„CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST
DOCTORAL SCHOOL
FIELD OF MEDICINE

Oncological Effectiveness of the VATS Approach in the Surgical Treatment of Bronchopulmonary Cancer

SUMMARY OF THE DOCTORAL THESIS

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Content

Abbreviatons

Abbreviation	English
NSCLC	Non-Small Cell Lung Cancer
VATS	Video-Assisted Thoracoscopic Surgery
RATS	Robotic-Assisted Thoracic Surgery
LDCT	Low-Dose Computed Tomography
S-LND	Systematic Lymph Node Dissection
LS-LND	Lobe-Specific Lymph Node Dissection
ERAS	Enhanced Recovery After Surgery
TNM	Tumor–Node–Metastasis
CCI	Charlson Comorbidity Index
FEV1	Forced Expiratory Volume in 1 Second
ASA	American Society of Anesthesiologists Physical Status Classification
ATI	Intensive Care Unit
NAT	Neoadjuvant Therapy
OS	Overall Survival
RFS	Recurrence-Free Survival
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
OR	Odds Ratio
IC	Confidence Interval
DS	Standard Deviation
LLL	Left Lower Lobe
LUL	Left Upper Lobe
RLL	Right Lower Lobe
RML	Right Middle Lobe
RUL	Right Upper Lobe
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Introduction

Non-small cell lung cancer (NSCLC) is the leading cause of cancer mortality worldwide, being responsible for approximately 18% of cancer deaths. Despite the therapeutic advances, the prognosis remains reserved, which requires the continuous development of more effective and less aggressive therapeutic strategies[1,2].

In recent decades, thoracic surgery has experienced a major change through the transition from to classical thoracotomy to minimally invasive techniques, especially video thoracoscopic surgery assisted (VATS). This transition aims to reduce surgical trauma and conservation functional pulmonary parenchyma, in the context of the increasingly frequent diagnosis of the disease in early stages through low-dose computed tomography screening programs (LDCT) [3].

There is major controversy regarding the optimal extent of nodal dissection mediastinal: systematic lymphadenectomy (S-LND), considered the traditional standard, versus lobe-specific lymph node dissection (LS-LND), proposed for reduction morbidity in the early stages without affecting the oncological radicality [4,5]. Optimization postoperative recovery and the reduction of complications are important objectives through integration of minimally invasive surgery with improved recovery protocols after surgery (ERAS), thus contributing to the improvement of the quality of life and the rapid reintegration of oncological patients [6].

The theme of this doctoral research is integrated into the current context of the guidelines international guidelines developed by the European Society of Thoracic Surgery and the National Network Cancer Comprehensive, which strongly recommends VATS as the therapeutic standard for resectable lung tumors, due to oncological efficiency and functional benefits postoperative.

However, in lymph node management, guidelines continue to consider S-LND the main standard for correct staging and complete oncological control. In parallel, Recent literature increasingly supports LS-LND for stages IA–IB, suggesting results comparable oncology, but associated with a lower morbidity [4,7].

Also, the clinical data from Eastern Europe regarding the application of the techniques minimally invasive in tertiary oncology centers. The present study aims to contribute to covering this deficit by analyzing the experience of the Oncological Institute "Prof. Dr. Alexandru Trestioreanu" from Bucharest, demonstrating the feasibility of implementation international standards in Romania [8].

The central hypothesis of this research is that minimally invasive approaches, especially VATS, associated with personalized nodal management strategies (LS-LND), can provide results equivalent to classic open surgery and systematic lymphadenectomy [4,7].

reducing surgical trauma by avoiding thoracotomy and limiting lymph node dissection at the relevant stations can significantly decrease postoperative morbidity and accelerate recovery, without affecting pathological staging or local tumor control. In the same time, these techniques could improve the quality of perioperative life without compromising it overall survival (OS) and long-term recurrence-free survival (RFS) [4,6].

The thesis is structured around three main objectives:

1. Comparison of VATS with thoracotomy: The first objective aims to assess oncological efficacy, safety and accuracy of inter-approach staging minimally invasive and open surgery in lung adenocarcinoma. The accent it is put on the quality of the nodal dissection, the phenomenon of upstaging and the evolution immediate postoperative [9,10].

2. Identification of predictors of postoperative morbidity: The second objective aims to identify independent predictive factors for complications clinically relevant postoperative. In particular, the Charlson index is analyzed (CCI) and lung function expressed by forced expiratory volume in the first second (FEV1) [11–13].

3. Comparison of LS-LND with S-LND: The last objective aims to evaluate

survival and safety between LS-LND and S-LND in NSCLC patients stages IA–IB, to demonstrate whether the limited approach can maintain oncological efficiency while reducing postoperative complications [14–17].

The limitations of these studies are generated by the retrospective nature and monocentric/bicentric of the studies, which may introduce selection bias and statistical limitations [4]. Also, relatively small sample size and heterogeneity of follow-up limits standardized assessment of long-term survival and recurrence. As directions the development of prospective, multicenter and randomized studies is proposed for validation of LS-LND and refinement of postoperative morbidity predictive models, later integrated into modern clinical guidelines [4,18].

I. General overview

1 Epidemiology and multimodal treatment of NSCLC

NSCLC is the leading cause of cancer mortality worldwide and its incidence is closely related to smoking, pollution and genetic factors. Adenocarcinoma is currently the most common histological subtype. Screening by LDCT allowed more frequent diagnosis of tumors in early stages and reduction of mortality by lung cancer [1].

Modern staging is based on the TNM system (tumor classification, nodule lymphatic, metastasis) updated by the International Association for the Study of Cancer Pulmonary and on the use of positron emission tomography combined with CT, aspiration endobronchial ultrasound-guided fine-needle transbronchial and fine-needle aspiration endoscopic echocardiography for mediastinal evaluation. Nodal management remains essential for prognosis and choice of treatment. Although S-LND is considered the standard oncology, increasing evidence supports LS-LND in carefully selected stages IA–IB, for reducing morbidity without compromising survival [4,5].

Surgical treatment has evolved towards minimally invasive techniques such as VATS and robotic-assisted thoracic surgery (RATS), which provides comparable oncological outcomes thoracotomy, with reduced pain, faster recovery and fewer complications [19,20]. In parallel, anatomical segmentectomy has become a valid alternative to lobectomy for small peripheral tumors, preserving lung function better [21,22].

Immunotherapy and neoadjuvant treatments have significantly changed management Locally advanced NSCLC, increasing pathologic complete response rates and integrating surgery in a multimodal and personalized approach [23].

2 Minimally invasive surgery in NSCLC: oncological and technical principles

Thoracic surgery has evolved from classic thoracotomy to minimally invasive approaches, especially VATS and later robotic surgery. These techniques have become the current standard for the treatment of resectable NSCLC due to reduced surgical trauma and recovery accelerated postoperative.

Comparative studies and meta-analyses have shown that VATS delivers similar to open surgery in terms of survival and local control tumor, but having important advantages: reduced postoperative pain, decrease complications, reduction of the inflammatory response and shorter length of hospitalization [20,24].

However, VATS implementation is limited by the learning curve, necessity of advanced surgical experience and the technical difficulties encountered in complex cases or after neoadjuvant treatments. Overall, minimally invasive surgery is presented as the modern development direction of thoracic oncological surgery, by combining radicality oncology with the reduction of surgical aggression.

II. Personal contributions

3 Working hypothesis and general objectives

The main hypothesis of the thesis is that minimally invasive approaches through VATS, associated with personalized nodal management strategies such as LS-LND can ensure results oncology comparable to classical surgery and systematic lymphadenectomy, reducing in at the same time post-operative morbidity and speeding up patients' recovery.

