Original Article

Analysis of clinical and oncological outcomes after simple and intentional lung segmentectomies: the deceptive simplicity of the S6 segment

Ivan Lomangino[1]^, Emanuele Addamo[2]^, Andrea Dell'Amore[3]^, Pietro Bertoglio[4], Simone Furia[5], Angela De Palma[6], William Grossi[7], Piergiorgio Muriana[8], Federico Femia[9], Maria Sole Gallazzi[1], Gabriele Maffeis[1], Armando Puglisi[1], Luca Vecchiarelli[1], Luca Melan[3], Stefano Silvestrin[3], Elena Garelli[4], Piergiorgio Solli[4], Cristiano Breda[5], Giuseppe Natale[5], Francesco De Blasi[6], Andrea Zuin[7], Giampiero Negri[8], Enrico Ruffini[9], Sara Alfonso[10], Matteo Rota[11], Federico Rea[3], Mauro Roberto Benvenuti[1], Giuseppe Marulli[12,13]^

[1]Cardiothoracic Department, Thoracic Surgery Unit, Spedali Civili, Brescia, Italy; [2]Cardiothoracic and Vascular Department, Thoracic Surgery Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy; [3]Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University Hospital of Padova, Padova, Italy; [4]Division of Thoracic Surgery, IRCSS Azienda Ospedaliero-Universitaria, Bologna, Italy; [5]Thoracic Surgery Unit, Ospedale dell'Angelo, Venezia Mestre, Italy; [6]Thoracic Surgery Unit, Department of Precision and Regenerative Medicine and Ionian Area (DIMEPREJ), University Hospital of Bari, Bari, Italy; [7]Department of Cardiothoracic Surgery, Santa Maria della Misericordia University Hospital, Udine, Italy; [8]Department of Thoracic Surgery, Scientific Institute and University Vita-Salute Ospedale San Raffaele, Milan, Italy; [9]Department of Thoracic Surgery, A.O.U. Città della Salute e della Scienza di Torino, Turin, Italy; [10]Department of Medical Biotechnologies, University of Siena, Siena, Italy; [11]Units of Biostatistics and Biomathematics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; [12]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [13]Thoracic Surgery Unit, IRCCS Humanitas Research Hospital, Milan, Italy

Contributions: (I) Conception and design: I Lomangino; (II) Administrative support: MR Benvenuti, G Marulli; (III) Provision of study materials or patients: A De Palma, E Ruffini, S Furia, A Zuin, L Melan, G Negri, P Bertoglio; (IV) Collection and assembly of data: A Dell'Amore, E Garelli, S Silvestrin, G Natale, W Grossi, P Muriana, F De Blasi; (V) Data analysis and interpretation: M Rota, E Addamo; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ivan Lomangino, MD. Cardiothoracic Department, Thoracic Surgery Unit, Spedali Civili, P.le Spedali Civili 1, 25123 Brescia, Italy. Email: i.lomangino@libero.it.

Background: Currently, few studies analyze postoperative outcomes for different types of segmental resections. Therefore, our aim was to compare lower lobe apex with other simple and intentional segmentectomies, in terms of clinical and oncological outcomes.

Methods: A retrospective and multicenter study was conducted on patients who underwent simple and intentional segmentectomies from 2015 to 2020. Inclusion criteria were stage cT1a/b N0 M0 disease, peripheral localization and predicted postoperative forced expiratory volume in one second (ppoFEV1) >60%. Pre, intra and post operative parameters were collected and we performed statistical analysis on overall survival and recurrence.

Results: The inclusion criteria were met by 252 patients, with 125 having an anatomical S6 resection ("S6" group) and 127 having another anatomical simple segmentectomy ("others" group). There were no significant differences in baseline data. We noted a worse 5-year disease-free survival (DFS) for the "S6" group (P=0.053). Twenty-eight of 46 patients with relapsed disease had loco-regional recurrence. Of these, 80% belonged to the "S6" group (P<0.001).

Conclusions: Oncological outcomes were not the same for all simple and intentional segmentectomies.

