

Advances in lung cancer surgery: the role of segmentectomy in early-stage management

Luca Bertolaccini, Monica Casiraghi, Clarissa Uslenghi, Cristina Diotti, Antonio Mazzella, Giovanni Caffarena & Lorenzo Spaggiari

To cite this article: Luca Bertolaccini, Monica Casiraghi, Clarissa Uslenghi, Cristina Diotti, Antonio Mazzella, Giovanni Caffarena & Lorenzo Spaggiari (08 Mar 2024): Advances in lung cancer surgery: the role of segmentectomy in early-stage management, Expert Review of Respiratory Medicine, DOI: [10.1080/17476348.2024.2324083](https://doi.org/10.1080/17476348.2024.2324083)

To link to this article: <https://doi.org/10.1080/17476348.2024.2324083>



© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.



Published online: 08 Mar 2024.



Submit your article to this journal [↗](#)



Article views: 293





View related articles [↗](#)



View Crossmark data [↗](#)

Advances in lung cancer surgery: the role of segmentectomy in early-stage management

Luca Bertolaccini ^a, Monica Casiraghi^{a,b}, Clarissa Uslenghi^a, Cristina Diotti^a, Antonio Mazzella^a, Giovanni Caffarena^a and Lorenzo Spaggiari ^{a,b}

^aDepartment of Thoracic Surgery, IEO, European Institute of Oncology IRCCS, Milan, Italy; ^bDepartment of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

ABSTRACT

Introduction: The evolving landscape of surgical interventions for early-stage non-small cell lung cancer (NSCLC) necessitates a reassessment of the traditional gold standard of lobectomy versus emerging sublobar resections, prompting this critical narrative review.

Areas covered: This review encompasses recent randomized controlled trials, notably JCOG0802/WJOG4607L and CALGB140503, comparing lobectomy and sublobar resections for early-stage NSCLC, focusing on tumor size and recurrence rates. It also discusses the importance of individualized decision-making, future research avenues, and technological advancements in lung cancer surgery.

Expert opinion: In this rapidly evolving field, sublobar resections emerge as a viable alternative to lobectomy for tumors smaller than 2 cm in early-stage NSCLC, necessitating precise patient selection and ongoing technological advancements to optimize outcomes.

ARTICLE HISTORY

Received 10 December 2023

Accepted 23 February 2024

KEYWORDS

Segmentectomy; lobectomy; lung cancer; early-stage; review

1. Introduction

Standard pulmonary architecture comprises five lobes in structure (right upper, middle, and lower, left upper and lower). Lobectomy is an anatomical procedure that necessitates the division of the lobar bronchus, pulmonary artery branches, and pulmonary venous drainage to each lobe individually. In contrast, anatomic segmentectomy involves the division of the segmental bronchus, artery, and vein (Table 1) [1]. The Lung Cancer Study Group (LCSG) published the findings of a randomized trial in 1995, which demonstrated that patients diagnosed with clinical T1 N0 non-small cell lung cancer (NSCLC) would benefit more from a lobectomy than a fewer resection [2]. Since then, lobar resections have become the therapy for patients with good cardiopulmonary function and early staging of lung neoplasm. However, limited resections were often reserved for patients with poor cardiopulmonary function [3]. The Japanese Clinical Oncology Group (JCOG) and the Cancer and Leukemia Group B (CALGB) co-operative group (now a part of the Alliance for Clinical Trials in Oncology) both initiated non-inferiority randomized trials to compare lobar and sublobar treatments for patients with clinical T1a N0 (measuring two centimeters or less in size), in response to significant advances in imaging technology and refinements in TNM staging [4,5]. In patients with clinical T1a N0 NSCLC measuring two centimeters or less, sublobar treatment was shown to be non-inferior to lobectomy, according to the results of both trials that were recently disclosed [6].

Our objective was to thoroughly examine the data published on lobectomy versus sublobar resections, critically addressing confounding factors and limitations to offer maximum clarity and trust in the applicability across different situations. This narrative review provides a comprehensive outline of the current published evidence and establishes a structure for clinical decision-making.

2. Before the randomized controlled trials

In contrast to small cell lung cancer, which typically shows greater sensitivity to radiation and chemotherapy, various stages of NSCLC exhibit improved survival outcomes when surgery is incorporated into the treatment regimen. This favorable response to surgical intervention can be attributed to the propensity of NSCLC tumors to attain larger dimensions and exhibit localized growth patterns, distinguishing them from their small-cell counterparts. The lesion size assumes particular importance in determining the most suitable surgical approach. Recent literature has highlighted that tumor size may not significantly impact lung cancer-specific survival in patients with NSCLC tumors of smaller dimensions. Specifically, studies comparing tumor sizes of less than 2 cm have shown comparable survival outcomes between lobectomy and sublobar resection, which encompasses segmentectomy and wedge resection.

