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„CAROL DAVILA”, BUCHAREST

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PHD THESIS SUMMARY

PhD supervisor:

PROF. UNIV. DR. HORVAT TEODOR

PhD student:

BURLACU ALIN IONUȚ

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***THE ROLE OF VIDEO-ASSISTED THORACIC SURGERY IN THE
TREATMENT OF LUNG CANCER***

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List of published scientific papers

Article 1

Tanase BC, **Burlacu AI**, Nistor CE, Horvat T, Oancea C, Marc M, Tudorache E, Manolescu D. Differential Outcomes of VATS and Open Surgery in Lung Cancer Patients with Oncological Antecedent Diagnosis. J Pers Med. 2023 Oct 15;13(10):1498. doi: 10.3390/jpm13101498. PMID: 37888110; PMCID: PMC10608346 (work made from data presented in Chapter 4, pages 95-103).

Title of the journal: Journal of Personalized Medicine,

Year: 2023, Volume: 13, Number: 10

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Work access links: <https://www.mdpi.com/2520354>,
<https://doi.org/10.3390/jpm13101498>

Quality: Corresponding author

Article 2

Tanase BC, **Burlacu AI**, Nistor CE, Horvat T, Oancea C, Marc M, Tudorache E, Mateescu T, Manolescu D. A Retrospective Analysis Comparing VATS Cost Discrepancies and Outcomes in Primary Lung Cancer vs. Used Primary Lung Cancer Patients. Healthcare (Basel). 2023 Jun 14;11(12):1745. doi: 10.3390/healthcare11121745. PMID: 37372863; PMCID: PMC10298099 (work made from data presented in Chapter 5, pages 104-112).

Title of the magazine: Healthcare

Year: 2023, Volume: 11, Number: 12

Journal indexing: BibCnrs, CNKI, National Library of Medicine, Web of Science;
<https://www.mdpi.com/journal/healthcare/indexing>

Impact factor at time of publication: 3.160

Work access links: <https://www.mdpi.com/2227-9032/11/12/1745>,
<https://doi.org/10.3390/healthcare11121745>

Quality: Corresponding author

Article 3

Burlacu AI, Tanase BC, Augustin I, Cozma GV. Evaluating VATS versus Open Surgery for Non- Small Cell Lung Cancer: A 5-year Retrospective Study. Surgery (Bucur). 2024 Aug;119(Ahead of print):1-11. two: 10.21614/chirurgia.2999. PMID: 39106471 (work made from data presented in Chapter 4, pages 95-103).

Title of the magazine: Surgery (Bucur)

Year: 2024, Volume: 119, Number: 4

Journal indexing: Web of Science Core Collection: ESCI, PubMed

Impact factor at the time of publication of the article: 0.8

Work access links: <https://revistachirurgia.ro/pdfs/2024-08-aop-alin-ionut-burlacu.pdf> , <https://www.revistachirurgia.ro/evaluating-vats-versus-open-surgery-for-nonsmall-cell-lung-cancer-a-5year-retrospective-study/>

Quality: First author

Article 4

Manolache V, Motas N, Davidescu M, Bluoss C, Rus O, Tanase B, Jianu E, Burlacu A, Alexe V, Cioalca -Iliescu M, Nicolae G, Dobritoiu F, Saon C, Paleru C, Bosinceanu M, Horvat T, Cordos I, Gonzalez-Rivas D. Minimally Invasive Thoracic Surgery - Video Assisted Thoracic Surgery: Technique and Indications. Surgery (Bucur). 2022 Feb;117(1):101-109. two: 10.21614/chirurgia.2608. PMID: 35272760 (work made from data presented in Chapter 4, pages 95-103).

