

Effect of surgery on survival of patients with small-cell lung cancer undiagnosed before resection

Brice Caput, Laura Peretti¹, Stephanie Lacomme², Angelica Tiotiu^{3,4}

Department of Thoracic Surgery, Private Hospital of Nancy-Lorraine, Nancy, ¹Department of Pulmonology, Hospital of Leman, Thonon-les-Bains, ²Center of Biological Resources BB-0033-00035, University Hospital of Nancy, Vandœuvre-lès-Nancy, France, ³Department of Pulmonology, University Hospital Saint-Luc, University of Louvain, ⁴Department of Pneumology, University Hospital Saint Luc, Brussels, Pole Pneumology, ENT, and Dermatology- LUNS, Institute of Experimental and Clinical Research, Brussels, Belgium

Address for correspondence:

Dr. Angelica Tiotiu,
Department of
Pulmonology, University
Hospital Saint-Luc, 10
Avenue Hippocrate,
1200 Brussels, Belgium.
E-mail: angelica.tiotiu@
yahoo.com

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Abstract:

BACKGROUND: Standards of treatment for limited-stage small-cell lung cancer (SCLC) include chemoradiotherapy. The place of the surgery in this indication is still debated. The objective of this study was to evaluate the overall survival (OS) in patients who underwent surgery for an SCLC undiagnosed before resection in the University Hospital of Nancy, France. Secondly, the impact of surgery on recurrence-free survival (RFS) was analyzed.

METHODS: All the patients who underwent lung resection in the Department of Thoracic Surgery, from 1991 to 2018, and a diagnosis of SCLC after surgery were included. OS and RFS were analyzed according to the resection type, postoperative staging, and lymph node extension.

RESULTS: Sixty-one patients were included. The median OS was higher in patients with lobectomy than those with pneumonectomy (26 [8.4–208.7] vs. 12 [3.4–27.6] months, $P < 0.001$) in stage I compared to other stages (58 [8.4–208.7] vs. 17 [3.4–83.5] months, $P = 0.002$), and N0-1 than N2 (25 [3.6–208.7] vs. 15 [3.4–83.5] months, $P = 0.01$). RFS was also significantly higher after lobectomy than after pneumonectomy (17 [1.6–184.9] vs. 8 [0.5–17.6], $P < 0.001$), stage I than stages II-III (35 [5–184.9] vs. 11 [0.5–42.4], $P < 0.001$) and N0-1 compared to N2 (25 [1.6–184.9] vs. 9 [0.5–16.5] months, $P = 0.006$). In multivariate analysis, the only independent factor influencing the OS was the pneumonectomy (hazard ratios = 3.19; 95% confidence interval [1.46–6.98], $P = 0.004$).

CONCLUSION: Surgical resection of stage I SCLC may lead to better OS and RFS. N1 patients should not automatically be excluded from surgery. Lobectomy with regional lymph node resection is the preferable choice of surgery.

Keywords:

Overall survival, small-cell lung cancer, surgery

Small-cell lung cancer (SCLC) represents 15%–20% of all primary lung cancers. SCLC is an aggressive cancer with a median doubling time of 50 days and high metastatic potential: Two-thirds of patients are diagnosed with at least one metastasis at baseline.^[1] Without treatment, its prognosis is very poor with a median survival of 2–4 months after diagnosis.^[2] In patients with one metastasis on diagnosis, 5-year survival is estimated at 5%.^[1] It is, therefore, an emergency to treat SCLC when diagnosed.

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The gold-standard treatment for the early stage of SCLC is chemotherapy with platinum-etoposide associated with mediastinal radiotherapy, to which may be added prophylactic cranial irradiation (PCI).^[3,4] In nonmetastatic SCLC receiving standard treatment, the overall 5-year survival rate is 16%–26%, and the median overall survival (OS) is 19–23 months.^[5]

The place of the surgery in the management of the SCLC should be better defined. Various studies report that 41%–57% of SCLCs are diagnosed during lung surgery on extemporaneous histological

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analysis.^[4] Despite that several international guidelines now recommend surgical resection in the early stage of SCLC (T1-2, N0-1) based on previous studies showing a longer survival in patients treated by surgery with adjuvant therapy than those receiving nonsurgical treatment, the surgery is referred to as “option” in the French guidelines.^[3,6-12] However, progress in practice was recently observed with the surgery more frequently performed in SCLC patients from only 7% in 2004 to 21% in 2013.^[13]

The present study had as its principal objective to evaluate the impact of surgery on the OS in patients with SCLC diagnosed during the intervention, depending on the type of resection and the stage of disease. The secondary aim was to estimate the effect of surgery on recurrence-free survival (RFS) in this population.