^ ORCID: Ivan Lomangino, 0009-0001-4234-4456; Emanuele Addamo, 0009-0001-6127-9610; Andrea Dell'Amore, 0000-0002-1384-7441; Giuseppe Marulli, 0000-0001-6570-615X.

Particularly, S6 exhibited worse oncological outcomes, mainly in terms of disease-free survival. This disparity could be explained by the unpredictable lymphatic drainage or by the smaller parenchymal volume removed during dissection.

Keywords: Lung segmentectomy; S6; early-stage lung cancer; intentional simple segmentectomy; sublobar resection

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Introduction

The widespread of screening programs and the increasing number of early-stage lung cancer diagnosis have led the clinicians to explore the feasibility and oncological safety of sublobar lung resection. Sublobar lung resection is currently considered the gold standard in the surgical treatment of early-stage non-small cell lung cancer (NSCLC) (1,2).

In the wide field of lung segmental resections, requiring the isolation of bronchovascular elements, two major categories can be distinguished, single segmentectomy and multiple segmentectomy, as suggested by the 2023 European Society of Thoracic Surgeons (ESTS) expert consensus on segmentectomies (3). For the purpose of our study, we applied another classification, which takes into account the multiplanar development of the inter-segmental planes and is still commonly used among surgeons. The first category includes the so-called "simple lung segmentectomies", identified by the need to isolate only one fissural plane during their execution. "Complex segmentectomies", on the other hand, are procedures that involve the resection of two or more fissural planes among segments. Another remarkable distinction is based on whether the sublobar resection is performed as intentional treatment or chosen due to the patient's predicted poor postoperative functional capacity. Currently, medical literature includes several studies comparing lobar lung resections with sublobar resections, but few studies compared the different types of segmental resections in terms of postoperative and oncological outcomes.

Segmental resection of the lower lobe apex (S6) is one of the most widely performed simple segmentectomy, also being the one requiring isolation of the fewest bronchovascular elements and ensuring greater parenchymal preservation.

The aim of our study was to compare the patient population undergoing segmental resection of the lower lobe apex (S6 group) with the population undergoing other types of intentional and simple pulmonary segmental resections (others) to assess the effectiveness and safety in terms of clinical-oncological middle and long-term outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1348/rc).

Highlight box

Key findings

- This study highlights that the oncological outcomes of simple and intentional lung segmentectomies are not uniform. Segmentectomy of the lower lobe apex (S6) shows worse disease-free survival (DFS) and higher recurrence rates compared to other simple segmentectomies, likely due to unpredictable lymphatic drainage and limited parenchymal volume resection.

What is known and what is new?

- Sublobar resections, including segmentectomies, are established as safe and effective for early-stage non-small cell lung cancer (NSCLC), offering comparable outcomes to lobectomy with reduced morbidity. However, differences in outcomes among specific segmentectomies remain underexplored. This study, focusing on simple segmentectomies, shows that S6 segmentectomy might be associated with worse DFS and higher locoregional recurrence rates, particularly in hilar lymph nodes.

What is the implication, and what should change now?

- Surgeons should consider the unique challenges of S6 segmentectomy, including its lymphatic unpredictability, during preoperative planning and intraoperative decision-making. Further studies are warranted to refine guidelines for segment-specific resections in NSCLC.

Methods

After approval by the ethics committee of "Spedali Civili" Hospital of Brescia (No. 5368) and with all participating

hospitals/institutions informed and in agreement, a retrospective multicenter study was conducted on patients who underwent simple and intentional segmental lung resection during the 5-year period going from 2015 to 2020, performed at 8 different institutions (Spedali Civili Hospital Brescia, University Hospital Padova, IRCSS "Azienda Ospedaliero-Universitaria" Bologna, "Ospedale dell'Angelo" Mestre, University Hospital Bari, Santa Maria della Misericordia University Hospital Udine, Scientific Institute and University Vita-Salute Ospedale San Raffaele Milan, A.O.U. Città della Salute e della Scienza Turin). Individual consent for this retrospective analysis was waived. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

All procedures performed were for curative purposes, and patients were required to have stage cT1a/b N0 M0 disease, peripheral localization, and be at least 2 cm distant from the visceral pleura margin and 1 cm from the fissure, according to the tumor-node-metastasis (TNM) classification (8th edition) for lung neoplasms.

