



HAL
open science

Outcomes after pulmonary lobectomy in patients with history of head and neck carcinoma

Josephine Chenesseau, Tchala Kassegne, Myriam Ammi, Sacha Mussot, Dominique Fabre, Delphine Mitilian, Stephane Temam, Olaf Mercier, David Boulate, Elie Fadel

► To cite this version:

Josephine Chenesseau, Tchala Kassegne, Myriam Ammi, Sacha Mussot, Dominique Fabre, et al.. Outcomes after pulmonary lobectomy in patients with history of head and neck carcinoma. *Respiratory Medicine and Research*, 2021, 80, pp.100857. 10.1016/j.resmer.2021.100857 . hal-04534999

HAL Id: hal-04534999

<https://hal.science/hal-04534999>

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Outcomes after Pulmonary Lobectomy in Patients with History of Head and Neck Carcinoma

Running Head: Lobectomy and head and neck carcinoma

Josephine Chenesseau¹, MD, MSc, Tchala Kassegne¹, MD, Myriam Ammi¹, MD, MSc, Sacha Mussot¹,
MD, MSc, Dominique Fabre¹, MD, PhD, Delphine Mitilian¹, MD, Stephane Temam², MD, Olaf
Mercier¹, MD, PhD, David Boulate^{1,¶,*}, MD, PhD, Elie Fadel^{1,¶}, MD, PhD

Institutions and Affiliations:

¹ Marie Lannelongue Hospital, Groupe Hospitalier Paris Saint-Joseph, Department of Thoracic Surgery, Le Plessis-Robinson, France

² Gustave Roussy Institute, Department of Otorhinolaryngology and Head and Neck Surgery, Villejuif, France

¶ David Boulate and Elie Fadel contributed equally to the work

Meeting presentation

A part of the study was presented at the World Conference on Lung Cancer in 2019 at Barcelona, Spain: Boulate, D., et al. "P2. 17-24 Minimally Invasive Surgery for Lung Cancer Improves Short Term Outcomes in Patients with History of Head and Neck Carcinoma." *Journal of Thoracic Oncology* 14.10 (2019): S893-S894.

Keywords: Head and neck carcinoma; lung cancer; minimally invasive surgery; lobectomy; outcomes.

Classification: Original article

Total Word count: 4498

Corresponding author

David Boulate at department of thoracic surgery, Hopital Marie Lannelongue, Groupe Hospitalier Paris Saint-Joseph, 133 avenue de la Résistance, 92350, le Plessis-Robinson, France.

Abstract

Background

We aimed to determine whether video assisted thoracic surgery (VATS) was associated with better short-term outcomes compared to open approach and to determine factors affecting long term survival after lobectomy in patients with history of head and neck carcinoma (HNC).

Methods

We performed a retrospective monocentric analysis of consecutive standard lobectomies performed for lung cancer in patients with history of HNC between 2010 and 2017. Patients' characteristics, surgical approach, lung tumor histology, in-hospital and 90-days morbi-mortality and long term survival were analyzed; VATS and open lobectomy groups were compared.

Results

Among 85 patients, 52 underwent an open lobectomy and 33 a VATS lobectomy. There was no significant difference between the two groups regarding age, preoperative characteristics, pathology and stage of lung cancer (All p=NS). In the VATS group, there was a significant decrease in proportion of in-hospital postoperative life-threatening complications requiring hospitalization in intensive care unit (12/52 vs. 1/33, p=0.01). The 90-days postoperative comprehensive complication index was significantly increased in the open thoracotomy group (median (interquartile range):33.5 (0-53.5) vs. 8.7 (0-34.1), p=0.018). Long term survival was not significantly different between the 2 groups - Log-rank test comparison, p=NS). Patients with squamous cell histology presented a significantly poorer survival (both Log-rank test comparison, p<0.01).

Conclusions

Minimally invasive approach improved in-hospital and 90-days outcomes compared to open surgery for lung cancer resection in patients with history of HNC. The poor long-term results in patients with squamous cell carcinoma highlight the need to improve therapeutic strategies for this subset of patients.

Abstract wordcount: 249 words.

Introduction

Patients with head and neck carcinoma (HNC) represent a particular group at risk to develop complications after anatomical resection of synchronous or metachronous lung carcinoma [1-3]. History of swallowing disorders, chemotherapy and radiation and chronic alcohol consumption confer a higher risk of postoperative complications. Minimally invasive surgical approaches are thought to limit the risk of postoperative complications in subset of patients presenting frailty as aging[4, 5] and has proven benefits in reduction of postoperative pain[6], hospital stay duration and postoperative complications [7-11].