Furthermore, evidence suggests that pulmonary function improves after sublobar resection compared to lobectomy. Despite lobectomy being the established standard of care for

Article highlights

- Recent randomized controlled trials (JCOG0802/WJOG4607L and CALGB140503) compare lobectomy and sublobar resections for early-stage NSCLC, revealing non-inferiority of sublobar resections for tumors ≤ 2 cm.
- Sublobar resections, including segmentectomy, emerge as viable alternatives to lobectomy, particularly for tumors smaller than 2 cm, with precise patient selection and ongoing technological advancements critical for optimizing outcomes.
- Critical analysis highlights complexities in comparing surgical approaches, with considerations ranging from postoperative mortality to long-term recurrence rates.
- Technological advancements, such as 3D modeling and robotic-assisted surgery, revolutionize preoperative planning and surgical precision in segmentectomy procedures, promising improved outcomes and reduced complications.
- Future research directions include refining patient selection criteria, exploring the role of neoadjuvant or adjuvant therapy, and investigating alternative treatments like stereotactic body radiation therapy to further optimize outcomes in early-stage NSCLC treatment.

stage IA NSCLC since 1995, recent findings have challenged the necessity of such an extensive resection for tumors smaller than 2 cm [2]. The landmark clinical trial by Ginsberg *et al.* comparing lobectomy versus limited resection for T1 N0 NSCLC played a pivotal role in establishing lobectomy as the preferred treatment approach. However, this trial had limitations, including its extended duration and possibly underpowered sample size, leading to nonsignificant survival differences between lobectomy and sublobar resection. Additionally, advancements in pulmonary function assessment and imaging techniques may offer more nuanced insights into treatment outcomes. The observed higher recurrence rates with limited resection suggest the presence of micrometastases beyond the visible tumor, a concern that modern imaging and nodal sampling techniques may address more effectively. Although the Ginsberg trial provides robust evidence supporting lobectomy, its relevance may be limited by the lack of minimally invasive approaches, which are now associated with reduced surgical morbidity [2]. Recent studies indicate a potential shift away from lobectomy as a necessary approach for smaller, node-negative lung cancers. However, thorough mediastinal lymph node assessment remains crucial for accurate staging

Table 1. Definition of the lobar and sublobar anatomical and non-anatomical procedures for lung cancer.

Procedure	Definition
Lobectomy	Anatomical procedure that necessitates the division of <ul style="list-style-type: none"> • Lobar bronchus • Lobar artery branches • Lobar venous drainage
Segmentectomy	Anatomical procedure that necessitates the division of <ul style="list-style-type: none"> • Segmental bronchus • Segmental artery • Segmental vein • Parenchymal division in accordance with segmental blood supply
Wedge resection	Non-anatomical procedure that eliminates lesion with bordering margin of healthy lung tissue

and potential therapeutic planning, regardless of the surgical approach chosen [7].

A comprehensive systematic review and meta-analysis comparing minimally invasive anatomical segmentectomy and lobectomy in stage IA NSCLC found that minimally invasive anatomical segmentectomy had similar outcomes to lobectomy in terms of survival and lymph node harvest but had lower rates of postoperative complications and shorter hospital stays. The authors note that the small number of studies and potential biases in the included studies limit the quality of the evidence. For example, many studies included in the analysis had a retrospective design. They were subject to selection bias, as patients who underwent minimally invasive segmentectomy were often declared ineligible for lobectomy. The studies included in the analysis were also conducted in different geographic regions and may need to be more generalizable to other populations. Therefore, minimally invasive anatomical segmentectomy may be a viable alternative to lobectomy for patients with stage IA non-small cell lung cancer, particularly for those who are not eligible for lobectomy due to comorbidities or other factors [3].

Another systematic review and meta-analysis of segmentectomy versus lobectomy for stage I non-small cell lung cancer aimed to provide a current state-of-the-art and better understanding of what has been published in the literature until today. The authors offer valuable insights into the benefits and drawbacks of these two surgical approaches and can help guide decision-making for patients and healthcare providers. Sublobar resections, such as segmentectomy, can preserve lung function and reduce the risk of postoperative complications, making them a viable option for patients who are not suitable for lobectomy. However, sublobar resections may be associated with a higher risk of local recurrence than lobectomy. Lobectomy was associated with better overall survival and lower recurrence rates than segmentectomy. However, they note that the difference in survival rates between the two procedures may be influenced by patient selection bias and other factors. When deciding between segmentectomy and lobectomy for stage I NSCLC patients, the guide factors include tumor size, location, histology, and patient comorbidities and preferences. The decision should be made on a case-by-case basis, considering the individual patient's circumstances [8].