Methods

Ethics

We included all the patients with an SCLC diagnosis on the histological examination of the resection specimen from January 1, 1991, to December 31, 2018, in the University Hospital of Nancy, France. The patients with metastatic disease, composite SCLC, and those receiving chemotherapy or radiotherapy before surgery were excluded. The study was approved by the Institutional Review Board of the French Learned Society for Respiratory Medicine – Société de Pneumologie de Langue Française (CEPRO 2022-036). Written consent was obtained from the patients or their families before the inclusion in the study.

Patient data and study design

We collected demographic and clinical data: age, gender, smoking status, the number of tobacco pack-years, date of surgery, surgical resection type (wedge-resection, lobectomy, bilobectomy, or pneumonectomy), stage of disease, date and site of recurrence, complementary treatments (chemotherapy/radiotherapy), vital status at inclusion in the study, and date of death. All histopathologic findings were checked, and each case was restaged on the basis of imaging according to the 8th tumor-node-metastasis (TNM) classification of the International Association for the Study of Lung Cancer.^[14] Recurrence was defined as signs of disease evolution on computed tomography (CT-scan) validated during the multidisciplinary meetings, including a thoracic oncologist, surgeon, radiologist, radiotherapy specialist, and pathologist without histopathological proof. Postoperative death was considered when occurring within 30 days after surgery.

The primary study endpoint was OS, defined as the time period elapsed between the date of surgery and the date

of death of any cause. The secondary endpoint was RFS, defined as the time from the date of surgery to the date of disease recurrence on the CT scan.

Statistics

Patient characteristics were reported using standard statistical descriptions: number, percentage (for the qualitative variables), median and interquartile, or mean and standard deviation (for the quantitative variables). Survival curves were estimated by the Kaplan–Meier method, analyzed, and compared by the log-rank test. OS and RFS were calculated and compared for the entire population and in the subgroups according to the surgical resection type, TNM staging, and mediastinal lymph node extension (N0-1 vs. N2 patients).

Potential factors influencing OS were identified through univariate analysis by Cox proportional hazard models. A multivariate analysis with step-wise logistic regression was performed after the univariate analysis. The results were presented as hazard ratios (HR) with a 95% confidence interval (CI). Statistical significance was defined as $P < 0.05$ for all the tests. The analyses were performed using SAS software 9.4 (SAS Institute, Cary, North Carolina).

Results

Patient characteristics

Eighty patients underwent lung surgery for SCLC in the University Hospital of Nancy, France, from 1991 to 2018. Nineteen patients were excluded, and 61 were analyzed [Figure 1]. At the end of the follow-up, only 14 (23%) patients were still alive. Forty-seven patients (77%) had died for different reasons: postoperative complications (4.9%), tumor recurrence (50.8%), or other causes unrelated to those enumerated (21.3%). Three patients died after surgery; two of them were treated by pneumonectomy.

The mean age of patients at surgery was 65.0 ± 7.0 years, and more than 95% of patients were current smokers with tobacco consumption evaluated at 40.1 ± 28.0 pack-years. The masculine gender was predominant in this study population (80.3% of patients). There were 42 lobectomies (68.9%) (including four bilobectomies), 15 pneumonectomies (24.6%), and 4 wedge resections (6.5%). Twenty patients (32.8%) were classified with postoperative stage I, 16 (26.2%) with stage II, and 25 (41%) with stage III (14 patients were IIIA and 11 patients IIIB). Fifty-one resections (83.6%) were complete (R0), seven resections (11.5%) were incomplete (R1), and margin involvement was not specified on the histological examination for 3 (4.9%) patients.