All selected patients underwent preoperative total body computed tomography (CT) scan and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET)-CT scan, with a preoperative diagnosis of NSCLC performed through either CT-guided needle biopsy or transbronchial biopsy, when feasible. Additional inclusion criteria included the execution of a simple segmental resection performed using open, video-assisted thoracic surgery (VATS), or robotic techniques and a definitive histological examination confirming NSCLC. In particular, all enrolled patients were required to have a predicted postoperative forced expiratory volume in one second (ppoFEV1) greater than 60%, emphasizing the intentional choice of performing a segmental resection as opposed to a feasible lobectomy.

Exclusion criteria included the administration of neoadjuvant chemoradiotherapy, the presence of secondary lung neoplasms (metastases) or benign lesions, tumors beyond stage I, atypical or non-anatomic resections, the need for intraoperative conversion, and the need for postoperative intensive care unit admission. Moreover, all patients with preoperative N1 lymph node involvement were excluded from our analysis. This selection resulted in the identification of a cohort of 252 patients, with 125 individuals undergoing simple and intentional non-S6 segmental lung resection ("others" group), and 127 undergoing S6 resection ("S6" group).

In addition, patients were stratified based on demographic and biometric data, preoperative comorbidities, risk scores [American Society of Anesthesiologists (ASA) score, Eurolung risk score], preoperative functional indices, and predictors of postoperative outcomes. The analysis also considered the presence of chronic obstructive pulmonary disease (COPD) and smoking habits in the study population.

The surgical choice was left to the discretion of the individual surgeon performing the procedure. For the isolation of the fissure plane, all surgeons chose to clamp the segmental bronchus, leading to the exclusion of the segmental parenchyma from ventilation, also all resections were performed with the section of the segmental vein at hilum. Technical characteristics assessed included the execution of lymphadenectomy with the associated number of nodes removed in both N1 and N2 regions, the laterality of the procedure, the presence of adhesions, the fissure opening, the fissure section technique, and the surgical time.

Postoperative analysis considered the most frequent cardio-respiratory complications occurring in the immediate perioperative period and the need for corrective interventions. Other factors considered were the length of hospital stay, the need for reintervention, transfusions, and placement of a new pleural drainage with or without associated air leaks and its duration. Complications and their management were stratified according to the Clavien-Dindo classification. Oncological follow-up was conducted every 6 months, utilizing total body contrast-enhanced (CT scan). Data collection was retrospective, utilizing respective institutional databases. Parameters analyzed included overall survival (OS) and disease-free survival (DFS).

Statistical analysis

Patients' baseline characteristics were summarized by frequencies and percentages for categorical variables and medians and interquartile range (IQR) for continuous variables. Comparisons between patients who underwent segmentectomy of the left lower lobe (S6) and those who underwent other segmentectomies were performed through the chi-square test for categorical variables and the non-parametric Mann-Whitney test for continuous variables.

OS and DFS were synthetized through the Kaplan-Meier estimator, with the log-rank test used to compare survival curves across strata of patients who underwent segmentectomy of the left lower lobe as compared to the other segmentectomies. The propensity score matching

was rendered useless because of the balance between the two groups, and it did not improve the comparability of the sample after testing. The analyses were performed using R-software (4.2.1).

Results

The inclusion criteria were met by 252 patients, with 125 having an anatomical S6 resection ("S6" group) and 127 having another anatomical simple segmentectomy ("others" group).

Preoperative characteristics

Table 1 summarizes the preoperative characteristics of the population. There were no significant differences in baseline data between the two groups. In the overall analysis, the median age of patients at the time of surgery was 71±6 years (IQR, 65–76 years). There was no significant difference in the comorbidities investigated, which included diabetes, hypertension, previous cancer, cardiovascular, pulmonary, and kidney diseases. Similarly, the predictive scores for morbidity and mortality were comparable in the groups (ASA score, Charlson score, Eurolung 1 and 2). The pre-operative functional respiratory study using predictive indices did not find any significant differences [forced expiratory volume in one second (FEV1), forced vital capacity (FVC), ppoFEV1, predicted postoperative diffusing capacity for carbon monoxide (ppoDLCO), and diffusing capacity for carbon monoxide (DLCO)].