Overall, both studies provide valuable insights into the benefits and drawbacks of segmentectomy versus lobectomy for stage I non-small cell lung cancer. However, their findings and recommendations differ, highlighting the importance of individualized decision-making based on patient-specific factors.

3. The randomized controlled trials

The two recently published randomized controlled trials (RCT) are compared in Table 2. JCOG0802/WJOG4607L was a randomized, multi-institutional, non-inferiority trial to test the hypothesis that segmentectomy is not inferior to lobectomy for the primary endpoint of overall survival in patients with clinical stage IA small-sized NSCLC (≤ 2 cm). Relapse-free survival and postoperative respiratory function were the

Table 2. Demographics and clinical characteristics of the patients enrolled in the randomized controlled trials [4,5]; modified from [15].

Trial	JCOG0802 [5]	CALGB140503 [4]
Enrolled	1319	1080
Randomized	1106	697
Male/Female Ratio	1.1	0.7
Smoker	55.7%	91.0%
Never smoker	44.3%	9.0%
ECOG Performance Status 0	97.9%	73.6%
Resections		
• Wedge	1	201
• Segmentectomy	544	129
• Lobectomy	533	357
Histological Types		
• Adenocarcinoma	90.7%	63.7%
• Squamous	6.8%	14.1%
• Other	2.5%	22.2%
5-years Overall Survival		
• Lobectomy	94.3%	80.3%
• Segmentectomy	91.1%	78.9%
5-year Disease-Free Survival		
• Lobectomy	87.9%	63.6%
• Segmentectomy	88.0%	64.1%
Loco-regional Recurrence		
• Lobectomy	11.0	13.4
• Segmentectomy	5.0	10.0

secondary objectives. Enrollment of patients occurred from August 2009 to October 2014. Eligible patients had computed tomography (CT)-detected tumors ≤ 2 cm in the outer one-third of the pulmonary parenchyma. One thousand three hundred nineteen patients were found, of which 161 could not undergo intraoperative randomization. This was primarily due to the detection of benign disease (6.3%) or N1/N2 upstaging (0.2%). A total of 1106 individuals were assigned at random to get either segmentectomy (552) or lobectomy (554). The patient population was predominately composed of males (53%), with 44% having never used tobacco. Moreover, 97.9% of the patients had an Eastern Cooperative Oncology Group (ECOG) zero performance score. In more than 90% of patients, adenocarcinoma was present. Comparatively, lobectomy resulted in a five-year overall survival rate of 91.1%, whereas segmentectomy yielded a 94.3% rate. It was determined that segmentectomy was superior and non-inferior in comparison to lobectomy. However, other causes of mortality were predominant in the lobectomy group; other cancers (including second primary lung cancer) were the most prevalent. 88% of patients achieved five years of disease-free survival following segmentectomy, compared to 87.9% following lobectomy. However, local relapse was considerably more commonplace after segmentectomy. In the segmentectomy group, patients who experienced relapse had a higher likelihood of survival at five years as opposed to the lobectomy group. Additionally, they were more likely to receive treatment for relapse and undergo re-operation for a second primary lung cancer. FEV1 decreased by 10.4% at six months, as opposed to 13.1% in favor of the segmentectomy [9].

CALGB140503 was an additional prospective, multicenter, phase three randomized, non-inferiority trial in which patients were randomly assigned to either sublobar resections or