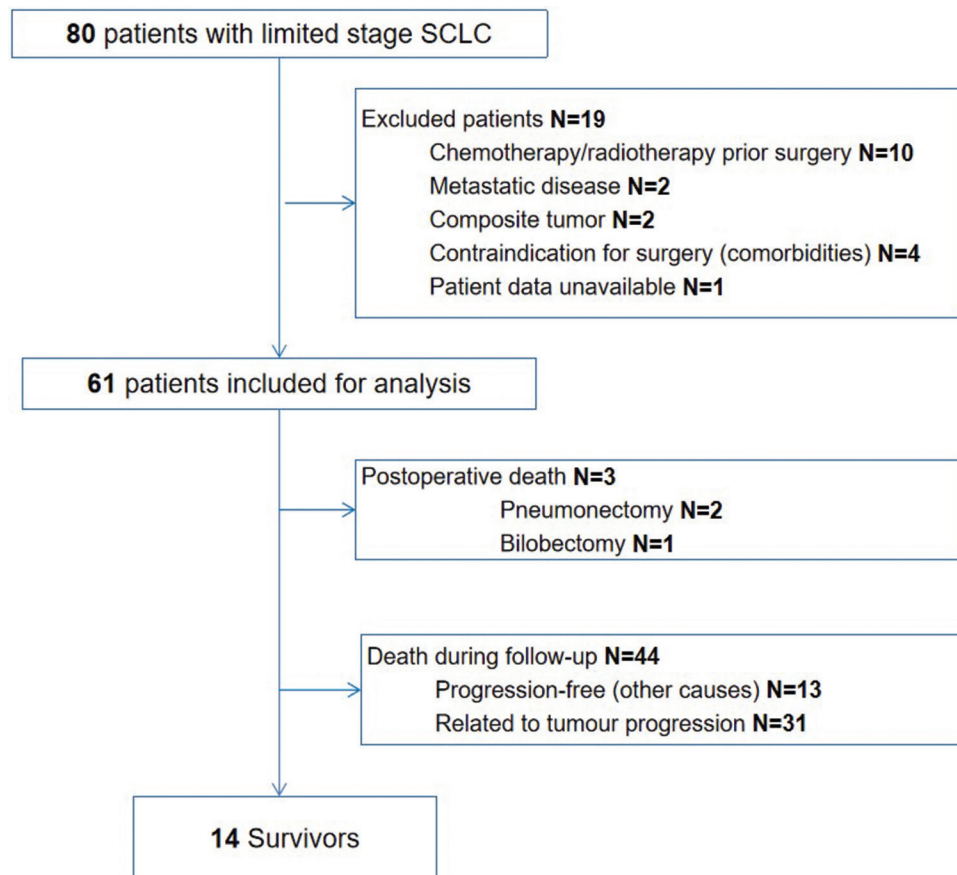


Figure 1: Flowchart of the patients operated for small-cell lung cancer between 1991 and 2018

Fourteen patients (22.9%) had no adjuvant treatment, 27 (44.3%) – concurrent radiochemotherapy, 18 (29.5%) – chemotherapy, and 2 (3.3%) – radiotherapy. Twenty patients (32.8%) received PCI. More than half of patients (54.1%) have a tumor recurrence during the follow-up. Population characteristics are summarized in Table 1.

Overall survival

The median OS for all surgical resection types and all stages of the disease was 21 (3.4–208.7) months, with corresponding 1-year, 5-year, and 10-year survival rates of 65.5%, 23.3%, and 8.9%. There were significant differences in OS according to surgical resection type. The median OS was significantly better after lobectomy/bilobectomy than after pneumonectomy (26 [8.4–208.7] months vs. 12 [3.4–27.6] months $P < 0.001$). One-year, 5-year, and 10-year survival rates after lobectomy/bilobectomy were 73.9%, 30%, and 10.9%, whereas there were no survivors 30 months after pneumonectomy. Very few patients underwent wedge resection, and the median OS was 26 (8.6–42.7) months [Figure 2a].

Similarly, the median OS was significantly higher in patients with stage I of the disease than for other

stages (58 [8.4–208.7] months vs. 17 [3.4–83.5] months, $P = 0.002$), with a 1-year, 5-year, and 10-year survival rates of 88.2%, 45%, and 13.5%, respectively, 51.4%, 2.9%, and 0% (all $P < 0.001$) [Figure 2b]. The median OS was also significantly better for N0-1 patients than in N2 patients (25 [3.6–208.7] months vs. 15 [3.4–83.5] months, $P = 0.01$) [Figure 2c]. One-year, 5-year, and 10-year survival rates for the patients with N0-1 were 54.8%, 12.9%, and 6.5%, while for those with N2 – 50%, 6.3%, and 0% (all $P \leq 0.01$). Ten patients (16.4%) had OS >5 years, and eight of them had no signs of disease recurrence at the end of the study.

Factors influencing overall survival

In univariate analysis, several factors were identified as associated with poor prognosis: pneumonectomy (HR = 4.47, 95% CI [2.21–9.04], $P < 0.001$), TNM stage $\geq$ II (HR = 2.79, 95% CI [1.39–5.56], $P = 0.004$), lymph node extension N2 (HR = 2.76, 95% CI [1.43–5.31], $P = 0.003$), and disease recurrence (HR = 2.22, 95% CI [1.13–4.36], $P = 0.02$). Multivariate analysis adjusted for these criteria found that the only one independent factor influencing OS was the pneumonectomy, with an HR of 3.19, 95% CI (1.46–6.98), $P = 0.004$. These data are summarized in Table 2.