Postoperative outcomes

The majority of surgeries were performed using a thoracoscopic approach (77% VATS segmentectomy, 195/252) using a triportal technique (38%, 95/252). Trisegmentectomies (culmen) were the most performed resection in "others" group (52.8%), followed by bisegmentectomies (lingula) (43.3%) and basal pyramid (3.15%). The two groups did not have any significant differences in intraoperative variables like pleuro-parenchymal adhesions or surgical technique to complete the fissure.

The "fissureless" technique was used less, and especially S6 group showed a statistically significant tendency to approach the bronchovascular elements in a trans-scissural way (P=0.03). The number of lymph nodes removed was also observed, revealing a lower number of lymph nodes removed in the S6 group (P=0.02), mostly concerning the hilar dissection (P=0.044). Between the two groups the procedure time was shorter in "S6" group (130 *vs.* 150 min, P=0.004). The postoperative results are summarized in *Table 2*. Complete R0 resections were achieved in the entire population. Overall, 13.9% of patients (35 patients) experienced postoperative complications, 12.8% in "S6" group (16 patients) and 14.9% in the other (19 patients) (P=0.40). The most frequent postoperative complication was prolonged air-leak, reported in 6.7% of all cases (17/252 patients) without differences between the groups (P=0.80). Additionally, there were no specific complications upon the type of segmentectomy (including atelectasis, pneumonia, reintubation, oedema, atrial fibrillation, emphysema, dysphonia, hemothorax, transfusion, reoperation, or re-drain). The overall median length of hospital stay was 6 days (IQR, 5–8 days) and the median duration of drainage was 2 days (IQR, 2–4 days), without difference between the two groups (both P=0.70). The Clavien-Dindo classification, applied to the two groups, demonstrated a comparable postoperative course and ultimately the majority of complications classified as grade 1 or 2 (P=0.60). The operative mortality was zero. As for oncological characteristics: the average diameter of the lesions in the pre-operative was 12 mm; a quarter of the patients arrived at the surgery with pre-operative diagnosis; histology in 75% of the sample was compatible with pulmonary adenocarcinoma; in 12 patients (4.7%) there was a lymph node upstaging (83.3% n0 to n1, on stations 11 or 12); in 95.3% pTNM confirmed stage I disease. Oncological characteristics are summarized in *Table 2*.

Survival estimates and recurrence

The average length of follow-up was 3.7 years. Five-year OS for entire cohort was 80.3% [95% confidence interval (CI): 74.4–86.6%], 75% for "S6" group and 86.2% for the other, respectively. As a function of time, the survival analysis demonstrated a worse outcome in "S6" group, although not statistically significant (P=0.11) (*Figure 1*). Five-year DFS for the entire population was 78.2% (95% CI: 72.4–84.5%), 72.1% in "S6" group and 84.8% for "others". The difference between the two groups is highlighted above all in the worse survival for "S6" group, with evidence bordering on statistical significance (P=0.053) (*Figure 2*).