lobectomy. Histology, smoking history, and tumor size were utilized to stratify the randomization process. Disease-free survival was the principal endpoint. Pulmonary function, overall survival, and locoregional recurrence constituted secondary objectives. Eligible patients had peripheral lung nodules with a solid component of 2 cm or less in diameter. Patients who presented with pathologically verified N1 or N2 disease or pure ground-glass opacities were ineligible. Patients who met the eligibility criteria were registered and randomized intraoperatively following pathological N0 status ascertained through frozen section examination of a minimum of two mediastinal nodal stations and a central hilar station and confirmation of NSCLC diagnosis (if not already done). sublobar resection modalities (wedge resection versus segmentectomy) were determined at the surgeon's discretion. Commencing in June 2007, the trial was concluded with accrual on 13 March 2017. The trial enrolled 1,808 patients, of which 35% were not randomized intraoperatively. 16.3% of these patients were ineligible for randomization because they lacked NSCLC, while 6.4% had N1/N2 disease. Successful randomization of 697 individuals into lobectomy (357) or sublobar resections (340) was accomplished. Wedge resection was performed on 59.1% in the sublobar resections group, while segmentectomy was performed on 37.9%. 57% were female. 91% had a current or prior smoking history. Among the patients, 73.6% were classified as ECOG 0. Adenocarcinoma comprised 63% of the patients' histological typology. Regarding disease-free survival, the primary outcome, sublobar resections, did not exhibit a lower level of inferiority than lobectomy. The lobectomy arm had a six-year disease-free survival rate of 64.1%, compared to 63.6% in the sublobar resections arm. The overall survival rate at five years was 80.3% compared to 78.9% last time. In the sublobar group, the overall recurrence rate was 30.4%, whereas in the lobar group, it was 29.3%. Furthermore, the sublobar group had a greater incidence of locoregional recurrence. Following sublobar resection, the five-year recurrence-free survival rate was 70.2%, whereas 71.2% followed lobectomy. Additionally, the lobectomy group exhibited a greater incidence of lung cancer-related mortality. At six months, the FEV1 decline was 6% instead of 4%, favoring the segmentectomy [4].

3.1. Critical analysis of the randomized controlled trials

A systematic review and meta-analysis of RCT found that sublobar resection was associated with a lower risk of postoperative mortality than lobectomy. However, sublobar resection was also associated with a higher risk of local recurrence. There was no significant difference in overall survival between the two surgical approaches. The authors noted that every outcome was considered of low certainty due to imprecision, which was downgraded twice because the confidence intervals for the effects were consistent with either an appreciable benefit or appreciable harm depending on the analyzed intervention. No trend of publication bias was observed by visual analysis of funnel plots. Therefore, while sublobar resection may be associated with a lower risk of postoperative mortality, it is also associated with a higher risk of local recurrence.

The JCOG0802/WJOG4607L trial failed to produce the anticipated results regarding the advantage of segmentectomies in the postoperative respiratory function [5]. As a result, a reduction in the excision of lung parenchyma would not invariably lead to enhanced function preservation; this may be attributed to the residual lobe expanding to an unacceptable degree after segmentectomy. Furthermore, expansion and compensation of the residual lobes in the ipsilateral or contralateral lung are enhanced after lobectomy compared to segmentectomy [10]. Because less lung parenchymal tissue is maintained, the JCOG0802/WJOG4607L study excluded basal segmentectomy, which entails the removal of all segments save the apical segment S6 in the lower lobe [5]. The same trial, however, approved apical trisegmentectomy. The JCOG0802/WJOG4607L trial failed to implement outcome stratification concerning the various segmentectomies performed. Despite the higher incidence of locoregional relapses in segmentectomies during the JCOG0802/WJOG4607L trial, the overall relapse pattern (including both distant and locoregional relapses) was found to be similar across the two procedures [5]. Systematic dissection of the mediastinal lymph nodes was recommended for the JCOG0802/WJOG4607L trial; however, selective dissection was also approved and permitted [5]. In CALGB140503, 59.1% of patients underwent wedge resection as sublobar resection [4].

4. Future research

Even with the inquiries that have been resolved by JCOG0802 and CALGB140503, the outcomes of these investigations perpetually give rise to fresh concerns. In the case of CALGB140503, should the five-year disease-free survival rate be below 64% and locoregional recurrence surpass 10% following lobectomy or sublobar resection? Should the potential benefits of neoadjuvant or adjuvant therapy be investigated in these patients? In patients with NSCLC stages, IB to IIIA, recent data from Checkmate 816 and IMpower010 indicate that combining chemotherapy and immunotherapy in the neoadjuvant or adjuvant setting significantly improves survival rates. Although there is limited evidence to support the use of chemotherapy alone in this context, combined immunotherapy, with or without chemotherapy, may become the standard therapeutic approach for stage IA NSCLC before or following surgery [11,12].