The research objectives aimed to compare oncological outcomes and staging

between VATS and thoracotomy, identifying predictive factors of postoperative complications and evaluating the efficacy and safety of LS-LND compared with S-LND in NSCLC stages IA–IB.

The observed results were aimed at demonstrating the fact that the reduction of surgical trauma and treatment individualization can improve perioperative outcome without compromising survival and oncological radicality.

4 General research methodology

The research was conducted through retrospective, observational and clinical studies

comparisons conducted on cohorts of patients diagnosed with NSCLC and treated surgically

with curative intent in the period 2016–2023, in two tertiary oncology centers in Romania.

Preoperative assessment and risk stratification used standardized tools international, such as the CCI, the physical status classification of the American Society of Anesthesiology (ASA) and pulmonary function parameters, especially FEV1. Morbidity postoperative was quantified by the Clavien-Dindo classification.

Statistical analysis included parametric and non-parametric comparative tests, models of univariate and multivariate logistic regression to identify independent predictors of

complications, as well as analyzing the receiver operating characteristic (ROC) and the area of under the curve (AUC) for validating the performance of predictive models.

The methodology aimed to evaluate oncological effectiveness, safety and impact minimally invasive surgery and adapted lymphadenectomy strategies in clinical practice real.

5 Comparative retrospective study of oncological outcomes and of staging between different surgical approaches — surgery video-assisted thoracoscopic versus thoracotomy in adenocarcinoma pulmonary

The study aimed to compare the minimally invasive VATS approach with classic thoracotomy in the treatment of lung adenocarcinoma, analyzing oncological efficiency, accuracy nodal staging and postoperative evolution. The starting premise was that VATS can provide oncological outcomes comparable to open surgery, with benefits additional effects on postoperative recovery and morbidity [25].

This comparative retrospective study was conducted on patients diagnosed with

lung adenocarcinoma and treat surgically with curative intent. Patients were divided into two groups: a group operated by VATS and a group operated by thoracotomy (Table 5-1).

Demographic and clinical characteristics, type of lung resection, number of resected nodes, upstaging phenomenon, postoperative complications, duration hospitalization and immediate postoperative course. Statistical analysis used comparative tests for assessing differences between groups.

The results demonstrated that the VATS approach was associated with a postoperative evolution more favorable, characterized by reduced length of hospitalization, faster recovery and rate lower postoperative complications. From an oncological point of view, VATS offered a adequate nodal dissection and staging comparable to thoracotomy. Moreover, the minimally invasive technique has demonstrated a superior yield in the harvesting of lymph nodes from certain deep stations, especially stations 7 and 10. No differences were observed significant differences regarding oncological radicality between the two approaches.

The main results of the study are illustrated in Tables 5-2 – 5-3 and Figures 5-1–5-2.

Table 5-1. Demographic and clinical data of patient diagnosed with adenocarcinoma pulmonary, undergoing open surgery versus video-assisted surgery

Variable	Open surgery (n = 52 pts)	VATS (n = 59 pts)	P value
Age (mean, years)	60,7	61,7	0,307
Sex			0,894
Male	24	29	
Female	28	30	
ASA Score			0,830
II	13	16	
III	39	43	
CCI			0,820
≤4	28	33	
>4	24	26	
Toxic Agents exposure			0,511
Yes	6	4	
No	46	55	
FEV1 (mean)	79	83	0,260
Left ventricular ejection fraction (mean)	60%	55%	0,540
Localisation			0,723
LLL	11	6	
LUL	12	20	
RLL	12	9	
RML	4	4	
RUL	13	20	
Clinical Stage			0,791
IA1	0	1	
IA2	3	14	
IA3	2	5	
IB	3	7	
IIA	2	0	
IIB	20	13	
IIIA	16	13	
IIIB	6	6	
Rezection type			0,005
Lobectomy	50	46	
Segmentectomy	2	13	
Istoric de NAT			0,125
Yes	7	3	
No	45	56	

Abbreviations: CCI = Charlson comorbidity Index; FEV1 = forced expiratory volume in 1st second; ASA = American Society of Anesthesiology LLL = left lower lobe; LUL = left upper lobe; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; VATS = video- assisted thoracoscopic surgery; NAT = Neoadjuvant Therapy

Table 4-1. Intraoperative and histopathological data of patients in the open VATS groups

Variable	Open approach (n = 52 pts)	VATS (n = 59 pts)	P value
Number of lymph nodes yielded per station (median and interval)			
2R + 4R	2 (0–9)	2 (0–14)	0.1134
4L	0 (0–2)	0 (0–2)	0.0893
5	0 (0–4)	0 (0–5)	0.1646
6	0 (0–3)	0 (0–3)	0.1521
7	0 (0–6)	4 (0–13)	0.0001
9	1 (0–9)	1 (0–2)	0.0867
10	4 (0–9)	4 (1–12)	0.0162
Number of invaded lymph nodes(median and interval)			
2R + 4R	0 (0–3)	0 (0–2)	0.2067
4L	0 (0)	0 (0)	0.5000
5	0 (0)	0 (0–2)	0.0525
6	0 (0)	0 (0–1)	0.4644
7	0 (0–2)	0 (0–3)	0.2441
9	0 (0–1)	0 (0)	0.5001
10	0 (0–4)	0 (0–8)	0.3036
Patological stage			
IA1	3	7	0.7272
IA2	9	14	
IA3	8	7	
IB	5	8	
IIA	2	2	
IIB	13	8	
IIIA	9	13	
IIIB	2	0	
IIIC	1	0	

Abbreviations: VATS = video- assisted thoracoscopic surgery.

Toracotomy group (n = 52)

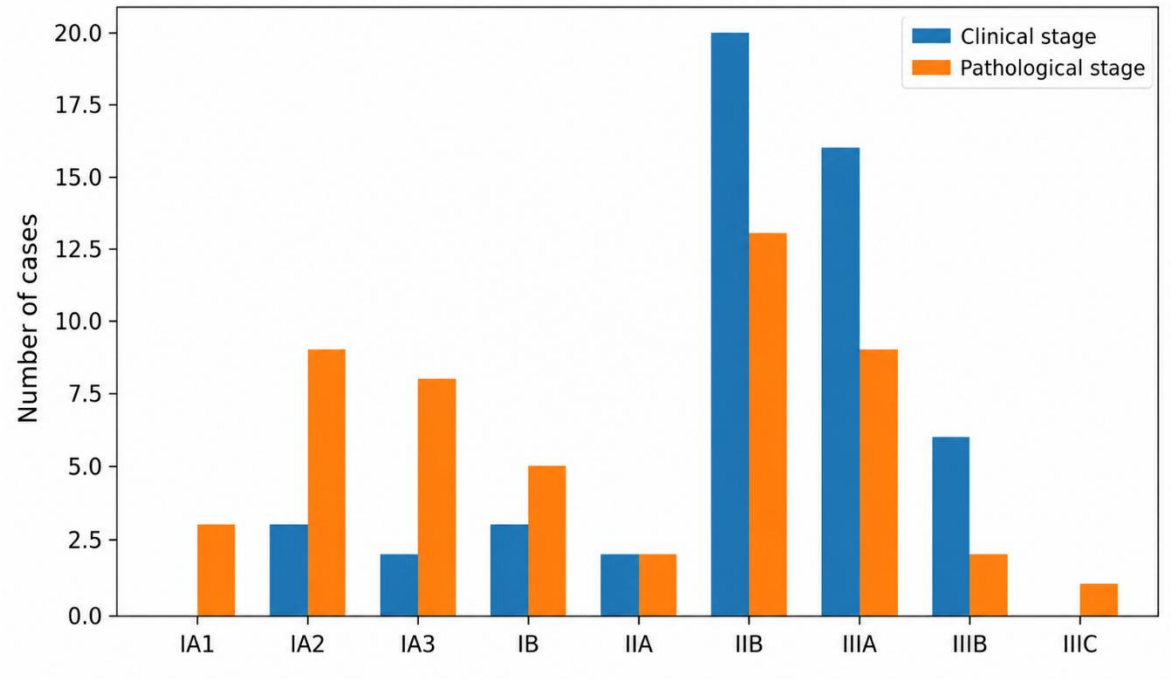

Figure 4-1. Comparation between initial clinical stadialization and postoperative patological stadialization in patients with thoracotomy.