Few studies have evaluated the benefits of minimally invasive surgery for anatomical lung cancer resection in patients with history of HNC despite secondary primary lung cancer presents an increased incidence among these patients [3, 12-14]. Furthermore, localized squamous cell carcinoma (SCC) eligible for VATS lobectomy may be either primary lung cancer or a metastasis from the HNC that could decrease the overall benefits of surgical lung resection. Within last decades minimally invasive thoracic surgery has shown to improve postoperative outcomes compared to open surgery. We estimated that short-term outcomes after lung cancer resection in patients with history of HNC could be of particular importance considering the higher operative risk and the potentially limited long-term benefits. Moreover, in the setting of synchronic HNC, limiting postoperative morbidity may be considered of utmost importance because postoperative morbidity could preclude optimal management of the HNC.

To date, superiority of minimally invasive approach has been long to establish and is supported by multicenter cohort and current prospective trial [15] in the general population of patients with primary lung cancer. In this study, we hypothesized that minimally invasive thoracic surgery compared to open thoracotomy could promote better short-term outcomes after lung cancer resection for patients with history of HNC. As SCC are more frequent in patients with history of HNC and because the distinction between a primary lung cancer and a single metastasis of HNC is

often impossible, we further evaluated the impact of the pathological sub-type of SCC on short term and long-term outcomes, hypothesizing that SCC were associated with worst short-term and long-term outcomes compared to non-SCC lung cancers.

The main objective was to determine whether minimally invasive surgery was associated with improved postoperative short-term outcomes compared to open thoracotomy. The secondary objective was to evaluate the impact the lung tumor pathology on long term survival. The period of this study includes the transition from the systematic open approach to the current minimally invasive approach which is performed by video-assisted thoracic surgery (VATS, not robotic) in our institution.

Patients and Methods

The study protocol was approved by our internal review board (IRB 00012157).

Study population and measurements

We performed a retrospective analysis of the consecutive patients with history of HNC who underwent a lobectomy for lung cancer at Marie Lannelongue Hospital between January 2010 and December 2017 and selected patients who underwent simple lobectomies. A total of 1874 patients underwent a lobectomy at the Hospital Marie Lannelongue between 2010 and 2017. Among these patients, 98 patients underwent a lobectomy for lung cancer with a history of HNC (5.4%), we excluded 13 of the 98 patients who underwent complex lobectomies (parietectomy, n=5; bronchoplasty, n=3; arterioplasty, n=5). The study population was constituted of 85 patients. We reported epidemiological data including HNC location, metachronous status (i.e. delay \geq 6 months between HNC diagnosis and lung cancer diagnosis), preoperative treatments undertaken for HNC, preoperative cardiac and respiratory conditions, preoperative biological inflammation, preoperative swallowing disorders and preoperative end tracheostomy and postoperative pathological classification. The follow-up was performed until October 1st 2020 by using the online INSEE (Institut

national de la statistique et des études économiques) database recording all the deaths occurring in France updated monthly (<http://phgervais.free.fr/>).

All decisions for surgery were validated at a preoperative multidisciplinary staff meeting. Anatomical lobectomies were performed along with systematic mediastinal lymph node dissection under the supervision of a staff surgeon. The surgical approach was let at the discretion of the surgeon. The VATS program started in 2014. Open resections were performed by posterolateral thoracotomy with systematic proposition for perioperative thoracic peridural analgesia. VATS resection were performed through a 3 ports anterior approach associated with peroperative subpleural analgesic catheter placement. In case of preoperative swallowing disorder, a peroperative tracheostomy was proposed to minimize the risk of postoperative aspiration pneumonia and the decision was let to the surgeon discretion after discussion with the patient. In case of synchronous HNC and lung cancer with indications for local treatments in both locations, we intended to prioritize lung cancer resection to limit the risk of postoperative aspiration.

The first postoperative night held in the continuous monitoring unit. The patient was transferred to the intensive care unit (ICU) only in case of life-threatening conditions.

Lung cancer were classified according to the 8th TNM classification[16]. In-hospital and 90-days postoperative complications were classified according to the Clavien-Dindo classification [17] and by computing the comprehensive complication index [18].

Statistical analysis

Continuous variables were expressed as median and interquartile range to address non-normal distribution; categorical variables were expressed as numbers and percentages. Comparisons between the 2 groups were performed using Mann Whitney test for continuous variables and Chi² or Fisher's exact test for categorical variables, adequately. To evaluate the association between potential risk factors and severe postoperative complications (Clavien-Dindo grade III to V), we performed an univariate logistic regression and reported Odd ratios, 95% confidence intervals and P

for each variable. P-value<0.05 was considered significant. To further identify potential risk factors for severe complications (Clavien-Dindo III, IV or V), we performed a multiple logistic regression approach based on the univariate analysis results by selecting manually the potentially independent explanatory variables with $p \leq 0.10$. Long term survival comparisons were performed by using Log-rank tests. Statistical analysis was performed with Graphpad *Prism* version 8.