Recent studies, including RCT and propensity score-matched studies, have sought to elucidate whether sublobar resection could achieve comparable outcomes to lobectomy. A meta-analysis was conducted in a comprehensive electronic literature search encompassing studies providing Kaplan-Meier curves for overall survival and disease-free survival. This involved a meticulous analysis of individual patient data, employing a graphical reconstructive algorithm and random-effects Cox models to determine hazard ratios. Sensitivity analyses, mainly focusing on RCT, were also carried out. The meta-analysis, involving 2528 patients across seven studies, revealed no significant differences in overall survival or disease-free survival between lobectomy and sublobar resection. Even upon restricting the analysis to RCTs, the comparison remained non-significant. Notably, pooled Kaplan-Meier curves suggested a potential divergence over time, favoring

sublobar resection, a trend confirmed by analysis of restricted mean survival time curves. This patient-level meta-analysis from high-quality studies indicates that sublobar resection is equivalent to lobectomy in patients with small-stage IA NSCLC. Moreover, sublobar resection may offer downstream advantages, particularly for patients experiencing recurrence or developing a second primary tumor, as the lung-sparing nature of this approach allows for further safe treatment. Despite the superiority of lobectomy in terms of overall survival, the lack of significant differences in disease-free and relapse-free survival suggests that sublobar resection warrants serious consideration, particularly given its potential long-term benefits and preservation of lung function [13,14].

Furthermore, specific individuals would undoubtedly push for non-surgical ablative treatments, such as stereotactic body radiation (SBRT) [1]. Nevertheless, it is critical to underscore that patients who were successfully randomized to sublobar resections underwent verification of a negative surgical margin of 2 cm or a distance equal to the size of the tumor, in addition to intraoperative lymph node sampling to reduce the risk of occult nodal disease. Important considerations regarding managing stage I lung cancer, particularly in selecting appropriate treatment modalities based on patient characteristics and tumor biology. Short-term differences between treatment modalities, such as SBRT and surgery, are more pronounced for compromised patients, while long-term differences become less significant. SBRT may offer clear short-term advantages over surgery, particularly for patients with compromised health status, but may result in worse long-term outcomes [1,15]. Specific tumor characteristics, such as GGO appearance, screen-detected, small size (≤ 1 cm), and slow-growing or low PET-avidity tumors, may suggest alternative treatments over lobectomy. GGO and screen-detected tumors generally have excellent long-term outcomes regardless of resection extent. However, late recurrence (>5 years) of GGO tumors after sublobar resection may occur [16]. Speculative extrapolation suggests that tumors with low PET-avidity or slow progression may also have favorable long-term outcomes regardless of resection extent. Decision-making for tumors with favorable characteristics revolves around long-term outcomes. For predominantly GGO tumors, sublobar resection may be reasonable, with no significant benefit or downside compared to lobectomy. Surveillance without immediate intervention may be sufficient for most predominantly GGO lesions, as prospective evidence suggests that most do not progress. Sublobar resection may be considered as an alternative to lobectomy for screen-detected, low PET-avidity, and slow-growing tumors, although confirmatory data is lacking. Margin distance may be an essential consideration in these cases. In healthy patients, current long-term outcomes support lobectomy over sublobar resection for tumors smaller than 1 cm. Additionally, there may be speculation regarding the advantage of resection over SBRT in this population. Individualized treatment selection for stage I lung cancer requires careful consideration of various factors, including patient health status, tumor characteristics, and long-term outcomes associated with different treatment modalities. Further research is needed to confirm the efficacy and safety of alternative treatments, particularly for tumors with

favorable characteristics [1]. Currently, prospective trials demonstrating SBRT's non-inferiority, equivalence, or superiority over surgical resection for stage IA NSCLC have yet to be conducted [15,17].

Segmentectomy should replace lobectomy as the conventional surgical treatment for patients with small (less than 2 cm) peripheral clinical stage IA NSCLC, according to the randomized research JCOG0802/WJOG4607L. However, this information must permit us to proceed confidently with the foundations of segmentectomy as the gold standard if two subgroups of Kaplan – Meyer could also estimate the overall survival of the various subtypes of segmentectomies and cancer-specific survival. Furthermore, anatomical segmentectomies, which involve the removal of segmentary lymphatic channels, are regarded as an approach for early-stage NSCLC. As a result, the disease-free survival and overall survival rates of patients who underwent wedge resections instead of lobectomies should be included in the CALGB140503 data, as this information may alter how early-stage lung cancer is currently managed in clinical practice. Subsequent investigations ought to employ randomized controlled trials to examine the impact of lobectomies and anatomical segmentectomies (stratified for complexity) on outcome variations. Lastly, suitable cost-effectiveness assessments should be carried out [10].