VATS group (n = 59)

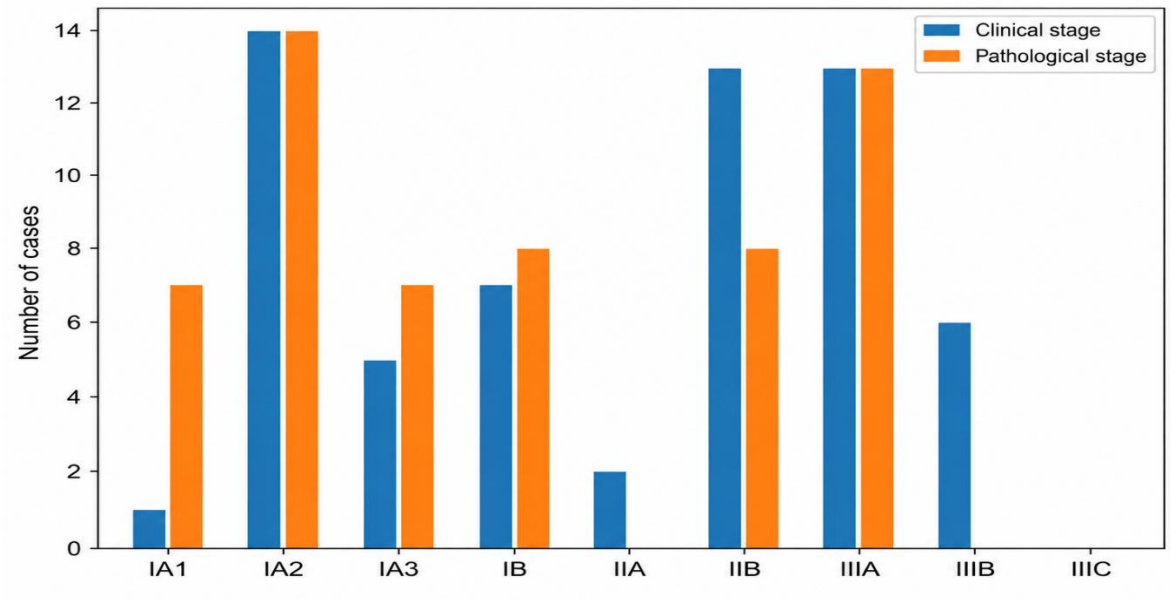

Figure 4-2. Comparation between initial clinical stadialization and postoperative patological stadialization in patients with video assisted thoracotomy (VATS).

Table 4-2. Clinical data of patients diagnosed with lung adenocarcinoma, undergoing open surgery versus video-assisted thoracoscopic surgery (VATS).

Variable	**Open surgery (n = 52 pts)**	**VATS (n = 59 pts)**	**P value**
ICU stay (days, median)	2.46	3.46	0.243
Hospitalization (days, median)	12.17	13.76	0.269
Complications (Clavien–Dindo)			0.714
Grade I	4	7	
Grade II	7	9	
Grade IIIA	2	3	
Grade IIIB	1	1	
Grade IVA	2	0	
Grade IVB	1	1	
Postoperative complications	32.6%	35.6%	0.840
30 days Postoperative mortality	0	0	

Abbreviations: ICU = Intensive Care Unit; VATS = video-assisted thoracoscopic surgery

The results of the study confirm the data from the international literature according to which VATS is non-inferior to thoracotomy from an oncological point of view and offers advantages important regarding postoperative recovery. It is emphasized that the magnified view and the technical precision offered by VATS may facilitate nodal dissection in certain regions deep anatomical. Also, the reduction of surgical trauma contributes to the reduction systemic inflammation and the accelerated recovery of patients.

The main limitations of the study are the retrospective nature and the relatively small size of the lot analyzed. VATS is a safe and effective alternative oncology to classic thoracotomy in the treatment of lung adenocarcinoma. The approach minimally invasive provides adequate nodal staging and comparable oncological outcomes open surgery, while providing important morbidity benefits postoperative and patient recovery.

6 Predictors of clinically relevant postoperative morbidity after surgical resection with curative intent for lung cancer non-microcellular

The study aimed to identify predictive factors associated with the occurrence of complicationsclinically significant postoperative complications after lung resections with curative intent for NSCLC. The importance of correct perioperative risk stratification for optimizing patient selection and reducing postoperative morbidity [26].

A retrospective study was performed on patients diagnosed with NSCLC and treated surgical with curative intent, demographic, clinical and functional data being analyzed such as age, sex, CCI, ASA status, lung function expressed as FEV1 and type surgery (Table 6-1).

Table 4-3. Basic demographic, clinical and surgical characteristics of the study group.

Variable	Total (n = 163)
Age, media ± SD (years)	61,3 ± 10,2
Sex	
Male	87 (53,4%)
Female	76 (46,6%)
ASA Score	
II	37 (22,7%)
III	126 (77,3%)
I, IV, V	0 (0%)
CCI ≥ 4	124 (76,1%)
Surgical procedure	
VATS	77 (47,2%)
Open thoracotomy	86 (52,8%)
Respiratory toxic exposure	14 (8,6%)
FEV1, media ± SD (%)	80,9 ± 14,7
Tumor localization	
LLL	30 (18,4%)
LUL	44 (27,0%)
RLL	28 (17,2%)
RML	10 (6,1%)
RUL	51 (31,3%)
Locally advanced stage	70 (42,9%)
Rezection type	
Lobectomy	144 (88,3%)
Segmentectomy	19 (11,7%)
NAT	15 (9,2%)

Abbreviations: CCI = Charlson comorbidity Index; FEV1 = forced expiratory volume in 1st second; ASA = American Society of Anesthesiology LLL = left lower lobe; LUL = left upper lobe; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; VATS = video- assisted thoracoscopic surgery; NAT = Neoadjuvant Therapy

Postoperative complications were classified using the Clavien-Dindo score, and clinically relevant morbidity was defined as grade ≥ II. Statistical analysis included regression univariate and multivariate logistic to identify independent predictors of postoperative complications. The results showed that patients with an increased CCI (CCI ≥ 4) and with low FEV1 values presented a significantly higher risk of developing a clinically relevant postoperative complications.

Also, postoperative morbidity was associated with advanced age, status functionally reduced, diminished pulmonary reserve and the complexity of the surgical intervention.

The developed statistical models demonstrated a good discrimination ability for prediction of postoperative complications.

The main results of the study are illustrated in Tables 6-2 – 6-4 and Figures 6-1– 6-3.

Table 4-4 Comparative analysis between patients with and without clinical postoperative morbidity .