Results

Patients Characteristics

Fifty-two patients (61%) underwent an open lobectomy and 33 (39%) a VATS lobectomy. There was no significant difference between groups regarding epidemiology, preoperative characteristics and lung cancer stages and pathology (Table 1, All $p = NS$).

Metachronous lung cancer developed in 57 patients with median delay of 36 months (extremes 6-300 months) between HNC and the lung cancer diagnoses. Among the 28 patients who were considered with simultaneous lung cancer and HNC 15 patients underwent lung cancer resection prior to local HNC treatment.

Operative characteristics and cancer staging

The 52 open lobectomies were performed between March 2010 and October 2017 and the 33 VATS lobectomies were performed between October 2013 and September 2017 (Figure 1A). The annual numbers of open and VATS lobectomy were reported in the Figure 1A. Two conversion into thoracotomy occurred in the VATS group, one for a non-palpable nodule, the other for a lymph node adherent to the pulmonary artery. We performed 5 additional peroperative wedge resection in remaining lobes including 4 in the open group.

In-hospital postoperative course

Two patients died within the in-hospital stay only in the open group secondary to cardiac arrhythmia associated with the development of severe acute respiratory distress syndrome (ARDS).

The postoperative outcomes comparisons were reported in the Table 2. The annual proportions of Clavien-Dindo grade III, IV and V complications were reported in the Figure 1B.

Reoperations were required in 10 patients (open, n=6; VATS, n=4; P=NS) because of bronchial fistula in 2 cases (VATS, n=1), persistent pneumothorax/airleak or pleural empyema in 5 cases (VATS, n=1), middle-lobe volvulus in 1 case (VATS, n=1) and bleeding in 2 case (VATS, n=1).

Postoperative discharge were at home in 67 patients (open, n= 40; VATS, n=27, p=NS), at postoperative rehabilitation departments in 11 patients (open, n = 6; VATS, n=5; p=NS), at HNC department in 3 (open, n=2; VATS, n=1; p=NS); death n=2 in the open group and unknown in 2 cases in the open group.

Among the 20 patients with preoperative swallowing disorders, 11 underwent a peroperative tracheostomy, of these 11 patients 5 patients were treated for pneumonia with antibiotics including 1 requiring ICU for severe sepsis, 2 required fibroscopy only and 1 required ICU for ARDS. Among the remaining 9 patients with preop swallowing disorders without peroperative tracheotomy, 7 developed a postoperative pneumonia treated with antibiotics including 1 who required ICU. Among patients with preoperative swallowing disorders, there was no significant difference between the proportions of pneumonia or ARDS between patients with or without peroperative tracheostomy (6/11 vs. 7/9, p=NS).

Among the 6 patients with preoperative end tracheostomy, 2 developed postoperative pneumonia treated with antibiotics including 1 who required ICU hospitalization, a third patient required postoperative fibroscopy for airway cleaning.

Evaluation of 90-days morbi-mortality

Eight required re-hospitalization within the postoperative 90 days for complications, 7 in the open group and 1 who died was in the VATS group (Table 2). At re-hospitalization, complications' severity were Grade I in 1 case, grade II in 1 case, grade III in 3 cases, grade IV in 1 case and grade V in

1 case (the patient of the VATS group). All of these 8 patients had presented at least one postoperative complication at time of the first hospitalization grade II (n=1), grade III (n=4) and grade IV (n=3). The 90-days comprehensive complication index was significantly increased in the open group (Table 2).

Univariate analysis of factors associated with severe postoperative complications

Factors associated with postoperative complication grade III, IV or V of the Clavien-Dindo classification were reported in the Table 3.

Multiple logistic regression

As the 8 patients with 90 days re-hospitalizations already presented grade III or IV Clavien-Dindo in-hospital complications, the same models were used to predict both in-hospital and 90 days postoperative grade III, IV or V complications.

Based on the univariate analysis we manually selected open surgical approach, preoperative CRP above normal, swallowing disorders and SCC as explanatory variables in a multiple logistic regression. Open surgical approach, preoperative swallowing disorders and SCC were significantly associated with occurrence of 90-days postoperative Clavien-Dindo grade III to V complications; Whereas preoperative CRP above normal was not (Table 4).

Long term survival

At October 10th 2020, the median follow-up was 37.8 months (IQR: 12.8 – 60.55) and median overall survival was 43.7 months.