The population's characteristics related to disease

Table 1 Patients baseline characteristics

Characteristics	Overall (n=252)	Others (n=127)	S6 (n=125)	P value
Age (years)	71 (65, 76)	72 (64, 76)	71 (66, 75)	>0.99
Sex				0.07
Male	143 [57]	65 [51]	78 [62]	
Female	109 [43]	62 [49]	47 [38]	
BMI (kg/m^2)				>0.99
Underweight (<18.5)	7 [2.8]	3 [2.4]	4 [3.2]	
Normal to overweight (18.5–30)	201 [80]	101 [80]	100 [80]	
Obese (>30)	44 [17]	23 [18]	21 [17]	
Diabetes	41 [16]	15 [12]	26 [21]	0.053
Hypertension	151 [60]	69 [54]	82 [66]	0.07
Cardiovascular disease	60 [24]	29 [23]	31 [25]	0.70
Congestive heart	10 [4.0]	3 [2.4]	7 [5.6]	0.20
Peripheral vasculopathy	55 [22]	25 [20]	30 [24]	0.40
Chronic kidney disease	14 [5.6]	2 [1.6]	12 [9.6]	0.006
ASA score				0.06
1	4 [1.6]	2 [1.6]	2 [1.6]	
2	115 [46]	60 [47]	55 [44]	
3	127 [50]	59 [46]	68 [54]	
4	6 [2.4]	6 [4.7]	0 [0]	
Charlson score	5.00 (4.00, 6.00)	5.00 (3.50, 6.00)	5.00 (3.50, 6.00)	0.30
Eurolong risk score (morbidity)	8.5 (5.0, 13.0)	8.0 (5.0, 13.5)	9.0 (5.0, 13.0)	0.50
Eurolung risk score (mortality)	0.93 (0.52, 1.48)	0.90 (0.50, 1.52)	0.95 (0.56, 1.45)	0.80
FEV1 (%)	95 (79, 109)	93 (78, 108)	97 (79, 109)	0.50
ppoFEV1 (%)	87 (72, 100)	86 (69, 95)	90 (75, 102)	0.08
FVC (%)	102 (88, 115)	99 (86, 115)	104 (92, 114)	0.40
DLCO/VA (%)	84 (72, 98)	84 (70, 93)	86 (75, 102)	0.33
ppoDLCO	87 (72, 100)	96 (73, 103)	85 (72, 96)	0.28
COPD	107 [42]	47 [37]	60 [48]	0.08
Smoking history				0.80
Never	61 [24]	30 [24]	31 [25]	
Former	128 [51]	67 [53]	61 [49]	
Current	63 [25]	30 [24]	33 [26]	

Values are n [%] or median (interquartile range). ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity for carbon monoxide; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; ppoDLCO, predicted postoperative diffusing capacity for carbon monoxide; ppoFEV1, predicted postoperative forced expiratory volume in one second; VA, alveolar volume.

Table 2 Post-operative outcomes

Characteristics	Overall (n=252)	Others (n=127)	S6 (n=125)	P value
Procedure access type				0.10
VATS	184 [73]	91 [72]	93 [74]	
Robotic	11 [4.4]	9 [7.1]	2 [1.6]	
Open	57 [23]	27 [21]	30 [24]	
VATS access				0.20
Uniportal	50 [20]	26 [20]	24 [19]	
Biportal	7 [2.8]	4 [3.1]	3 [2.4]	
Triportal	95 [38]	43 [34]	52 [42]	
Simple segmentectomy type				
Tri-segmentectomy (culmen)	–	67 [52.8]	–	
Bisegmentectomy (lingula)	–	55 [43.3]	–	
Basal pyramid	–	4 [3.15]	–	
Adhesions	60 [24]	26 [20]	34 [27]	0.20
Fissure completion	184 [73]	85 [67]	99 [79]	0.03
Fissureless technique	59 [23]	35 [28]	24 [19]	0.12
Fissure completion technique				>0.99
Stapling fissure	224 [89]	113 [89]	111 [89]	>0.99
Fissure cauterization	10 [4.0]	4 [3.1]	6 [4.8]	0.50
Coagulating fissure	18 [7.1]	10 [7.9]	8 [6.4]	0.60
Number of resected lymph nodes	6.0 (4.0, 8.0)	6.0 (5.0, 8.0)	6.0 (4.0, 7.0)	0.02
N1	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	0.04
N2	3.00 (2.00, 4.00)	3.00 (2.00, 4.50)	3.00 (1.00, 4.00)	0.20
Procedure time (min)	140 (110, 185)	150 (120, 192)	130 (100, 173)	0.003
Post-operative complications	35 [13.9]	19 [14.9]	16 [12.8]	0.40
Clavien-Dindo classification				0.60
0	79 [33]	43 [36]	36 [30]	
1	146 [61]	70 [58]	76 [64]	
2	8 [3.3]	5 [4.2]	3 [2.5]	
3	6 [2.5]	2 [1.7]	4 [3.4]	
Unknown	13 [5.2]	7 [5.5]	6 [4.8]	
Atelectasis	3 [1.2]	2 [1.6]	1 [0.8]	>0.99
Pneumonia	8 [3.2]	4 [3.1]	4 [3.2]	>0.99
Reintubation	3 [1.2]	2 [1.6]	1 [0.8]	>0.99
Oedema	1 [0.4]	1 [0.8]	0 [0]	>0.99
Arrhythmia (atrial fibrillation)	6 [2.4]	4 [3.1]	2 [1.6]	0.70