Variable	**Without morbidity(n = 128)**	**Relevant morbidity (n = 35)**	**Test**	**p Value**
Age (years)	62 (26–84)	65 (37–81)	Mann–Whitney U	0,0788
FEV1 (%)	80 (55–140)	78 (47–129)	Mann–Whitney U	0,0693
VATS	58 (45,3%)	19 (54,3%)	Chi-square	0,4525
Locally advanced stage	56 (43,8%)	14 (40,0%)	Chi-square	0,8380
Segmentectomy	16 (12,5%)	3 (8,6%)	Exact Fisher	0,7669
NAT	12 (9,4%)	3 (8,6%)	Exact Fisher	1,0000
Scuamous histology	44 (34,4%)	8 (22,9%)	Chi-square	0,2753
Male	68 (53,1%)	19 (54,3%)	Chi-square	1,0000
CCI ≥ 4	93 (72,7%)	31 (88,6%)	Exact Fisher	0,0720
ASA III	96 (75,0%)	30 (85,7%)	Chi-square	0,2656
Respiratory toxic exposure	10 (7,8%)	4 (11,4%)	Exact Fisher	0,5023

Abbreviations: CCI = Charlson comorbidity Index; FEV1 = forced expiratory volume in 1st second; ASA = American Society of

Anesthesiology; VATS = video- assisted thoracoscopic surgery; NAT= Neoadjuvant Therapy

Table 4-5. Univariate logistic regression analysis for clinically relevant postoperative morbidity.

Variable	OR	CI 95%	P value
Age	1,04	0,99–1,08	0,0657
FEV1	0,97	0,94–1,00	0,0991
VATS	1,43	0,68–3,04	0,3473
Locally advanced stage	0,86	0,40–1,83	0,6914
Segmentectomy	0,66	0,18–2,39	0,5235
NAT	0,91	0,24–3,41	0,8842
Scuamous histology	0,57	0,24–1,35	0,1989
Male	1,05	0,49–2,22	0,9029
CCI ≥ 4	2,92	0,96–8,86	0,0591
ASA III	2,00	0,72–5,59	0,1862
Respiratory toxic exposure	1,52	0,45–5,18	0,5012

Abbreviations: OR = Odds ratio; CI = Confidence interval ; CCI = Charlson comorbidity Index; FEV1 = forced expiratory volume in 1st second; ASA = American Society of Anesthesiology; VATS = video-assisted thoracoscopic surgery; NAT= Neoadjuvant Therapy

Table 4-6. Multivariate logistic regression analysis for clinically relevant postoperative morbidity.

Variable	adjusted OR	CI 95%	P Value
VATS	1,50	0,69–3,24	0,3044
CCI ≥ 4	2,04	0,54–7,70	0,2948
FEV1	0,98	0,95–1,01	0,1859
Age	1,02	0,97–1,07	0,4618

Abbreviations: OR = Odds ratio; CI= Confidence interval ; CCI=Charlson comorbidity Index; FEV1 = forced expiratory volume in 1st second; VATS = video- assisted thoracoscopic surgery;

The results confirm the major role of comorbidities and pulmonary function in the postoperative outcome of NSCLC patients. It is highlighted that rigorous preoperative assessment is essential for individualizing treatment and reducing perioperative risk.

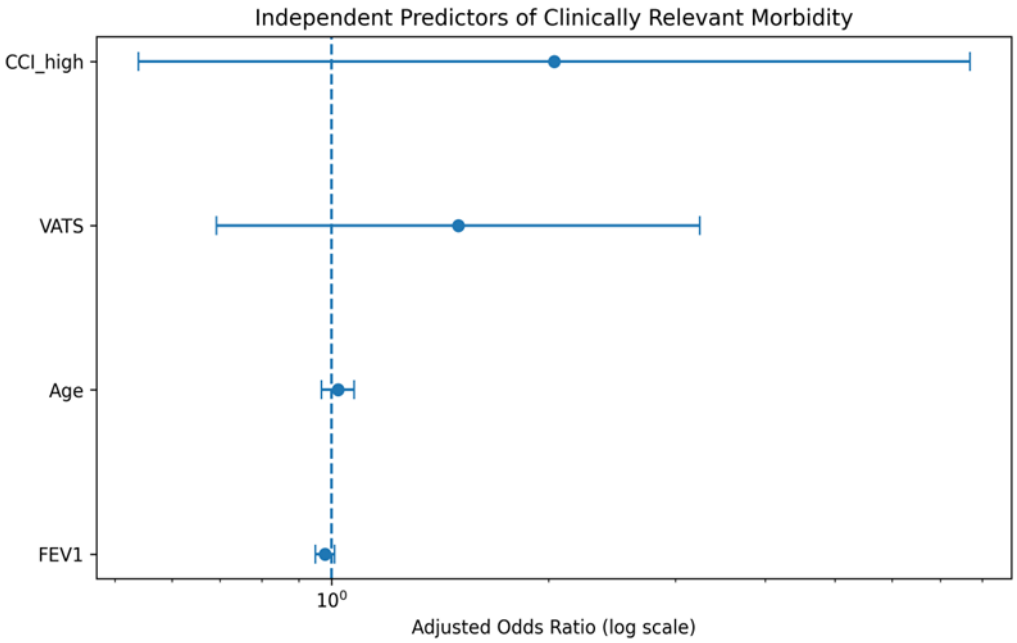

Figure 6-1. Forest plot of variables associated with clinically relevant postoperative morbidity.

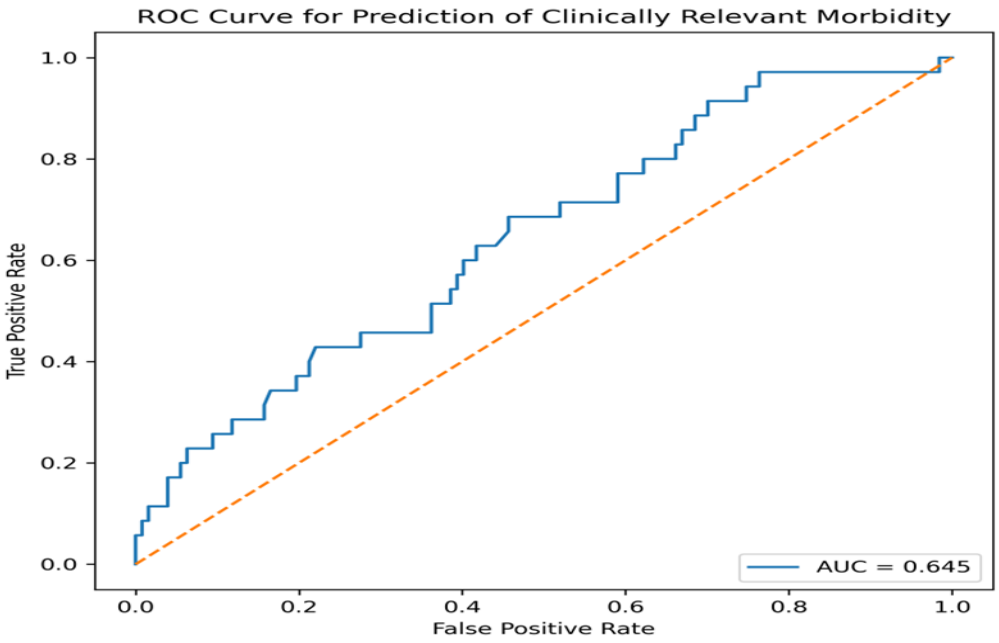

Figure 4-3 ROC curve analysis of the multivariate predictive model for clinically relevant postoperative morbidity**.**