Open surgical approach presented similar long-term outcomes compared to VATS (Figure 2); in the open group the estimated median survival was 34.1 months vs. 44.3 months in the VATS group (P=NS); whereas SCC histology was associated with poorer long term survival with an estimated median survival of 21 months vs. 69 months in the group with non-SCC (p<0.001)(Figure 2).

Proportions of lung cancer stage I, stage II and stage III were not significantly different between patients with SCC histology (n=35) vs. patients with non-SCC histology (n=50) (respectively 60%, 29% and 11% vs. 80%, 12% and 4%, p=0.11). Among patients with stage I lung cancer, the long term survival was significantly decreased in patients with SCC compared to patients with non-SCC histology (Figure 3).

Discussion

This study confirmed the high morbi-mortality burden among patients undergoing pulmonary lobectomy with history of HNC and VATS approach was associated with reduction of postoperative major complications and hospital-stay duration compared to open approach. As this study was performed during the learning curve of VATS lobectomy, the VATS benefits may be even greater than observed. However, this benefit did not remain over time. Importantly, SCC was associated with impaired short- and long-term outcomes, even in the main subgroup of patients with stage I carcinoma. Taken together, our results confirm the already known benefits of VATS lobectomy over open approach in this particular group of patients and highlight the need to improve our recognition of lung metastasis of SCC that preclude the long term benefits of lobectomy. Also preoperative swallowing disorders was associated with poorer short term outcomes after surgery.

To our knowledge, this is the first study evaluating VATS approach in patients with history of HNC. Despite the limited power of the study, the magnitude of the benefits of VATS lobectomy in this population may explain the significance of the results. This is in line with previously reported benefits of VATS lobectomy patients with frailty [5, 19]. Briend et al. reported a significantly increase rate of postoperative mortality among 65 patients with history of HNC compared with 120 patients without history of HNC operated for lung cancer resection in a single center between 2006 and 2012 (8.5% vs. 1.7%) [3]. Our study was underpowered to prove benefits of VATS lobectomy on mortality alone as the overall postoperative 90-days mortality was 3.5% (3/85). In the general population of patients with operable lung cancer, in-hospital mortality after lobectomy is reported between 1.3% after

VATS and 2.5% after open lobectomy ($p < 0.001$) among 9393 patients who underwent a lobectomy with a proportion of VATS of 35% and of open of 65% between 2009 and 2012[20]. To date, the standard of postoperative in-hospital mortality after lobectomy is around 2%[21]. Despite our results of overall mortality after lobectomy may be considered acceptable compared to the existing standards, we observed 43.5% of grade III + IV + V in-hospital complications (28.2% + 12.9% + 2.4%, respectively). Consistently, Briend et al. reported a rate of 42.4% of severe postoperative complications (death, shock, need for mechanical ventilation or pneumonia) in the group with history of HNC compared to 15.8% ($P < 0.001$) in the group without [3].

The poorer long term prognosis of stage I SCC compared to stage I adenocarcinoma highlights the hypothesis that single SCC nodules correspond more likely to a metastasis of the HNC rather than to primary lung cancer. Misclassification of patients with pulmonary SCC as primary lung cancer instead of metastatic HNC disease is further supported by the high proportion of squamous cell histology (42.4%) and the rate of 48.8% of synchronous HNC. The observed proportion of SCC in our study is concordant with a Surveillance, Epidemiology and End result database study reporting SCC proportion of 42% of lung cancers among 101 856 patients treated for HNC compared to 21,0% ($P < 0.01$) in the population of 1 160 853 lung cancer patients extracted from the same database [22]. Poorer long term results in patients with localized pulmonary SCC and history of HNC suggest that dedicated studies should be undertaken to better predict the long term outcomes after sublobar resections including wedge resections in the population of patients with localized pulmonary SCC and history of HNC.

Our results further promote minimally invasive approach in line with the current recommendations for early-stage lung cancer resection [23]. Preoperative histological documentation of the tumor may help to evaluate the long-term benefit/risk balance of surgery and help to avoid futile lobectomy in higher risk patients. Furthermore, adjuvant therapy should be evaluated in clinical trials in pathological stage I SCC with history of HNC. Given the limited mortality

after lobectomy, lung cancer screening after 5 years of HNC control could be of benefit in these patients with higher risk of secondary primary lung cancer [24].

Our study presents major limitations. There is a recruitment bias due to the proximity of a high volume HNC program at Gustave Roussy, Villejuif, France. The retrospective nature of the study precluded full HNC characteristics evaluation. The preoperative swallowing disorders were not systematically evaluated or reported and the nature of postoperative pneumonia (aspiration vs. other) was not feasible. Despite preoperative swallowing disorders were associated with postoperative complications, this study did not allowed to determine whether preventive tracheostomy would prevent postoperative aspiration because of unpowered. This highlights the need for specific clinical investigations to determine indications for preoperative tracheostomy in patients with history of HNC. We acknowledge that human papilloma virus detection in pathological samples of SCC of head and neck and lung tumors could provide some insight into determination of the primary or metastatic nature of lung cancer; however, this retrospective analysis was not performed in this study.