Table 1: Patient characteristics (n=61) in the study population

Characteristics	n (%)
Sex (male)	49 (80.3)
Smoking status (current smoker)	58 (95.1)
Resection type	
Wedge resection	4 (6.5)
Lobectomy/bilobectomy	42 (68.9)
Pneumonectomy	15 (24.6)
Stage IASLC	
Stage I	20 (32.8)
Stage II	16 (26.2)
Stage III	25 (4.0)
Tumor classification	
T1	24 (39.3)
T2	17 (27.8)
T3	12 (19.7)
T4	8 (13.1)
Mediastinal lymph node staging	
N0	23 (37.7)
N1	20 (32.8)
N2	18 (29.5)
Histological analysis of resection specimen	
Capsular invasion	6 (9.8)
Incomplete resection	7 (11.5)
Invaded visceral pleura	12 (19.7)
Adjuvant treatment	
None	14 (22.9)
Chemotherapy	18 (29.5)
Radiotherapy	2 (3.3)
Concurrent radiochemotherapy	27 (44.3)
PCI	20 (32.8)
Tumor recurrence	33 (54.1)
Survival rate	14 (23.0)

IASLC=International Association for the Study of Lung Cancer,
PCI=Prophylactic cranial irradiation

Recurrence-free survival

The median RFS was 18 (0.5–184.9) months. RFS rates at 1 year, 5 years, and 10 years after surgery were 68.4%, 32.7%, and 29%. During the 1st-year follow-up, 16 (27.4%) patients had disease recurrence (eight patients after pneumonectomy, six after lobectomy/bilobectomy, and two after wedge resection). The median survival time after disease recurrence was 4.5 (0.3–6.9) months, and 75% of patients died within 6 months after recurrence.

The median RFS was significantly higher after lobectomy/bilobectomy (17 [1.6–184.9] months) than after pneumonectomy (8 [0.5–17.6] months) or wedge resection (6.4 [5–7.7]) (all $P < 0.001$) [Figure 3a]. RFS was also significantly higher in stage I than in stages II–III (35 [5–184.9] vs. 11 [0.5–42.4], $P < 0.001$) [Figure 3b]. Patients with N0-1 extension had a significantly higher median RFS than those with N2 (25 [1.6–184.9] vs. 9 [0.5–16.5] months, $P = 0.006$) [Figure 3c].

All seven patients with R1 had disease recurrence in the first 21 months after surgery despite the adjuvant chemotherapy. Four of them received also thoracic radiotherapy.

Discussion

Despite that several international guidelines recommend surgery for patients with early-stage N0 SCLC, the implementation of this treatment option in practice remains suboptimal and most patients receive the standard of care including platinum-based chemotherapy, with or without thoracic radiotherapy according to the stage of disease.^[7-9] The present study including patients having resections for histological diagnosis suggests that the surgery represents an interesting therapeutic option for patients with early-stage of SCLC and N0-1 in terms of OS and RFS.

The median OS after resection in our study was 21 months, lower than the value of 36 months found in another similar study, including patients with stages I–III SCLC.^[15] Similarly, 1-year, 5-year, and 10-year survival rates were 65.5%, 23.3%, and 8.9%, smaller than the values reported by another one, 73.6%, 42%, and 25.6%. A possible explanation for this difference is that in the Italian study, the diagnosis of SCLC was well established before the surgery, and all patients underwent surgical resection with curative intent in contrast with our study where the histological diagnosis was obtained after resection. Our results are comparable to those found in other similar studies in terms of median OS (18 months) and 5-year survival rate (21.7% in a Caucasian population and 28.6% in an Asiatic population).^[16,17] Only 77% of patients included in the present study had adjuvant therapy after surgery as recommended by current guidelines from stage I of SCLC.^[7-9] Effectively, a recent large study showed that the median OS of patients treated by surgery-plus-chemotherapy was significantly higher than that of those treated by surgery-alone (35 months vs. 23 months, $P = 0.002$).^[17] In the same line, another study showed better results than ours with a median OS of 56 months and a 5-year survival rate of 46% in patients with stage IA–IIIB SCLC treated by surgery combined with chemotherapy and/or thoracic radiotherapy.^[16] The patients who did not receive adjuvant treatment in our study were those with postoperative complications and/or important comorbidities.

There were significantly different survival rates depending on the type of surgery, with better results after lobectomy. There was no survivor 30 months after pneumonectomy, while the 5-year OS rate was 30% after lobectomy and 50% after wedge resection.