3D modeling approaches have significantly transformed segmentectomy preoperative planning and surgical guiding. Sophisticated imaging technologies enable the generation of three-dimensional depictions of the patient's anatomy that are exceptionally precise and comprehensive, hence promoting enhanced comprehension of intricate pulmonary segmental structures. These models could allow surgeons to determine intersegmental planes accurately, assess vascular and bronchial architecture, and simulate surgical resection methods [18,19]. The heightened visibility level could facilitate optimizing surgical results and reducing potential problems in segmentectomy operations.

In addition, robotic surgery has become a highly advantageous instrument for conducting segmentectomy procedures with enhanced accuracy and skill. Additional benefits of the da Vinci Surgical System and comparable automated platforms include improved instrument control, ergonomic enhancements, and increased visibility. Surgeons can access complex anatomical sites with enhanced mobility and maneuverability using robotic-assisted segmentectomy. By employing this methodology, the surgeon is better equipped to maneuver within the pulmonary parenchyma, arteries and bronchi are dissected with greater precision, and the reconstruction of the lung parenchyma is executed with greater accuracy. Robotic segmentectomy has exhibited encouraging outcomes, such as abbreviated hospital stays and expedited surgical recuperation. These developments signify substantial progress in individualized surgical methodologies, enhanced patient results, and refined surgical procedures [20].

5. Conclusions

Segmentectomy may be employed in elderly and/or multimorbid patients to spare parenchyma from peripheral tumors (≤ 2 cm) that do not involve the lining of the nerve and tumors that are

synchronous or metachronous in nature. In addition, segmental resection may be conducted on benign tumors verified histologically and ground glass opacities lesions measuring less than 1 cm. The technical difficulty of segmental resection stems from the vascular and bronchial architecture. A bisegmentectomy or trisegmentectomy may be performed if adequate resection margins cannot be reached, such as when the tumor invades the intersegmental plane or when anatomic differences complicate the procedure. The selection between thoracoscopic intercostal and subxiphoid access methods is contingent upon the tumor's site and the expertise of the surgeons. While it is possible to retain pulmonary function by segmental excision, care must be taken to prevent technical complications. Ensuring the appropriate selection of patients for this surgery is critical. Malignant infiltration of resection margins at macroscopic and micronodular levels, extracapsular extension, lymph node involvement, and low differentiation grade are all associated with recurrence. It is critical to guarantee more than one margin-to-tumor ratio and conduct enough lymph node dissection and sampling. Without this, segmental resection must be converted to lobar resection per oncological principles. A meticulous evaluation of the condition of the nodes is associated with a reduced likelihood of recurrence due to the avoidance of understaging. A mock and mediastinal sampling or dissection is recommended. At least three lymph node stations should be sampled for mediastinal sampling, although subcarinal lymph nodes should always be included. Systematic dissection is superior to systematic sampling for conducting a comprehensive nodal evaluation due to its ability to identify skip metastases and micrometastasis. However, the American College of Chest Physicians [21], the European Society of Thoracic Surgeons [22], and the National Comprehensive Cancer Network [23] criteria have not excluded systematic sampling [20].

JCOG0802 and CALGB140503 provide substantial evidence that sublobar resections are not inferior to lobectomy for peripheral stage IA NSCLC. Intraoperative pathological or cytological assessment to confirm the absence of nodal metastases is a critical component of various treatment methods. It should not be substituted with imaging modalities whose sensitivity varies. Prior retrospective investigations have consistently found that sublobar resections yield survival rates comparable to those observed in patients who underwent lobectomy when accompanied by sufficient lymph node removal. Hence, a comprehensive lymph node assessment and guaranteeing enough negative margin to achieve a successful sublobar resection is imperative.

Regarding the future, treating early-stage lung cancers has both considerable potential and unpredictability. Catheter-based ablations will vie for therapy in this region with stereotactic radiosurgery and surgical resection as sophisticated navigational bronchoscopy advances. Accurate staging will ultimately be critical for future research comparing these strategies.

6. Expert opinion

The treatment landscape for early-stage NSCLC has witnessed significant transformations, particularly with the shift toward less invasive sublobar resections from the traditional standard