To conclude, patients with history of HNC who underwent a lobectomy presented an acceptable postoperative mortality but a significantly increased morbidity burden in case of open approach and/or SCC histology of the lung tumor. Our results revealed clear benefit of VATS regarding the 90-days outcomes but was not significant for long-term outcomes. VATS lobectomy for local non-SCC seems the preferred approach in an intent to cure strategy in patients with history of HNC, while patients with SCC should benefit from further evaluation to define the best strategy.

Funding Support

None

Acknowledgements

We would like to thank Professor Pascal-Alexandre Thomas from the department of thoracic surgery of the Hopital Nord at Aix-Marseille University, France, for his kind technical assistance.

Cite References

- [1] Massard G, Wihlm JM, Ameur S, et al. Association of bronchial and pharyngo-laryngeal malignancies. A reappraisal. *Eur J Cardiothorac Surg.* 1996;10(6):397-402.
- [2] Herrera LJ, Correa AM, Vaporciyan AA, et al. Increased risk of aspiration and pulmonary complications after lung resection in head and neck cancer patients. *Ann Thorac Surg.* 2006;82(6):1982-7; discussion 7-8.
- [3] Briend G, Planquette B, Badia A, et al. Impact of previous head and neck cancer on postoperative complications after surgical resection for lung cancer: a case-control study. *J Thorac Dis.* 2018;10(7):3948-56.
- [4] Berry MF, Hanna J, Tong BC, et al. Risk factors for morbidity after lobectomy for lung cancer in elderly patients. *Ann Thorac Surg.* 2009;88(4):1093-9.
- [5] Pagès PB, Mariet AS, Madelaine L, et al. Impact of video-assisted thoracic surgery approach on postoperative mortality after lobectomy in octogenarians. *J Thorac Cardiovasc Surg.* 2019;157(4):1660-7.

- [6] Bendixen M, Jørgensen OD, Kronborg C, Andersen C, Licht PB. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: a randomised controlled trial. *Lancet Oncol.* 2016;17(6):836-44.
- [7] Laursen L, Petersen RH, Hansen HJ, Jensen TK, Ravn J, Konge L. Video-assisted thoracoscopic surgery lobectomy for lung cancer is associated with a lower 30-day morbidity compared with lobectomy by thoracotomy. *Eur J Cardiothorac Surg.* 2016;49(3):870-5.
- [8] Pagès PB, Delpy JP, Orsini B, et al. Propensity Score Analysis Comparing Videothoracoscopic Lobectomy With Thoracotomy: A French Nationwide Study. *Ann Thorac Surg.* 2016;101(4):1370-8.
- [9] Falcoz PE, Puyraveau M, Thomas PA, et al. Video-assisted thoracoscopic surgery versus open lobectomy for primary non-small-cell lung cancer: a propensity-matched analysis of outcome from the European Society of Thoracic Surgeon database. *Eur J Cardiothorac Surg.* 2016;49(2):602-9.
- [10] Boffa DJ, Dhamija A, Kosinski AS, et al. Fewer complications result from a video-assisted approach to anatomic resection of clinical stage I lung cancer. *J Thorac Cardiovasc Surg.* 2014;148(2):637-43.
- [11] Paul S, Altorki NK, Sheng S, et al. Thoracoscopic lobectomy is associated with lower morbidity than open lobectomy: a propensity-matched analysis from the STS database. *J Thorac Cardiovasc Surg.* 2010;139(2):366-78.
- [12] Dikshit RP, Boffetta P, Bouchardy C, et al. Risk factors for the development of second primary tumors among men after laryngeal and hypopharyngeal carcinoma. *Cancer.* 2005;103(11):2326-33.
- [13] Furák J, Troján I, Szöke T, et al. Lung cancer as a second primary malignant tumor: prognostic values after surgical resection. *Interact Cardiovasc Thorac Surg.* 2008;7(1):50-3.
- [14] Gao X, Fisher SG, Mohideen N, Emami B. Second primary cancers in patients with laryngeal cancer: a population-based study. *Int J Radiat Oncol Biol Phys.* 2003;56(2):427-35.

