terms and appropriate filters was designed; the searching strategy was developed in MEDLINE (via PubMed) from 2014 until 2019. Records identified through our search strategy were imported into reference management software. The eligibility criteria were: "non-small cell lung cancer AND lobectomy AND/OR sublobar resection (anatomical segmentectomy, wedge resection) AND outcome". Two authors worked independently to assess each identified study based on the eligibility criteria; when multiple studies contained overlapping data, a most informative study was included. Two independent reviewers and disagreements assessed the risk of bias were settled by discussion and consensus. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to improve the report of this systematic review. The literature search was conducted by two reviewers independently. Any discrepancies in the final list of articles to be included were discussed and resolved by consensus. The following items were extracted from each study if available: first author's surname, publication year, surgical strategy, recurrence, complications, overall survival.

Results

The selection of the articles was carried out by interrogating five databases: Medline, Scopus, CINAHL, Web of Science, Cochrane. The following search string was used: "non-small cell lung cancer AND lobectomy AND/OR sublobar resection (anatomical segmentectomy, wedge resection) AND outcome". One-hundred eight results were obtained and, after removing of duplicates and article not in English, 103 articles were identified. Of these, 53 were found interesting after reading the title and the abstract. Afterwards, only 24 were evaluated relevant after reading the full text. This step was performed independently by two researchers. In case of doubt, a third independent researcher intervened from the previous ones. For the data analysis, 24 articles (13-36) were identified and taken into consideration (*Figure 1*). These provided overall information on 43,469 patients treated for NSCLC. Of these, 25,584 patients were treated with lobectomy and 17,885 were treated with sublobar resection (wedge or anatomical segmentectomy). Patients were divided into two distinct groups based on the surgical strategy and we have considered three parameters: complications, recurrence and overall survival. Sublobar resections compared to lobectomies showed (*Table 1*) an overall range in regard to: (I) the complication rate, between 0% and 46.6% and 0% and 48% respectively; (II) the incidence of recurrence, from 3.6% to 53.4% and 6.2% and 32% respectively; (III) the overall survival, from 38.6% to 100% and from 50.2% to 93.8% respectively. Therefore, from the analysis of individual studies was highlighted that sublobar resections are characterized by a reduced overall complication index but by a higher risk of developing local recurrence which it is translated into a lower overall survival index compared to lobectomies.

Discussion

Surgery is the best strategy treatment in NSCLC patients' early stages (37), although the type of intervention is still debated. Pulmonary lobectomy represents the safest and oncologically correct choice (38,39). However, sublobar lung resections seem to reach the same levels of efficacy and accuracy compared to lobectomy (40) favoring the recruitment of elderly patients with poor functional respiratory reserve and/or high comorbidity index according to the saving of lung parenchyma (41). Indisputably, lobectomy seem to reduce the risk of local recurrence, improving overall survival (42,43). In our review the total number of patients enrolled in the various studies was 43,469 and data appear particularly significant. The first parameter taken into consideration is the complication rate. As can be deduced from *Table 1*, lobectomy shows a maximum value of 48% while sublobar resections show a maximum value of 46.6%. Echavarria *et al.* (27) displayed a higher complication rate compared to all Authors. This data can be explained by the characteristics of the study in which only patients with pneumological problems underwent segmentectomy and the complications were basically linked to basic respiratory insufficiency. Dell'Amore *et al.* (35) studied octogenarian patients with a high comorbidity index, responsible of 31% complications rate in sublobar resections. In fact, other comparative studies highlighted the complication rate not exceeding 15.3%. The higher rate of complications in lung lobectomies compared to sublobar resections can be explained with the greater stress on the cardiovascular system, due to the hemodynamic effects following the functional and anatomical reduction of the intrapulmonary vascular bed (44,45). Therefore, the careful patients selection associated with an accurate preoperative evaluation is essential to reduce the risks of intraoperative and postoperative complications. The second