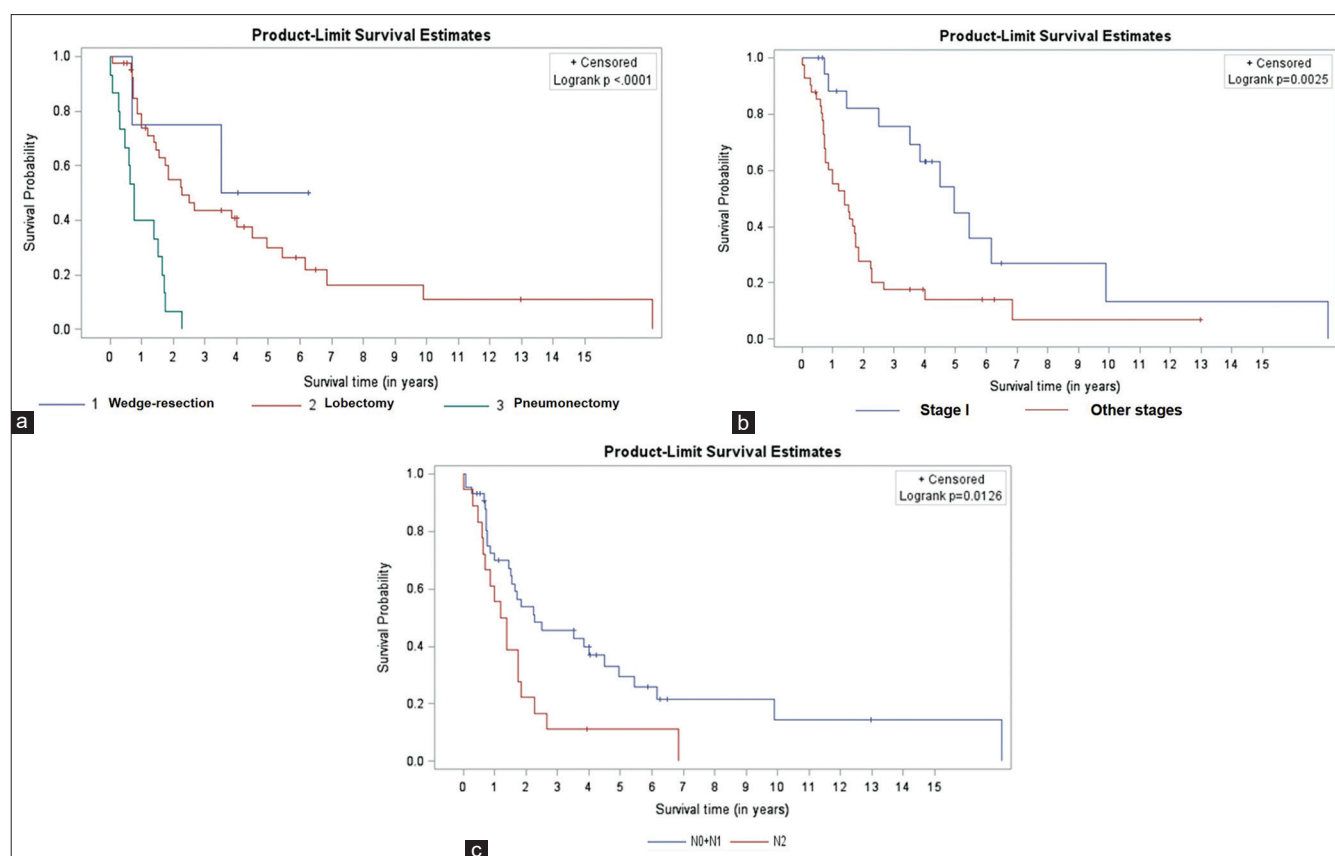


Figure 2: (a) Overall survival (OS) according to surgery resection type. (b) OS according to the International Association for the Study of Lung Cancer stage. (c) OS according to mediastinal lymph node extension (N0-N1 vs. N2)

Table 2: Factors influencing overall survival identified by univariate and multivariate analyses

Parameter	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	0.98 (0.94–1.02)	0.430		
Gender (male vs. female)	1.12 (0.55–2.29)	0.750		
Tobacco consumption (pack-year)	0.99 (0.98–1.00)	0.110		
Stage IASCL ($\geq$ II vs. I)	2.79 (1.39–5.56)	0.004	1.08 (0.13–9.06)	0.950
Surgery resection type				
Lobectomy/bilobectomy	1			
Wedge resection	0.58 (0.13–2.46)	0.463	0.62 (0.14–2.71)	0.530
Pneumonectomy	4.47 (2.21–9.04)	<0.001	3.19 (1.46–6.98)	0.004
Incomplete resection	1.19 (0.46–3.05)	0.720		
Adjuvant treatment				
None	1			
Concurrent radiochemotherapy	0.75 (0.29–1.93)	0.560		
Chemotherapy	1.52 (0.55–4.23)	0.420		
Radiotherapy	5.37 (0.95–30.17)	0.060		
Mediastinal lymph node extension	2.76 (1.43–5.31)	0.003	2.55 (0.34–19.39)	0.370
Recurrence	2.22 (1.13–4.36)	0.020	1.32 (0.61–2.86)	0.480