- [15] Lim E, Batchelor T, Shackcloth M, et al. Study protocol for Video assisted thoracoscopic lobectomy versus conventional Open Lobectomy for lung cancer, a UK multicentre randomised controlled trial with an internal pilot (the VIOLET study). *BMJ Open*. 2019;9(10):e029507.
- [16] Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT. The Eighth Edition Lung Cancer Stage Classification. *Chest*. 2017;151(1):193-203.
- [17] Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250(2):187-96.
- [18] Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. *Ann Surg*. 2013;258(1):1-7.
- [19] Ezer N, Kale M, Sigel K, et al. Outcomes after Video-assisted Thoracoscopic Lobectomy versus Open Lobectomy for Early-Stage Lung Cancer in Older Adults. *Ann Am Thorac Soc*. 2018;15(1):76-82.
- [20] Desai H, Natt B, Kim S, Bime C. Decreased In-Hospital Mortality after Lobectomy Using Video-assisted Thoracoscopic Surgery Compared with Open Thoracotomy. *Ann Am Thorac Soc*. 2017;14(2):262-6.
- [21] Hannan EL, Radzyner M, Rubin D, Dougherty J, Brennan MF. The influence of hospital and surgeon volume on in-hospital mortality for colectomy, gastrectomy, and lung lobectomy in patients with cancer. *Surgery*. 2002;131(1):6-15.
- [22] Crippen MM, Brady JS, Burke LA, Eloy JA, Baredes S, Park RCW. Second primary lung malignancy following head and neck squamous cell carcinoma. *Laryngoscope*. 2019;129(4):903-9.
- [23] Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg*. 2019;55(1):91-115.

[24] Liu WS, Chang YJ, Lin CL, et al. Secondary primary cancer in patients with head and neck carcinoma: the differences among hypopharyngeal, laryngeal, and other sites of head and neck cancer. *Eur J Cancer Care (Engl)*. 2014;23(1):36-42.

Illustrations

Figure 1. A: Relative numbers of open and Video Assisted Thoracic Surgery (VATS) lobectomies per year between 2010 and 2017. **B:** Numbers of postoperative in-hospital complications of grade III, IV and V per year between 2010 and 2017.

Figure 2. A: estimated survival comparison between patients with squamous cell carcinoma and other pathological types. **B:** estimated survival comparison between open and Video Assisted Thoracic Surgery (VATS) approach for lobectomy in patients with history of Head-Neck Carcinoma (HNC).

Figure 3. A: Kaplan-Meier survival curves of patients with classified stage I lung carcinoma. Comparison between squamous cell carcinoma (SCC) and non-SCC. **B:** Kaplan-Meier survival curves of patients with classified stage II lung carcinoma. Comparison between SCC and non-SCC. Cure comparisons were performed using Log-rank test. $p < 0.05$ was considered significant.

Tables

Table 1: Patients characteristics among patients with history of head and neck carcinoma (HNC) who underwent video-assisted (VATS) or open lobectomy.

	All (n=85)	Open lobectomy (n=52)	VATS lobectomy (n=33)	P-value
Age (median [IQR], y)	63 [59; 70]	64 [59; 71]	63 [59; 69]	0.81
Sex (male/female)	68/17	44/8	24/9	0.29
BMI (median [IQR], kg/m²)	22.5 [20.0; 24.9]	23.4 [20.3; 31.3]	23.0 [20.0; 24.6]	0.18
HNC location				
Oral cavity	25 (29.4%)	18 (34.6%)	7 (21.2%)	0.14
Oropharynx / nasopharynx	13 (15.3%)	5 (9.6%)	8 (24.2%)	
Hypopharynx	18 (21.2%)	13 (25.0%)	5 (15.2%)	
Larynx	21 (24.7%)	13 (25%)	8 (24.2%)	
Other	8 (9.4%)	3 (5.8%)	5 (15.2%)	
Metachronous lung cancer (≥6months delay)	57 (61.2%)	39 (75.0%)	18 (54.5%)	0.09
HNC treatments				
Preop HNC surgery ± other	44 (51.8%)	28 (53.8%)	16 (48.5%)	0.80
Preop radio chemo ± HNC surgery	38 (44.7%)	20 (38.5%)	18 (54.5%)	0.22
Preop radio ± HNC surgery	15 (17.6%)	9 (17.3%)	6 (18.2%)	>.99
Preop chemo ± HNC surgery	6 (7.0%)	5 (9.6%)	1 (3.0%)	0.40
HNC treatment pending	13 (15.3%)	7 (13.5%)	6 (18.2%)	0.55
Comorbidities				
Coronary artery disease	10 (11.8%)	4 (6.1%)	6 (18.2%)	0.18
PreopFEV ₁ (%), mean, SD	86 ± 17	87 ± 15	84 ± 21	0.25
Preop CRP above normal	28/81	19/51	9/33	0.48
Preop N/L ratio (median [IQR])	4.2 [2.4; 6.3]	3.9 [2.3; 6.2]	4.8 [3.0; 6.9]	0.37
Preop end tracheostomy	6 (7.1%)	3 (5.8%)	3 (9.1%)	0.67
Preop swallowing disorder	20 (23.5%)	15 (28.8%)	5 (15.2%)	0.19
Peroperative tracheotomy	6 (7.1%)	4 (7.7%)	2 (6.1%)	>.99
Lung cancer pathological staging (8th edition)				
Stage I	61 (71.8%)	36 (69.2%)	25 (75.8%)	0.34
Stage II	16 (18.8%)	9 (13.3%)	7 (21.2%)	
Stage III	8 (9.4%)	7 (13.5%)	1 (3.0%)	
Stage IV	0 (0%)	0 (0%)	0 (0%)	
Lung cancer pathology				
Adenocarcinoma	43 (50.6%)	23 (44.2%)	20 (60.6%)	0.35
SCC	36 (42.4%)	25 (48.7%)	11 (33.3%)	
Other	6 (7.1%)	4 (7.7%)	2 (6.1%)	