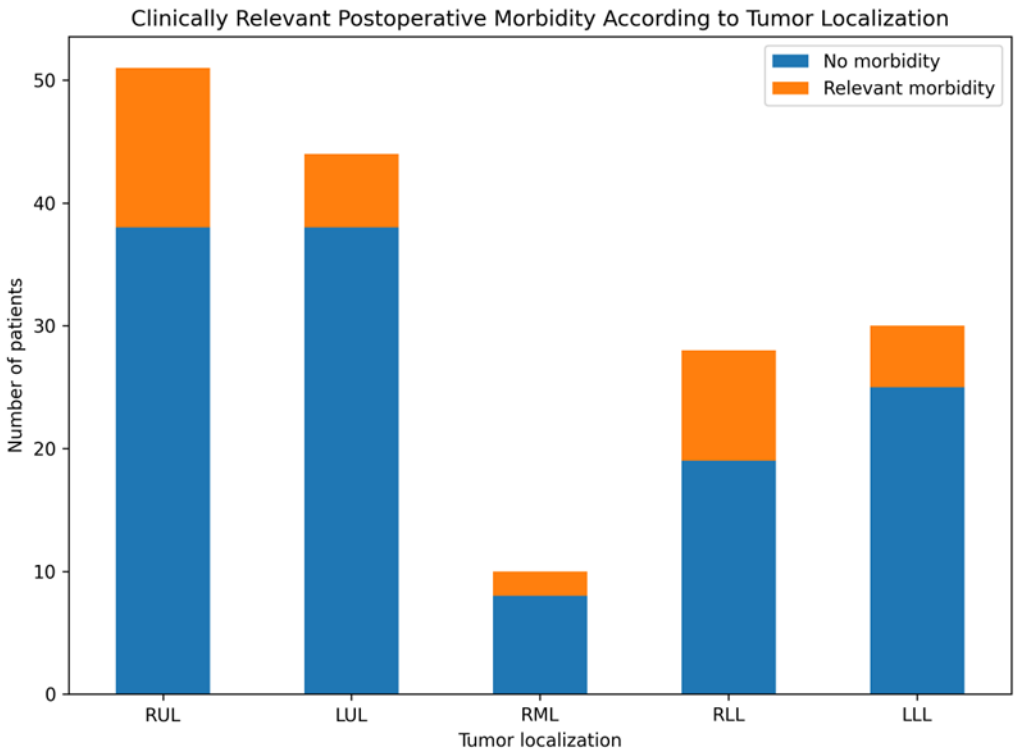

Figure 6-3. Distribution of clinically relevant postoperative morbidity according to tumor localization. Blue bars represent patients without clinically relevant postoperative morbidity, while orange bars represent patients with Clavien–Dindo grade ≥ II complications. Abbreviations: LLL - Left Lower Lobe, LUL - Left Upper Lobe, RLL - Right Lower Lobe, RML - Right Middle Lobe, RUL – Right Upper Lobe.

Integrating clinical and functional parameters into predictive models can contribute to the optimal selection of patients for surgery and the implementation of perioperative measures adapted

Limitations of the study are its retrospective nature and size relatively low of the analyzed batch.

Increased CCI and reduced FEV1 values are independent predictors of clinically relevant postoperative morbidity after lung resections for NSCLC.

Careful perioperative risk stratification and rigorous functional assessment are essential to optimize surgical management and reduce postoperative complications.

7 Surgery with curative intent associated with lymph node dissection lobe-specific versus systematic lymphadenectomy in cancer non-microcellular lung in clinical stage IA–IB

The study looked at whether LS-LND can represent a safe alternative to S-LND at patients with NSCLC in clinical stages IA–IB. The starting premise is that the limitation extension of lymphadenectomy could reduce surgical trauma and complications postoperatively without affecting oncological control and survival [27].

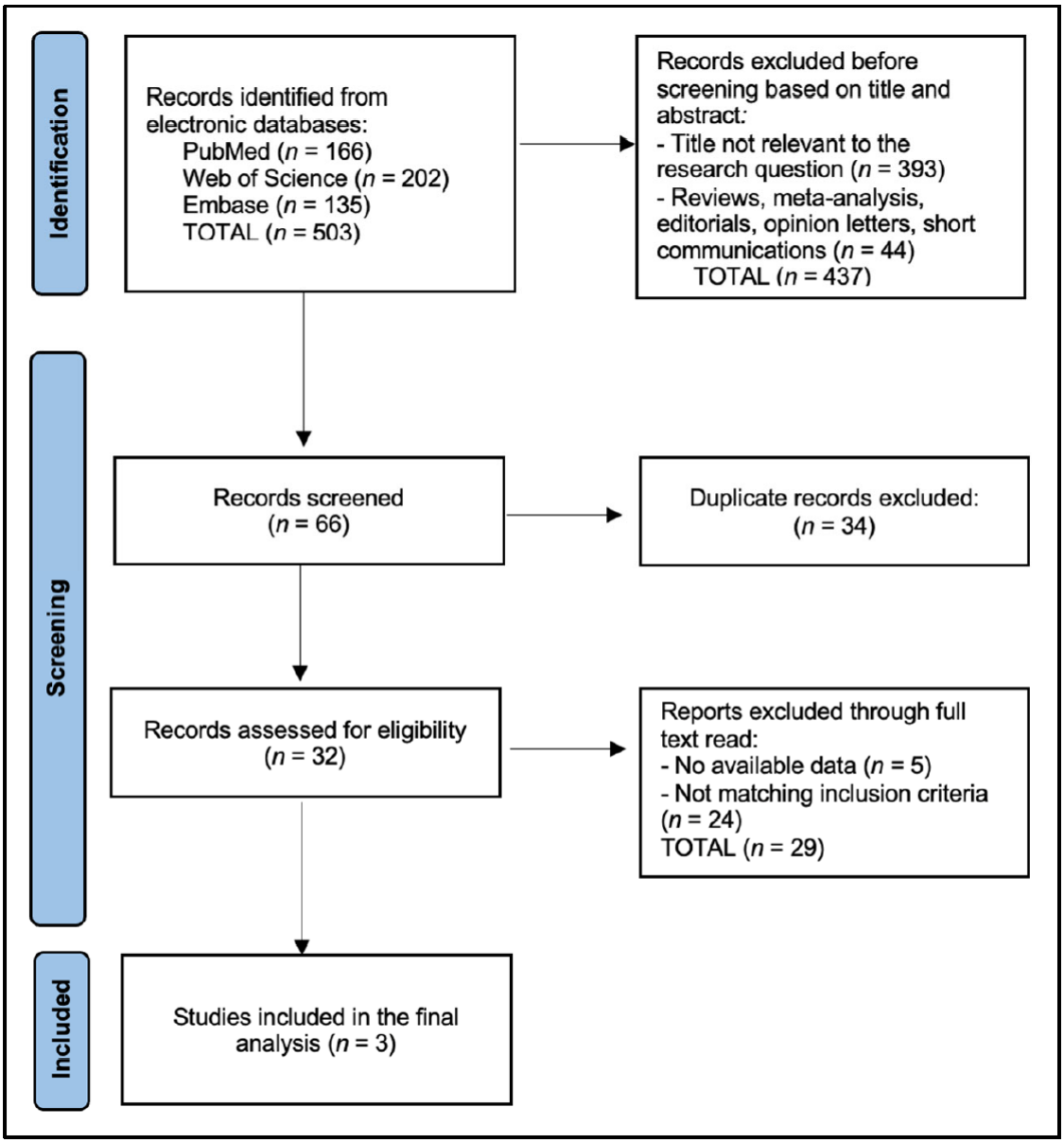

Figure 4-4. PRISMA flowchart.

A retrospective comparative study was conducted on patients diagnosed with NSCLC stages IA–IB and treat surgically with curative intent. The patients were divided into two groups: group with LS-LND and group with S-LND. Clinical features were analyzed and

pathology, type of lung resection, postoperative complications, OS and RFS. Analysis statistical analysis looked at the comparison of oncological outcomes and safety profile between those two techniques. Data extraction from included studies was performed independently by two evaluators, using the PRISMA diagram (preferred elements for reporting analyses systematic reviews and meta-analyses) shown in Figure 7-1.

The results demonstrated that LS-LND provided overall survival values and

relapse-free survival comparable to those achieved by S-LND at 5 years. Treated patients

by LS-LND showed reduced postoperative morbidity, faster recovery and duration lower of the surgical intervention. No significant differences were identified regarding oncological control between the two approaches in the carefully selected groups.