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	Overall (n=252)	Others (n=127)	S6 (n=125)	P value
Emphysema	10 [4.0]	6 [4.7]	4 [3.2]	0.70
Dysphonia	3 [1.2]	3 [2.4]	0 [0]	0.20
Hemothorax	1 [0.4]	0 [0]	1 [0.8]	0.50
Transfusion	4 [1.6]	1 [0.8]	3 [2.4]	0.40
Reoperation	5 [2.0]	3 [2.4]	2 [1.6]	>0.99
Re-drain	4 [1.6]	3 [2.4]	1 [0.8]	0.60
Drainage duration (days)	2.00 (2.00, 4.00)	2.00 (2.00, 4.00)	2.00 (2.00, 4.00)	0.70
Length of stay (days)	6.00 (5.00, 8.00)	6.00 (4.00, 8.00)	6.00 (5.00, 8.00)	0.70
Prolonged air leak (>7 days)	17 [6.7]	8 [6.3]	9 [7.2]	0.80
Diameter (mm)	1.2 (0.8, 1.8)	–	–	
Lymph nodal upstaging	12 [4.7]	7 [2.7]	5 [1.98]	0.70
N1	10 [3.9]	–	–	
N2	2 [0.8]	–	–	
Histology				–
Adenocarcinoma	189 [75]	–	–	
Squamous	63 [25]	–	–	
Post-operative staging				–
Stage I	243 [96.4]	–	–	
Other stage	9 [4.6]	–	–	

Values are n [%] or median (interquartile range). In the VATS group not all specific types of access were consistently reported. VATS, video-assisted thoracic surgery.

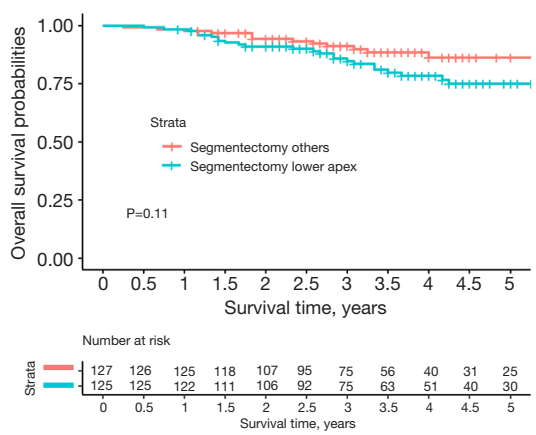

Figure 1 The 5-year overall survival.

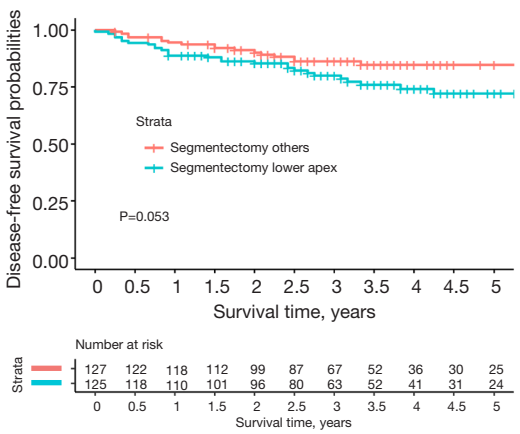

Figure 2 The 5-year disease-free survival.