BMI: body mass index; IQR: interquartile range; N/L ratio: neutrophil to lymphocyte ratio; preop: preoperative; CRP: C-reactive Protein; SCC: squamous cell carcinoma; Video Assisted Thoracic Surgery (VATS); Body Mass Index (BMI); Head and Neck Carcinoma (HNC). Qualitative variables were compared using Chi2 or Fischer's exact test. Continuous variables were compared using Mann-Whitney test. $P < 0.05$ was considered significant.

Table 2: Patients short term outcomes after video-assisted (VATS) or open lobectomy among patients with history of head and neck carcinoma (HNC).

	All (n=85)	Open lobectomy (n=52)	VATS lobectomy (n=33)	P-value
Postoperative outcomes				
In-hospital mortality	2 (2.4%)	2 (3.8%)	0 (0%)	-
90-days mortality	9 (10.6%)	7 (13.5%)	2 (6.1%)	0.47
Unexpected postoperative ICU	14 (16.4%)	12 (23%)	2 (6.1%)	0.07
Postoperative hospital stay duration	9.0 [7.0; 16.0]	9.5 [7.0; 21.0]	8.0 [4.0; 15.0]	0.045
Pneumonia	27 (31.8%)	21 (40.4%)	6 (18.2%)	0.035
90 days re-hospitalization	8 (9.4%)	7 (13.5%)	1 (3.0%)	0.15
In-hospital complications				
Clavien-Dindo highest grade				
Grade I	6 (7.1%)	2(3.8%)	4 (12.1%)	0.16
Grade II	10 (11.8%)	5 (9.6%)	5 (15.2%)	
Grade III	24 (28.8%)	17 (32.7%)	7 (21.2%)	0.014
Grade IV	12 (14%)	10 (19.2%)	2 (6.1%)	
Grade V	2 (2.4%)	2 (3.8%)	0 (0%)	
CCI, median (IQR)	20.9 (0; 40.8)	33.5 (0; 45.9)	8.7 (0; 24.1)	0.034
90-days complications				
Clavien-Dindo highest grade				
Grade I	6 (7.1%)	2(3.8%)	4 (12.1%)	0.16
Grade II	10 (11.8%)	5 (9.6%)	5 (15.2%)	
Grade III	24 (28.8%)	17 (32.7%)	7 (21.2%)	0.027
Grade IV	12 (14%)	10 (19.2%)	2 (6.1%)	
Grade V	3 (2.4%)	2 (3.8%)	1 (3.0%)	
CCI, median (IQR)	22.6 (0; 47.4)	33.5 (0; 53.5)	8.7 (0; 34.1)	0.018

ICU: intensive care unit; Video Assisted Thoracic Surgery (VATS). Qualitative variables were compared using Chi2 or Fischer's exact test. Continuous variables were compared using Mann-Whitney test. $P < 0.05$ was considered significant.

Table 3: Univariable analysis for prediction of 90-days postoperative grade III, IV or V complication according to Clavien-Dindo classification.

	Odd Ratio	95% CI	P-value
Age > 63 years old	1.39	0.59 – 3.39	0.45
Sex (male)	2.13	0.72 – 5.90	0.19
BMI ≤ 23.2	0.67	0.30 – 1.5	0.34
Lung cancer stage III	4.45	1.00 – 22.43	0.22
Preoperative CRP above normal	2.77	1.13 – 6.94	0.032
Preoperative N/L ratio ≥ 4.15	0.65	0.26 – 1.58	0.34
Preoperative FEV1 < 80% predicted value	0.96	0.34 – 2.31	0.95
Open surgical approach (i.e. thoracotomy)	3.11	1.19 – 7.57	0.016
Preoperative swallowing disorder	2.40	0.79 – 6.37	0.10
Squamous cell carcinoma (SCC) (vs. non-SCC)	3.72	1.48 – 9.43	0.039