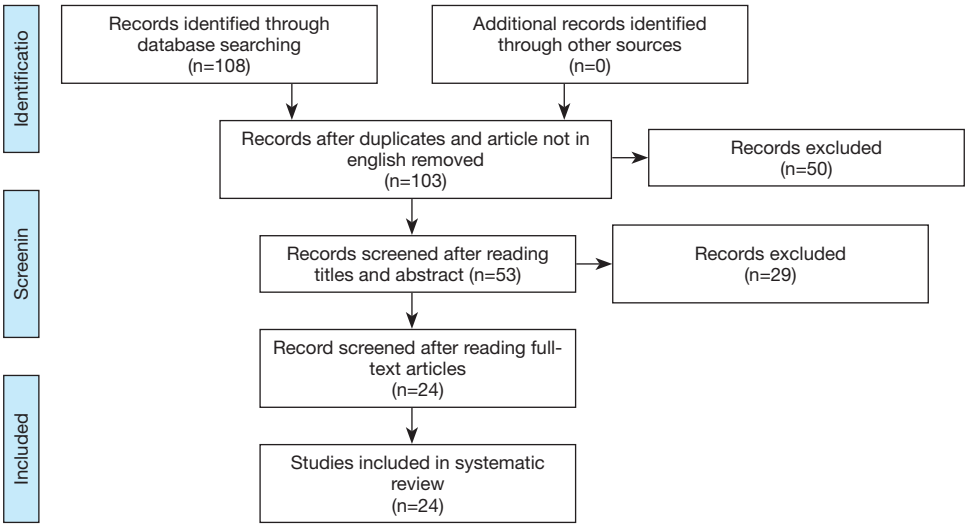

Figure 1 Flow chart according PRISMA statement. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1 Selected papers

Author	Number of patients/ procedures	Type of resection	Complications	Incidence of recurrence	Overall survival
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%
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	–	–; (risk) 39%	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%

parameter evaluated was the incidence of recurrence. Percentages derived from the comparative articles in our study appear similar. However, considering also the studies analyzing the two techniques individually, it is clear that patients underwent sublobar resections have a greater possibility of recurrence than patients underwent lobectomy with maximum risk percentage equal to 53.4% and 32% respectively. This is due to the better oncological radicality obtainable with pulmonary lobectomy. In fact, during sublobar resections in not easy to sample the interlobar lymph nodes (station 11) whose cancer invasion can explain recurrences (46,47). Currently, has found consensus among the Authors the hypothesis about bronchial airspace involvement by locally spread of malignant cell elements (48-50). Kadota *et al.* (51) analyzed 411 adenocarcinoma patients (stage I) underwent lung resection. One hundred fifty-five of these (38%) showed spread tumor air space (STAS). The risk of developing recurrence in STAS patients underwent sublobar resections and lobectomy was 42.6% and 12.7% respectively. The third parameter considered in our study was the overall survival. One study (18) showed a survival equal to 100%. The bias is due to only 30-days survival is assessed in 242 patients underwent VATS sublobar resections. Moon *et al.* (22) studied the margin tumor ratio in 133 patients underwent sublobar resection and experienced 5-year recurrence-free survival (RFS) rate equal to 100% only in lepidic tumors with T <2 cm-N0M0. In non-lepidic tumor Groups RFS decreased up to 49.9%. Razi *et al.* (32) highlighted 5-year survival in NSCLC patients of 38.6% for wedge resection and of 43.8% for anatomical segmentectomy. Ito *et al.* (36) studied 65 NSCLC octogenarian patients, 43 of these treated by lobectomy while 22 by sublobar resection. Survival was higher in patients underwent lobectomy compared to limited resection with a rate equal to 78.4% and to 48.5% respectively. In conclusion, sublobar resections seem to be indicated in elderly patients with a high comorbidity index and reduced respiratory functional reserve. Pulmonary lobectomy still remains the safest and oncologically suitable method in patients with good performance status, reducing the risk of recurrence.

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Footnote

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