IASCL=International Association for the Study of Lung Cancer, HR=Hazard ratio, CI=Confidence interval

The consequences of postoperative complications were not evaluated here, except the death occurred in three patients. The lobectomy was performed for nearly 70% of patients and is usually associated with a better OS in SCLC than pneumonectomy.^[5,6,15] In multivariate analysis, pneumonectomy was an independent risk

factor for mortality. This result confirms those of other studies that found that pneumonectomy is associated with worse long-term survival in SCLC, probably related also to higher stage and more lymph node involvement.^[6,15,18] The OS results in this study were probably impacted by the high rate of

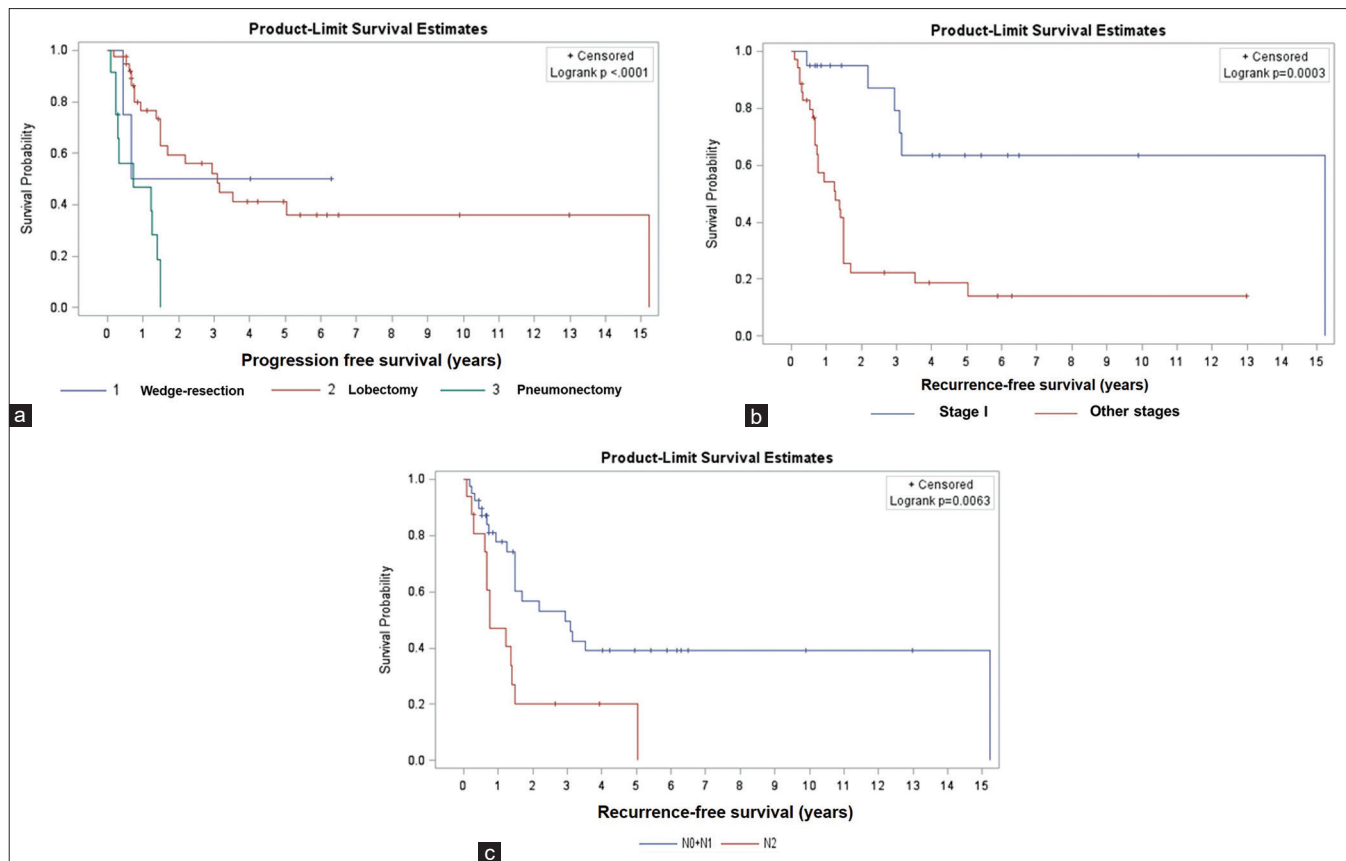


Figure 3: (a) Recurrence-free survival (RFS) according to surgery resection type. (b) RFS according to the International Association for the Study of Lung Cancer stage. (c) RFS according to mediastinal lymph node extension (N0-N1 vs. N2)

pneumonectomies (nearly 25% of patients) compared to other studies (17%).^[15] Fortunately, over time, we observed that the proportion of lobectomies increased, while the number of pneumonectomies decreased, suggesting changes in our practice. In our study, the OS for patients with wedge resection was similar to other previous data.^[1,10,11] However, the RFS was shorter in these patients compared to those treated by lobectomy. Usually, wedge resection is reserved for patients with poor lung function or histological diagnosis. A previous study showed that the survival of patients after wedge resection was still significantly longer than survival in those receiving medical treatment alone.^[11]