Table 3 Survival estimates and recurrence

Event	Overall (n=252), n [%]	Others (n=127), n [%]	S6 (n=125), n [%]	P value
Alive without disease	151 [80]	82 [79]	69 [82]	–
Death due to disease	7 [3.7]	3 [2.9]	4 [4.8]	–
Death due to other causes	11 [5.9]	9 [8.7]	2 [2.4]	–
Alive with disease	19 [10]	10 [9.6]	9 [11]	–
Unknown	64 [42.4]	23 [18.1]	41 [32.8]	–
Recurrence	46 [18]	17 [14]	29 [23]	0.041
Regional recurrence	28 [60.8]	–	–	–
Hilar lymph nodes	22 [8.7]	15 [80]	7 [20]	<0.001

recurrence and survival estimates are described in *Table 3*. Forty-six (18.3%) patients had recurrent disease either locoregional or distant. The analysis indicated that "S6" was negatively affected by a higher number of relapses (P=0.041). The analysis of tumor's aggressiveness—through histological data on vascular, peripheral, and spread through air spaces (STAS) invasiveness—did not reveal any correlations worth mentioning. However, we point out that—out of 46 patients with relapsed disease—28 patients (60.8%) had loco-regional recurrence in the parenchyma contiguous to the surgical resection (6 patients) or to the hilar lymph nodes (22 patients). Of these, 15 patients (80%) with recurrent hilar lymph node disease belonged to the "S6" group (P<0.001).

Discussion

Segmentectomy is a valid surgical option for early-stage lung cancer. As demonstrated by different studies in carefully selected patients, sublobar resection ensures oncological outcomes comparable to lobectomy with lower postoperative morbidity and mortality, offering an advantage in terms of pulmonary function preservation (4,5).

With the increasing adoption of this procedure, it is crucial to understand whether there are differences in outcomes based on the specific lung segment removed. In our retrospective and multicenter study, 252 patients with cT1N0M0 NSCLC [8th edition International Association for the Study of Lung Cancer (IASLC)] underwent intentional segmentectomy. Our study is in line with the literature (6): no perioperative differences, such as complications or length of hospital stay, were observed between "other simple" segmentectomies and those involving the S6 segment. Data analysis revealed that, after the removal of segment S6, both DFS and OS were lower compared to other types of segmentectomy. Recurrence rates were higher in S6 group compared to others (23% *vs.* 15%). Despite no statistical significance, the data suggest that S6 may independently predict worse DFS (P=0.053).

In the majority of literature reports, survival estimates after segmentectomy show considerable variability, with an OS ranging from 58% to 93% in stage I NSCLC patients (7,8). Our research group identified a 5-year OS rate for all patients of 80.3% (95% CI: 74.4–86.6%), comparable to that reported by other retrospective studies and database reviews of patients undergoing elective segmentectomy for stage I cancer (9,10).

A retrospective study by Jones *et al.* from the United States, reported similar results, with poorer oncological outcomes in S6 NSCLC patients compared to other types of segmentectomy (11). Specifically, the 5-year DFS was 57.6% for the S6 group compared to 77.1% for S7–S10 group (P=0.15), while the 5-year OS respectively was 66.3% compared to 79.5% (S7–S10) (P=0.03). In our study, the 5-year DFS for S6 group was 76.0%, and the 5-year OS was 76.0% compared with 81.4% (P=0.053) and 80.3% (P=0.11) for the "others" group of simple segmentectomies, respectively. Additionally, the authors noted a difference based on the laterality of the procedure: right S6 showed worse OS than left S6 [hazard ratio (HR) =2.07; 95% CI: 1.09–3.95; P=0.03], but not related to DFS (HR =1.73; 95% CI: 0.96–3.12; P=0.07). This difference was partly explained by a higher incidence of lymphovascular invasion in right S6 tumors and aggressive adenocarcinoma histotype. Nevertheless, no differences were found in our study regarding the laterality. It is noteworthy that our

patient selection required accurate preoperative imaging evaluation and pulmonary function parameters that were not requested by our colleagues.