of lobectomy. This transition underscores the need for a nuanced and individualized approach to treatment selection, where factors such as patient demographics, tumor characteristics, and surgeon expertise play crucial roles. As the decision between lobectomy and sublobar resection becomes increasingly complex, it is imperative to involve experienced surgeons who can assess each patient's unique circumstances and recommend the most appropriate course of action. Surgeon experience, particularly in performing both lobectomy and sublobar resection, is paramount in ensuring optimal outcomes and minimizing potential complications. The role of neoadjuvant or adjuvant therapy in conjunction with sublobar resection remains an area of active investigation. Understanding the impact of these additional treatment modalities on recurrence rates and overall survival is essential for optimizing treatment strategies and improving patient outcomes. Non-surgical ablative treatments, such as SBRT, are promising alternatives for early-stage NSCLC, particularly in patients unsuitable for surgery. While SBRT has demonstrated efficacy in achieving local tumor control, further research is needed to compare its effectiveness with surgical resection and elucidate its role within the broader treatment paradigm. Technological advancements, including 3D modeling and robotic-assisted surgery, promise to enhance the precision and visibility of sublobar resections. These innovations aim to reduce the risk of complications and improve surgical outcomes, ultimately benefiting patients undergoing minimally invasive lung cancer surgeries. Given the dynamic nature of NSCLC treatment paradigms, healthcare providers must stay abreast of the latest research findings and clinical guidelines. Patients should be actively engaged in shared decision-making processes, where they can discuss their preferences, concerns, and treatment goals with their healthcare team. In conclusion, while subjectivity inevitably plays a role in treatment decision-making, objective criteria such as tumor characteristics, surgical outcomes, and technological advancements serve as guiding principles for optimizing patient care. By embracing a multidisciplinary approach and incorporating the latest evidence-based practices, healthcare providers can ensure that patients with early-stage NSCLC receive the most effective and personalized treatment interventions.

Funding

This work was partially supported by the Italian Ministry of Health with Ricerca Corrente and 5x1000 funds.

Declarations of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

ORCID

Luca Bertolaccini  <http://orcid.org/0000-0002-1153-3334>
Lorenzo Spaggiari  <http://orcid.org/0000-0002-1068-3541>

References

Papers of special note have been highlighted as either of interest (*) or of considerable interest () to readers.**

1. Detterbeck FC, Blasberg JD, Woodard GA, et al. A guide for managing patients with stage I NSCLC: deciding between lobectomy, segmentectomy, wedge, SBRT and ablation-part 1: a guide to decision-making. *J Thorac Dis.* 2022 Jun;14(6):2340–2356.
2. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung cancer study group. *Ann Thorac Surg.* 1995 Sep;60(3):615–622. discussion 622–3. doi: [10.1016/0003-4975\(95\)00537-U](https://doi.org/10.1016/0003-4975(95)00537-U)
3. Bedetti B, Bertolaccini L, Rocco R, et al. Segmentectomy versus lobectomy for stage I non-small cell lung cancer: a systematic review and meta-analysis. *J Thorac Dis.* 2017 Jun;9(6):1615–1623.
4. Altorki N, Wang X, Kozono D, et al. Lobar or sublobar resection for peripheral stage IA non-small-cell lung cancer. *N Engl J Med.* 2023 Feb 9;388(6):489–498. doi: [10.1056/NEJMoa2212083](https://doi.org/10.1056/NEJMoa2212083)
- **This study provides valuable insights into comparing lobar and sublobar resection for peripheral stage IA NSCLC, offering crucial evidence for surgical decision-making in early-stage lung cancer.**
5. Saji H, Okada M, Tsuboi M, 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. *Lancet.* 2022 Apr 23;399(10335):1607–1617. doi: [10.1016/S0140-6736\(21\)02333-3](https://doi.org/10.1016/S0140-6736(21)02333-3)
- **This study provides valuable insights into comparing lobar and sublobar resection for peripheral stage IA NSCLC, offering crucial evidence for surgical decision-making in early-stage lung cancer.**
6. Lee B, Mynard N, Nasar A, et al. Surgical resection after neoadjuvant durvalumab and radiation is feasible and safe in non-small cell lung cancer: results from a randomized trial. *J Thorac Cardiovasc Surg.* 2023 Jan;165(1):327–334 e2. doi: [10.1016/j.jtcvs.2022.07.017](https://doi.org/10.1016/j.jtcvs.2022.07.017)
- **This randomised trial explores the feasibility and safety of surgical resection following neoadjuvant immunotherapy and radiation, addressing a critical aspect of multidisciplinary treatment approaches in NSCLC.**
7. Behinaein P, Treffalls J, Hutchings H, et al. The role of sublobar resection for the surgical treatment of non-small cell lung cancer. *Curr Oncol.* 2023 Jul 22;30(7):7019–7030. doi: [10.3390/curroncol30070509](https://doi.org/10.3390/curroncol30070509)
8. Bertolaccini L, Prisciandaro E, Bardoni C, et al. Minimally invasive anatomical segmentectomy versus Lobectomy in stage IA non-small cell lung cancer: a systematic review and meta-analysis. *Cancers (Basel).* 2022 Dec 14;14(24). doi: [10.3390/cancers14246157](https://doi.org/10.3390/cancers14246157)
- **This systematic review and meta-analysis shed light on the comparison between minimally invasive anatomical segmentectomy and lobectomy in stage IA NSCLC, providing valuable insights for surgical decision-making and potential advancements in minimally invasive techniques.**
9. Meldola PF, Toth OAS, Schnorrenberger E, et al. Sublobar resection versus lobectomy for stage IA non-small-cell lung cancer: a systematic review and meta-analysis of randomized controlled trials. *Surg Oncol.* 2023 Dec;51:101995.
10. Bertolaccini L, Spaggiari L. Is it time to cross the pillars of evidence in favor of segmentectomies in early-stage non-small cell lung cancer? *Cancers (Basel).* 2023;15(7):1993. doi: [10.3390/cancers15071993](https://doi.org/10.3390/cancers15071993)
11. Forde PM, Spicer J, Lu S, et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. *N Engl J Med.* 2022 May 26;386(21):1973–1985. doi: [10.1056/NEJMoa2202170](https://doi.org/10.1056/NEJMoa2202170)
12. Felip E, Altorki N, Zhou C, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIa non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label,