Several studies showed that the quality of surgical resection has an impact on survival with better OS and lower risk of locoregional relapse after R0 resection, respectively, and shorter OS after R1 resection.^[19] In addition, the absence of an adjuvant treatment after R1 resection allowed for no benefit of the surgery.^[12] In our study, OS was not affected by the quality of surgical resection, but all seven patients with R1 resection had disease recurrence in the first 21 months after surgery despite the adjuvant treatment.

The stage I patients had a longer OS and RFS than those with stage II or III. The 5-year OS for the patients with stage I in our study was 45%, comparable to the value found in another study on an Asiatic population (43.4%) but lower than those reported by a similar study on a Caucasian population (62.9%).^[18] Despite that the OS is better for stage I compared to the others, recent data suggest the benefits of surgery followed by adjuvant treatment even for stage II–IIIA compared to the nonsurgical strategy.^[7,13,17,20–22] The lymph node extension influenced also the OS with a longer median survival for the patients N0–1 compared to those N2. The N0 stage is widely recognized as a favorable prognosis factor, associated with a 5-year OS rate of 41.5%–66%, against only 6.8%–10% for N + patients.^[15] In another French study, the median OS was 10 months in N2 patients, justifying that lymph node staging should be performed systematically before surgery.^[16] However, staging must not delay treatment, and it is important to select patients eligible for surgery, using a diagnostic method with the highest possible specificity and sensitivity.^[21] Furthermore, several studies showed a positive impact of surgery combined with adjuvant treatment on OS even in N + patients compared to the standard medical care.^[10,12] Lymph node involvement and stage ≥ 2 were

identified as negative prognosis factors for OS in our study, as previously reported.^[10,15,17,20]

To the best of our knowledge, this is the first time in the literature that the RFS is analyzed in a SCLC population treated by surgery and we found a median of 18 months. Stage I patients who underwent lobectomy had significantly superior RFS than other patients, as well as N0-N1 patients compared to N2 patients. Unfortunately, disease recurrence was enregistered 4.5 months after surgery, and three-quarters of patients died within 6 months after recurrence. These data confirm the well-recognized aggressivity of this cancer and our limited resources to treat it. However, the surgery could have a positive impact on the RFS in selected early-stage patients.

This study has several limitations. It is a retrospective, monocentric study, including a limited number of patients, despite a long duration of inclusions. As the aim of the study was to analyze the survival in patients treated by surgery for an SCLC without histology before the resection, the presence of a control group was not considered necessary. Despite these limitations, our results are in line with other current data that showed the benefits of the surgery associated with chemoradiotherapy compared to the nonsurgical strategy in patients with early stages of SCLC in terms of OS.^[6,7,10,13,20,22,23]

Conclusion

In summary, even in patients who underwent surgical resection for histology, surgery showed benefits in terms of survival comparable to those obtained in studies realized with curative intent for localized SCLC. According to our results for OS and RFS, and considering current evidence, patients with stage I could be considered the best candidates for surgery, in a multidisciplinary setting. Patients with stage II and III disease should be carefully selected for surgery in raison of worse survival. Chemoradiotherapy after surgery is mandatory in the case of mediastinal lymph node extension.

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Conflicts of interest

There are no conflicts of interest.