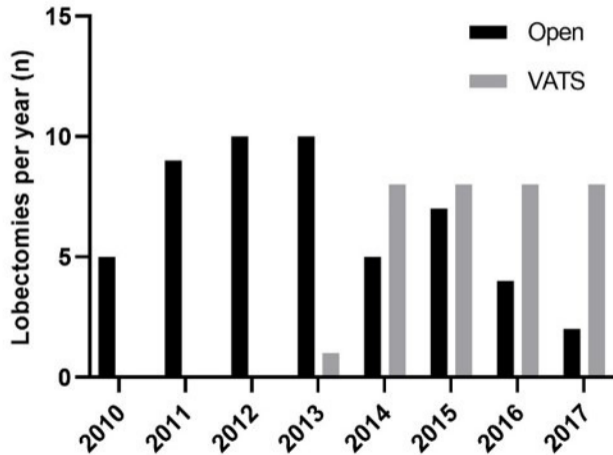
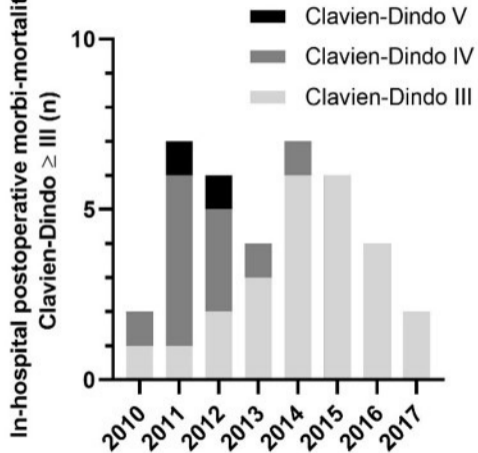
BMI: body mass index; CRP: C-reactive protein; CI: confidence interval; FEV1: Forced expiratory volume in 1 second; N/L: neutrophil / lymphocyte ratio.

Table 4: Odd Ratio (OR) and 95% Confidence Intervals (95% CI) of variables included in the multiple logistic regression model to predict 90-days postoperative Clavien-Dindo grade III, IV or V complications.

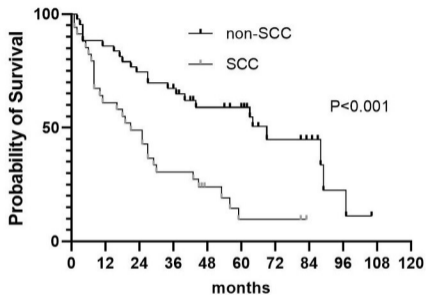
	OR	95% CI
Preoperative CRP above normal	2.17	0.73 – 6.65

Open surgical approach	2.94	1.02 – 8.87
Preoperative swallowing disorder	3.84	1.12 – 15.06
Squamous cell carcinoma (SCC) (vs. non-SCC)	3.45	1.21 – 10.39

CRP: C-reactive protein); SCC: Squamous Cell Carcinoma.

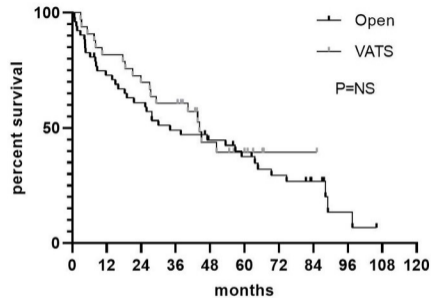
A**B**

A



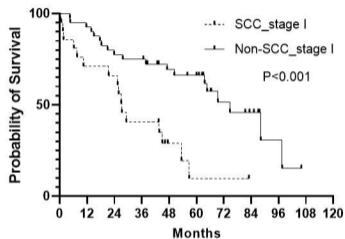
N at risk non-SCC	43	38	33	29	20	17	9	7	3	1
N at risk SCC	34	21	17	11	6	3	3	1	1	1

B



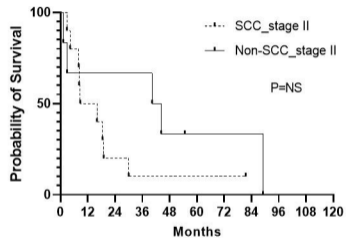
N at risk Open	52	38	32	25	20	16	12	7	3	1
N at risk VATS	33	28	24	21	11	7	2	2	1	0

A



N at risk SCC	21	15	14	9	4	2	2	1	1	1
N at risk non-SCC	40	38	32	31	23	20	10	7	3	1

B



N at risk SCC	10	6	3	2	2	2	2	0	0	0
N at risk non-SCC	6	5	5	5	3	2	2	2	1	1