The main results of the study are illustrated in Tables 7-1 – 7-4 and Figures 7-2– 7-3.

Table 4-7. Comparative studies between S-LND and LS-LND in pacients with NSCLC stages IA–IB.

Study (year)	**Country**	**Study design**	**Study period**	**Recruitment (S-LND vs. LS-LND)**
Hattori et al. (2021) [17]	Japan	Retrospective	2008–2016	459 (181 vs. 278)
Zhao et al. (2021) [14]	China	Retrospective	2014–2017	546 (446 vs. 100)
Ma et al. (2013) [28]	China	Prospective	2004–2008	96 (51 vs. 45)
Curent study	Romania	Retrospective	2018–2020	24 (14 vs. 10)

Abbreviations: S-LND, Systematic lymph node dissection; LS-LND, Lobe specific lymph node dissection.

Table 4-8. Baseline clinical-demographic characteristics of patients included in comparative studies S-LND versus LS-LND.

Study	Medium age (years) (S-LND vs. LS-LND)	Male (%) (S-LND vs. LS-LND)	Adenocarcinoma (%) (S-LND vs. LS-LND)
Hattori et al. (2021) [17]	66 vs. 65	64.1 vs. 67.6	70.7 vs. 68.7
Zhao et al. (2021) [14]	58 vs. 57	47.8 vs. 36.0	80.7 vs. 92.0
Ma et al. (2013) [28]	60 vs. 59	Unreported	Unreported
Curent study	57 vs. 60	50.0 vs. 40.0	71.4 vs. 70.0

Not reported (NR) indicates that data were not available in the study.

Abbreviations: S-LND, Systematic lymph node dissection; LS-LND, Lobe-specific lymph node dissection.

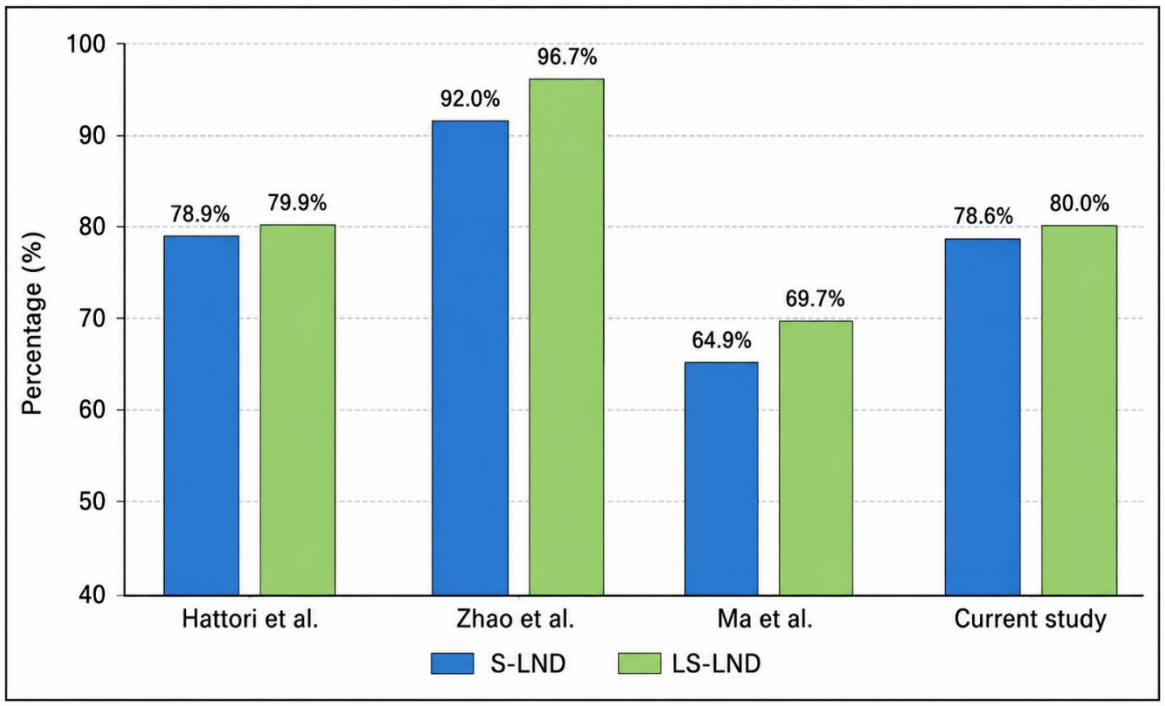

Figure 4-5. Five-year Overall survival (OS). Hattori and colab. (2021)[22], Zhao and colab. (2021)[7], Ma and colab. (2013)[59].

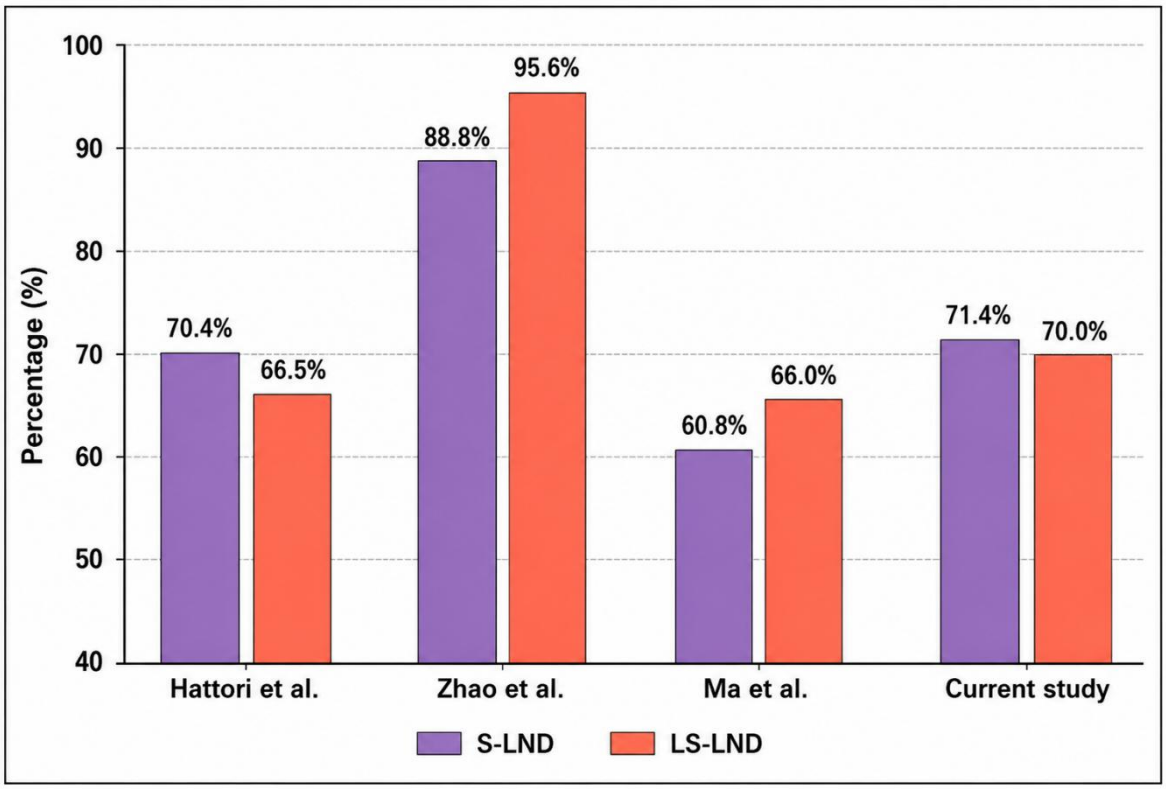

Figure 4-6. Five-Year Recurrence-Free Survival (RFS). Hattori et al. (2021) [21]. Hattori and colab. (2021)[22], Zhao and colab. (2021)[7], Ma and colab. (2013)[59].