- phase 3 trial. *Lancet*. 2021 Oct 9;398(10308):1344–1357. doi: [10.1016/S0140-6736\(21\)02098-5](https://doi.org/10.1016/S0140-6736(21)02098-5)
- **This randomised, multicenter, phase 3 trial evaluates the efficacy of adjuvant atezolizumab after chemotherapy in resected stage IB-IIIa NSCLC, offering critical evidence for the role of immunotherapy in improving outcomes for patients with early-stage NSCLC.**
13. Shi Y, Wu S, Ma S, et al. Comparison between wedge resection and lobectomy/segmentectomy for early-stage non-small cell lung cancer: a bayesian meta-analysis and systematic review. *Ann Surg Oncol*. 2022 Mar;29(3):1868–1879.
 14. Fong KY, Chan YH, Chia CML, et al. Sublobar resection versus lobectomy for stage IA non-small-cell lung cancer. *Updates Surg*. 2023 Dec;75(8):2343–2354.
 15. Kocak Uzel E, Bagci Kilic M, Morcali H, et al. Stereotactic body radiation therapy for stage I medically operable non-small cell lung cancer. *Sci Rep*. 2023 Jun 27;13(1):10384.
 16. Bertolaccini L, Terzi A, Ricchetti F, et al. Surgery or stereotactic ablative radiation therapy: how will be treated operable patients with early stage not small cell lung cancer in the next future? *Ann Transl Med*. 2015 Feb;3(2):25.
 17. Lee BE, Altorki N. Sub-lobar resection: the new standard of care for early-stage lung cancer. *Cancers (Basel)*. 2023 May 25;15(11). doi: [10.3390/cancers15112914](https://doi.org/10.3390/cancers15112914)
 18. Zaraca F, Kirschbaum A, Pipitone MD, et al. Prospective randomized study on the efficacy of three-dimensional reconstructions of bronchovascular structures on preoperative chest CT scan in patients who are candidates for pulmonary segmentectomy surgery: the PATCHES (prospective rAndomized sTudy effiCaCy of tHree-dimensional rEconstructions segmentecomy) study protocol. *Trials*. 2023 Sep 16;24(1):594.
 19. Zaraca F, Kirschbaum A, Pipitone MD, et al. Correction: prospective randomized study on the efficacy of three-dimensional reconstructions of bronchovascular structures on preoperative chest CT scan in patients who are candidates for pulmonary segmentectomy surgery: the PATCHES (prospective rAndomized sTudy effiCaCy of tHree-dimensional rEconstructions segmentecomy) study protocol. *Trials*. 2023 Oct 3;24(1):629.
 20. Galanis M, Leivaditis V, Gioutsos K, et al. Segmentectomy versus lobectomy. Which factors are decisive for an optimal oncological outcome? *Kardiochir Torakochirurgia Pol*. 2023 Sep;20(3):179–186.
 21. Detterbeck FC, Lewis SZ, Diekemper R, et al. Executive summary: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):7S–37S.
 22. De Leyn P, Doooms C, Kuzdzal J, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2014 May;45(5):787–98.
 23. Ettinger DS, Wood DE, Aisner DL, et al. NCCN guidelines(R) insights: non-small cell lung cancer, version 2.2023. *J Natl Compr Canc Netw*. 2023 Apr;21(4):340–350.