References

- Combs SE, Hancock JG, Boffa DJ, Decker RH, Detterbeck FC, Kim AW. Bolstering the case for lobectomy in stages I, II, and IIIA small-cell lung cancer using the national cancer data base. *J Thorac Oncol* 2015;10:316-23.
- Le Péchoux C, Besse B, Ferreira I, Bretel JJ, Bruna A, Mazeron R, *et al.* Small cell lung cancer (CPC). Management of patients presenting with limited stage small cell carcinoma of the lung. *Rev Mal Respir* 2006;23:16S188-97.
- Cancer Bronchique à Petites Cellules – Référentiel National de RCP – Ref : RECOKBRAPETCEL15. Available from: <https://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Cancer-bronchique-a-petites-cellules-Referentiel-national-de-RCP>. [Last accessed on 2024 Feb 08].
- Turrisi AT 3rd. Limited stage small cell lung cancer: Treatment and therapy. *Curr Treat Options Oncol* 2003;4:61-4.
- Turrisi AT 3rd, Kim K, Blum R, Sause WT, Livingston RB, Komaki R, *et al.* Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *N Engl J Med* 1999;340:265-71.
- Lüchtenborg M, Riaz SP, Lim E, Page R, Baldwin DR, Jakobsen E, *et al.* Survival of patients with small cell lung cancer undergoing lung resection in England, 1998-2009. *Thorax* 2014;69:269-73.
- Rudin CM, Ismaila N, Hann CL, Malhotra N, Movsas B, Norris K, *et al.* Treatment of small-cell lung cancer: American society of clinical oncology endorsement of the American college of chest physicians guideline. *J Clin Oncol* 2015;33:4106-11.
- Früh M, De Ruysscher D, Popat S, Crinò L, Peters S, Felip E, *et al.* Small-cell lung cancer (SCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013;24 Suppl 6:i99-105.
- Kalemkerian GP, Loo BW, Akerley W, Attia A, Bassetti M, Bumber Y, *et al.* NCCN guidelines insights: Small cell lung cancer, version 2.2018. *J Natl Compr Canc Netw* 2018;16:1171-82.
- Schreiber D, Rineer J, Weedon J, Vongtama D, Wortham A, Kim A, *et al.* Survival outcomes with the use of surgery in limited-stage small cell lung cancer: Should its role be re-evaluated? *Cancer* 2010;116:1350-7.
- Weksler B, Nason KS, Shende M, Landreneau RJ, Pennathur A. Surgical resection should be considered for stage I and II small cell carcinoma of the lung. *Ann Thorac Surg* 2012;94:889-93.
- Wakeam E, Acuna SA, Leighl NB, Giuliani ME, Finlayson SR, Varghese TK, *et al.* Surgery versus chemotherapy and radiotherapy for early and locally advanced small cell lung cancer: A propensity-matched analysis of survival. *Lung Cancer* 2017;109:78-88.
- Wakeam E, Varghese TK Jr., Leighl NB, Giuliani M, Finlayson SR, Darling GE. Trends, practice patterns and underuse of surgery in the treatment of early stage small cell lung cancer. *Lung Cancer* 2017;109:117-23.
- Chansky K, Detterbeck FC, Nicholson AG, Rusch VW, Vallières E, Groome P, *et al.* The IASLC lung cancer staging project: External validation of the revision of the TNM stage groupings in the eighth edition of the TNM classification of lung cancer. *J Thorac Oncol* 2017;12:1109-21.
- Casiraghi M, Sedda G, Del Signore E, Piperno G, Maisonneuve P, Petrella F, *et al.* Surgery for small cell lung cancer: When and how. *Lung Cancer* 2021;152:71-7.
- Riquet M, Le Pimpec Barthes F, Scotté F, Fabre E, Cazes A, Foucault C, *et al.* Relevance of surgery in small cell lung cancer. *Rev Pneumol Clin* 2009;65:129-35.
- Ye P, Guo Z, Zhang Y, Dong C, Li M. Surgery plus chemotherapy versus surgery alone for limited-stage small-cell lung cancer: A population-based survival outcome analysis. *Front Oncol* 2021;11:676598.
- Kawano D, Okamoto T, Fujishita T, Suzuki Y, Kitahara H, Shimamatsu S, *et al.* Surgical results of resectable small cell lung cancer. *Thorac Cancer* 2015;6:141-5.
- Weckler BC, Baldes N, Schirren J. Survival following multimodality treatment including surgery for stage IA-IIIB small-cell lung cancer. *Thorac Cardiovasc Surg* 2019;67:291-8.

20. Yang Y, Yuan G, Zhan C, Huang Y, Zhao M, Yang X, *et al.* Benefits of surgery in the multimodality treatment of stage IIB-IIIC small cell lung cancer. *J Cancer* 2019;10:5404-12.
21. Veronesi G, Bottoni E, Finocchiaro G, Alloisio M. When is surgery indicated for small-cell lung cancer? *Lung Cancer* 2015;90:582-9.
22. Chai Y, Ma Y, Feng W, Lu H, Jin L. Effect of surgery on survival in patients with stage III N2 small cell lung cancer: Propensity score matching analysis and nomogram development and validation. *World J Surg Oncol* 2021;19:258.
23. Yang CJ, Chan DY, Shah SA, Yerokun BA, Wang XF, D'Amico TA, *et al.* Long-term survival after surgery compared with concurrent chemoradiation for node-negative small cell lung cancer. *Ann Surg* 2018;268:1105-12.