The data analysis highlighted that the rigorous approach in patient selection prior to surgery resulted in a cohort with pathological stages (pTNM) similarly to the initially determined stages. Indeed, only 4.7% of patients showed a lymph node upstaging, specifically 83.3% from n0 to n1 in stations 11 or 12. This result integrates the evidence that with a lower number of lymph nodes resected in s6 group (P=0.02), in most cases this gap concerns the hilar ones (P=0.044).

During the follow-up, we identified 46 patients who developed either local (28 patients) or distant recurrences. Locoregional recurrences occurred in 21.4% (6 patients), involving the parenchyma, while 78.6% (22 patients) affected the hilar lymph nodes. It is remarkable that 80% cases of recurrences in the hilar lymph nodes belonged to group S6 (P<0.001): this is indicative of the greater unpredictability in the lymphatic drainage of the apical segment of the lower lobe and it could potentially depend on the aforementioned intraoperative lymph-nodes dissection.

This result is in line with what has been reported in the literature (12,13), in fact it is recognized that lymphatic drainage pathways can vary based on the location of the neoplasm. Some lung segments may have less predictable drainage paths. Deng *et al.* described a predictive model for metastatic pathways, highlighting that—among patients with stage I NSCLC localized to the upper lobes—metastases to lower mediastinal lymph nodes were present in only 0.3% of cases (13). Furthermore, additional studies have investigated possible differences in drainage pathways within the same lung lobe. For instance, Watanabe *et al.* (14) analyzing patients with pathologically positive N2 lymph nodes, showed that tumors located on S6 had a higher incidence of upper mediastinal metastases than S7–S10 tumors (64% *vs.* 36%, P=0.001), with fewer subcarinal metastases (57% *vs.* 80%, P=0.004). These results, in patients with S6 tumors, suggest the need for a complete mediastinal lymphadenectomy due to a higher risk of metastasis to upper mediastinal lymph nodes.

These discrepancies in the results indicate the complexity of assessing the impact of different removed segments on the survival of patients undergoing segmentectomy for stage I lung cancer.

In both groups of our study (S6 *vs.* "other simple segmentectomies"), all resections were evaluated as R0, with a resection margin from the neoplasm greater than 1 cm. However, we could hypothesize that the higher local recurrence rate observed might be associated with the lesser amount of resected lung parenchyma and the smaller number of dissected hilar lymph nodes, being the only single-segment segmentectomy in the study. In fact, as the 2023 ESTS expert consensus on segmentectomies recommends, a distinction between single and multiple segmentectomies should be made. Indeed, the term "segmentectomy" refers to a variety of surgical resections, and the different outcomes among segments might also be attributed to the varying amounts of lung parenchyma and lymph nodes removed, even with similar surgical indications. The surgical indication for single or multiple segmentectomy is determined by the anatomical position of the tumor, ultimately influencing the amount of resected parenchyma and lymph-nodes removed, thereby potentially impacting the oncological outcome.

As recently indicated by two randomized trials (1,2), current guidelines for segmentectomy in stage I NSCLC clearly establish indications for sublobar resection without specifically considering the tumor's location. Although statistical significance was not reached, likely given the small sample size and the stringent inclusion criteria, data suggest that the involvement of the S6 segment could represent a negative prognostic factor, associated with worse DFS. Further limitations of the present study include its multicentric nature, precluding the standardization of surgical techniques, the retrospective design, and the inability to analyze the impact of solid, semi-solid, and non-solid lesions on therapeutic decisions and prognosis. Older cases lacked reliable radiological data, and a critical re-evaluation was not feasible. Including incomplete or uncertain data could have compromised the validity of our findings, so we chose to exclude this aspect.

Conclusions

In conclusion, the results suggest that the oncological outcome is not the same for all simple and intentional segmentectomies. Particularly the S6 segment, being the only single segmentectomy, exhibits worse oncological outcomes mainly in terms of DFS. This disparity could be explained by the unpredictable lymphatic drainage or by the

smaller parenchymal volume removed during dissection.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1348/rc

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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. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional ethics committee of "Spedali Civili" Hospital of Brescia (No. 5368) and individual consent for this retrospective analysis was waived.

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