Table 4-9 Oncologic Outcomes: Five-Year Overall Survival (OS) and Recurrence-Free Survival

Study	**5 years OS (S-LND vs. LS-LND)**	**5 years RFS (S-LND vs. LS-LND)**	**p value(OS)**	**P value (RFS)**
Hattori et al. [17]	78.8% vs. 79.9%	70.4% vs. 66.5%	0.665	0.669
Zhao et al. [14]	92.0% vs. 96.7%	88.8% vs. 95.6%	0.411	0.13
Ma et al. [28]	64.9% vs. 69.7%	60.8% vs. 66.0%	0.552	0.241
Studiul curent	78.6% vs. 80.0%	71.4% vs. 70.0%	0.892	0.911

Abbreviations: OS, Overall Survival; RFS, Recurrence-Free Survival; S-LND, Standard Lymph Node Dissection; LS-LND, Lobe-Specific Lymph Node Dissection.

Table 4-10. Postoperative complications

Study	Pneumonia (S-LND vs. LS-LND	Arrhythmia (S-LND vs. LS-LND)	Chylothorax (S-LND vs. LS-LND)	Early Mortality (S-LND vs. LS-LND
Hattori et al. [17]	4.9% vs. 3.2%	13.3% vs. 10.1%	NR	0.5% vs. 1.1%
Zhao et al. [14]	NR	3% vs. 1%	NR	NR
Ma et al. [28]	9.8% vs. 4.4%	4% vs. 2.2%	4% vs. 0%	NR
Current study	7.1% vs. 10.0%	14.3% vs. 10.0%	0% vs. 0%	0% vs. 0%

NR indicates 'Not Reported'. Early Mortality is reported as the number of deaths per the total number of participants in each group. Abbreviations: S-LND, Standard Lymph Node Dissection; LS-LND, Lobe-Specific Lymph Node Dissection.

The results support the idea that LS-LND may represent a safe and effective option

for carefully selected early-stage NSCLC patients. It is highlighted that predictable patterns of lymphatic drainage allow limitation of nodal dissection without compromising oncological radicality. Reducing the extent of lymphadenectomy can decrease the risk of associated complications, such as recurrent nerve damage, arrhythmias or chylothorax, contributing to a more favorable postoperative recovery.

Limitations of the study are the retrospective design and relative size reduced the analyzed batch. LS-LND proved non-inferior to S-LND in terms of overall survival and relapse-free survival in patients with NSCLC stages IA–IB carefully select. The lobe-specific approach can reduce postoperative morbidity and surgical trauma without affecting oncological efficiency.

8 Conclusions and personal contributions

The results of the thesis confirm that minimally invasive approaches through VATS represent safe and oncologically effective alternatives to classic thoracotomy in the treatment of NSCLC, offering important benefits regarding the reduction of postoperative morbidity, recovery accelerated and shortening the length of hospitalization.

Studies have shown that VATS provides adequate nodal dissection and oncological staging comparable to open surgery, including nodal stations deep. Also, increased CCI and reduced FEV1 values were identified as independent predictors of clinically relevant postoperative complications, emphasizing the importance of functional assessment and rigorous perioperative risk stratification.

In terms of nodal management, LS-LND proved non-inferior systematic lymphadenectomy in carefully selected patients with NSCLC stages IA–IB, helping to reduce surgical trauma and complications without compromise survival and cancer control.

The original contribution of the thesis is represented by the results from the experience "Prof. Dr. Alexandru Trestioreanu" Oncological Institute from Bucharest as an oncological center tertiary care in Romania regarding the implementation of minimally invasive surgery and strategies modern nodal management in NSCLC. Through this research I managed to demonstrate the feasibility and efficiency of VATS in Romanian oncology practice. Also we identified the role of clinical and functional factors in predicting postoperative morbidity and we proposed the possibility of using LS-LND as a safe alternative to S-LND in early stages carefully selected.

Thus this thesis represents a contribution to support the personalization of treatment surgery in NSCLC and to the integration of minimally invasive approaches in oncological practice modern from Romania.

Bibliography

1. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer J Clinicians* **2021**, *71*, 209–249, doi:10.3322/caac.21660.
2. Siegel, R.L.; Kratzer, T.B.; Giaquinto, A.N.; Sung, H.; Jemal, A. Cancer Statistics, 2025. *CA A Cancer J Clinicians* **2025**, *75*, 10–45, doi:10.3322/caac.21871.
3. Howington, J.A.; Blum, M.G.; Chang, A.C.; Balekian, A.A.; Murthy, S.C. Treatment of Stage I and II Non-Small Cell Lung Cancer. *Chest* **2013**, *143*, e278S-e313S, doi:10.1378/chest.12-2359.
4. Darling, G.; Malthaner, R.; Dickie, J.; McKnight, L.; Nhan, C.; Hunter, A.; McLeod, R.S. Quality Indicators for Non-Small Cell Lung Cancer Operations With Use of a Modified Delphi Consensus Process. *The Annals of Thoracic Surgery* **2014**, *98*, 183–190, doi:10.1016/j.athoracsur.2014.03.001.
5. Lardinois, D.; Deleyn, P.; Vanschil, P.; Porta, R.; Waller, D.; Passlick, B.; Zielinski, M.; Junker, K.; Rendina, E.; Ris, H. ESTS Guidelines for Intraoperative Lymph Node Staging in Non-Small Cell Lung Cancer☆. *European Journal of Cardio-Thoracic Surgery* **2006**, *30*, 787–792, doi:10.1016/j.ejcts.2006.08.008.
6. Batchelor, T.J.P.; Rasburn, N.J.; Abdelnour-Berchtold, E.; Brunelli, A.; Cerfolio, R.J.; Gonzalez, M.; Ljungqvist, O.; Petersen, R.H.; Popescu, W.M.; Slinger, P.D.; 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). *European Journal of Cardio-Thoracic Surgery* **2019**, *55*, 91–115, doi:10.1093/ejcts/ezy301.
7. Rami-Porta, R. The TNM Classification of Lung Cancer—a Historic Perspective. *J Thorac Dis* **2024**, *16*, 8053–8067, doi:10.21037/jtd-24-1212.
8. Tanase, B.C.; Burlacu, A.I.; Nistor, C.E.; Horvat, T.; Oancea, C.; Marc, M.; Tudorache, E.; Manolescu, D. Differential Outcomes of VATS and Open Surgery in Lung Cancer Patients with Antecedent Oncological Diagnoses. *JPM* **2023**, *13*, 1498, doi:10.3390/jpm13101498.
9. Nath, T.S.; Mohamed, N.; Gill, P.K.; Khan, S. A Comparative Analysis of Video-Assisted Thoracoscopic Surgery and Thoracotomy in Non-Small-Cell Lung Cancer

in Terms of Their Oncological Efficacy in Resection: A Systematic Review. *Cureus* **2022**, doi:10.7759/cureus.25443.

10. Kim, D.; Woo, W.; Shin, J.I.; Lee, S. The Uncomfortable Truth: Open Thoracotomy versus Minimally Invasive Surgery in Lung Cancer: A Systematic Review and Meta-Analysis. *Cancers* **2023**, *15*, 2630, doi:10.3390/cancers15092630.
11. Birim, O. Validation of the Charlson Comorbidity Index in Patients with Operated Primary Non-Small Cell Lung Cancer. *European Journal of Cardio-Thoracic Surgery* **2003**, *23*, 30–34, doi:10.1016/S1010-7940(02)00721-2.
12. Berry, M.F.; Onaitis, M.W.; Tong, B.C.; Harpole, D.H.; D'Amico, T.A. A Model for Morbidity after Lung Resection in Octogenarians. *European Journal of Cardio-Thoracic Surgery* **2011**, *39*, 989–994, doi:10.1016/j.ejcts.2010.09.038.
13. Ferguson, M.K.; Durkin, A.E. A Comparison of Three Scoring Systems for Predicting Complications after Major Lung Resectionq.
14. Zhao, Y.; Mao, Y.; He, J.; Gao, S.; Zhang, Z.; Ding, N.; Xue, Q.; Gao, Y.; Wang, D.; Zhao, J.; et al. Lobe-Specific Lymph Node Dissection in Clinical Stage IA Solid-Dominant Non–Small-Cell Lung Cancer: A Propensity Score Matching Study. *Clinical Lung Cancer* **2021**, *22*, e201–e210, doi:10.1016/j.cllc.2020.09.012.
15. Subramanian, M.P.; Eaton, D.B.; Heiden, B.T.; Brandt, W.S.; Labilles, U.L.; Chang, S.-H.; Yan, Y.; Schoen, M.W.; Patel, M.R.; Kreisel, D.; et al. Lobe-Specific Lymph Node Sampling Is Associated with Lower Risk of Cancer Recurrence. *JTCVS Open* **2024**, *17*, 271–283, doi:10.1016/j.xjon.2023.11.009.
16. Adachi, H.; Sakamaki, K.; Nishii, T.; Yamamoto, T.; Nagashima, T.; Ishikawa, Y.; Ando, K.; Yamanaka, K.; Watanabe, K.; Kumakiri, Y.; et al. Lobe-Specific Lymph Node Dissection as a Standard Procedure in Surgery for Non–Small Cell Lung Cancer: A Propensity Score Matching Study. *Journal of Thoracic Oncology* **2017**, *12*, 85–93, doi:10.1016/j.jtho.2016.08.127.
17. Hattori, A.; Matsunaga, T.; Takamochi, K.; Oh, S.; Suzuki, K. Extent of Mediastinal Nodal Dissection in Stage I Non-Small Cell Lung Cancer with a Radiological Pure-Solid Appearance. *European Journal of Surgical Oncology* **2021**, *47*, 1797–1804, doi:10.1016/j.ejso.2021.03.232.
18. Brunelli, A.; Refai, M.; Xiumé, F.; Salati, M.; Sciarra, V.; Socci, L.; Sabbatini, A. Performance at Symptom-Limited Stair-Climbing Test Is Associated With Increased Cardiopulmonary Complications, Mortality, and Costs After Major Lung Resection.

The Annals of Thoracic Surgery **2008**, *86*, 240–248, doi:10.1016/j.athoracsur.2008.03.025.

19. McKenna, R.J. Lobectomy by Video-Assisted Thoracic Surgery with Mediastinal Node Sampling for Lung Cancer. *The Journal of Thoracic and Cardiovascular Surgery* **1994**, *107*, 879–882, doi:10.1016/S0022-5223(94)70344-2.
20. Yan, T.D.; Black, D.; Bannon, P.G.; McCaughan, B.C. Systematic Review and Meta-Analysis of Randomized and Nonrandomized Trials on Safety and Efficacy of Video-Assisted Thoracic Surgery Lobectomy for Early-Stage Non–Small-Cell Lung Cancer. *JCO* **2009**, *27*, 2553–2562, doi:10.1200/JCO.2008.18.2733.
21. Saji, H.; Okada, M.; Tsuboi, M.; Nakajima, R.; Suzuki, K.; Aokage, K.; Aoki, T.; Okami, J.; Yoshino, I.; Ito, H.; et al. Segmentectomy versus Lobectomy in Small-Sized Peripheral Non-Small-Cell Lung Cancer (JCOG0802/WJOG4607L): A Multicentre, Open-Label, Phase 3, Randomised, Controlled, Non-Inferiority Trial. *The Lancet* **2022**, *399*, 1607–1617, doi:10.1016/S0140-6736(21)02333-3.
22. Altorki, N.K.; Wang, X.; Wigle, D.; Gu, L.; Darling, G.; Ashrafi, A.S.; Landrenau, R.; Miller, D.; Liberman, M.; Jones, D.R.; et al. Perioperative Mortality and Morbidity after Sublobar versus Lobar Resection for Early-Stage Non-Small-Cell Lung Cancer: Post-Hoc Analysis of an International, Randomised, Phase 3 Trial (CALGB/Alliance 140503). *The Lancet Respiratory Medicine* **2018**, *6*, 915–924, doi:10.1016/S2213-2600(18)30411-9.
23. Provencio, M.; Serna-Blasco, R.; Nadal, E.; Insa, A.; García-Campelo, M.R.; Casal Rubio, J.; Dómine, M.; Majem, M.; Rodríguez-Abreu, D.; Martínez-Martí, A.; et al. Overall Survival and Biomarker Analysis of Neoadjuvant Nivolumab Plus Chemotherapy in Operable Stage IIIA Non–Small-Cell Lung Cancer (NADIM Phase II Trial). *JCO* **2022**, *40*, 2924–2933, doi:10.1200/JCO.21.02660.
24. Whitson, B.A.; Groth, S.S.; Duval, S.J.; Swanson, S.J.; Maddaus, M.A. Surgery for Early-Stage Non-Small Cell Lung Cancer: A Systematic Review of the Video-Assisted Thoracoscopic Surgery Versus Thoracotomy Approaches to Lobectomy. *The Annals of Thoracic Surgery* **2008**, *86*, 2008–2018, doi:10.1016/j.athoracsur.2008.07.009.
25. Tanase, B.C.; Horvat, T.; Burlacu, A.; Chitoran, E.; Rotaru, V.; Pătrașcu, T.; Simion, L. A Retrospective Comparison of Oncologic and Staging Outcomes Between Surgical Procedures–Video-Assisted Thoracoscopic Surgery Versus Thoracotomy in

Pulmonary Adenocarcinoma. *Medicina* **2026**, *62*, 702, doi:10.3390/medicina62040702.

26. Tanase, C.B.; Chitoran, E.; Rotaru, V.; Gullo, G.; Horvat, T. Predictors of Clinically Relevant Postoperative Morbidity Fol- 2 Lowing Curative Intent Surgical Resection for Non-Small Cell 3 Lung Cancer 4.
27. Tanase, B.C.; Horvat, T.; Davidescu, M.; Nistor, C.E.; Muntean, C.; Cozma, G.V.; Nicola, A.; Bratosin, F.; Laitin, S.M.D.; Burlacu, A. Curative-Intention Surgery with Lobe-Specific Versus Systematic Lymph Node Dissection in Clinical Stage IA–IB Non-Small Cell Lung Cancer: Our Experience and Literature Review. *Healthcare* **2025**, *13*, 957, doi:10.3390/healthcare13080957.
28. Ma, W.; Zhang, Z.-J.; Li, Y.; Ma, G.-Y.; Zhang, L. Comparison of Lobe-Specific Mediastinal Lymphadenectomy versus Systematic Mediastinal Lymphadenectomy for Clinical Stage T_{1a} N_0 M_0 Non-Small Cell Lung Cancer. *J Can Res Ther* **2013**, *9*, 101, doi:10.4103/0973-1482.119119.

List of published scientific papers

Article 1:

Burlacu, Alin Ionut, **Bogdan Cosmin Tanase**, Iolanda Augustin, and Gabriel Veniamin Cozma. "Evaluating VATS versus Open Surgery for Non-Small Cell Lung Cancer: A 5-Year Retrospective Study." *Chirurgia* 119, no. 4 (2024): 393. https://doi.org/10.21614/chirurgia.2999.

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Article 2:

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Article 3:

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Article 4:

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