Title of the magazine: Surgery (Bucur)

Year: 2022, Volume: 117, Number: 1

Journal indexing: Web of Science Core Collection: ESCI, PubMed

Impact factor at the time of publication of the article: 0.6

Access links to the work: <https://www.revistachirurgia.ro/pdfs/2022-1-101.pdf> , <https://www.revistachirurgia.ro/minimally-invasive-thoracic-surgery-video-assisted-thoracic-surgery-technique-and-indications/>

Quality: co-author

List of abbreviations

CCI	<i>Charlson comorbidity index</i>
CMLND	<i>Complete mediastinal lymph node dissection</i>
COPD	<i>Chronic obstructive pulmonary disease</i>
DOS	<i>Distal obstructive syndrome</i>
MRD	<i>Mixed respiratory dysfunction</i>
NSCLC	<i>Non-small cell lung cancer</i>
ORD	<i>Obstructive respiratory dysfunction</i>
PAD	<i>Peripheral arterial disease</i>
PFT	<i>Pulmonary function tests</i>
PLC	<i>Primary lung cancer</i>
RRD	<i>Restrictive respiratory dysfunction</i>
SPLC	<i>Second primary lung cancer</i>
TB	<i>Tuberculosis</i>
uVATS	<i>Uniportal video-assisted thoracic surgery</i>
VATS	<i>Video-assisted thoracic surgery</i>

Introduction

Video-assisted thoracic surgery (VATS) is the minimally invasive approach used to access the chest without the use of a rib retractor, the image of the operative field being obtained through a video telescope.

The choice of the theme thesis "The role of video-assisted thoracic surgery in the treatment of bronchopulmonary cancer" comes in response to long specialist, national and international debates regarding the surgical treatment of bronchopulmonary cancer. In Romania, attempts to introduce video-assisted thoracic surgery in the treatment of bronchopulmonary cancer as a standard therapeutic strategy for early stages lung cancer (stages I and II) still represent a challenge [1] . It should be mentioned right from the introduction, as a recognition for the work of our predecessors, teachers and even mentors, that the first anatomical resection in Romania, a right lower lobectomy, was performed at the Elias Hospital by Dan Ulmeanu and Ioan Cordoș, and the second, a middle lobectomy was performed at the Clinical Central Military Hospital by Teodor Horvat [2] . I mention that the idea of this work appeared with the video-assisted thoracic surgery program carried out in the clinic I am part of and in which I was trained during my residency years, namely the Thoracic Surgery Clinic within the Oncological Institute "Professor Doctor Alexandru Trestioreanu" Bucharest.

The concept of video-assisted thoracic surgery includes a wide range of approaches, such as: multiportal (two or more access ports are used to perform the surgical intervention), uniportal (the use of a single working port through which the telescope is inserted to obtain the image, as well as work tools).

If at the beginning of video-assisted thoracic surgery, the multiportal approach was frequently practiced, today the standard is uniportal surgery or surgery with an accessory working port [3]. The present paper wants to finally support the need to introduce the minimally invasive approach in bronchopulmonary cancer surgery as a quality standard, an aspect otherwise supported by the international guidelines for the management of bronchopulmonary cancer.

I mention the fact that the video-assisted thoracic surgery approach, regardless of its type, aims to carry out a surgical intervention that respects the oncological principles, without there being a consistent difference in the way to practice the resection between the two major approaches: the classic way and the minimally invasive [4] . Analyzing the role

of the minimally invasive approach in bronchopulmonary cancer surgery, I will emphasize, through the results obtained from the studies carried out in the framework of scientific research, the advantages of video-assisted thoracic surgery in general, as well as the advantages of each approach used in our clinic compared to thoracotomy surgeries. At the end of the scientific research, I mention that we obtained results that will help to establish some indications regarding the type of approach used in bronchopulmonary cancer resection surgery according to different factors (age, associated comorbidities, staging, risks or costs). At the same time, these results can represent a substantiation note to support the use of the minimally invasive approach in bronchopulmonary cancer surgery.

I. The general part

1. Video-assisted thoracic surgery – generalities

1.1. Basic principles in VATS

Video-assisted thoracic surgery (VATS) is defined as a minimally invasive approach to the chest that requires the observance of two rules: the first - obtaining the image of the operating field through a video telescope, image processed and displayed on a screen, and the second - lack of use of a rib spacer, which has been shown to be responsible for postoperative pain. Regarding the number or size of the incisions performed, a working mini-thoracotomy of up to 7 cm is considered optimal [5] .

1.2. Types of minimally invasive approach

From the point of view of access to the pleural cavity, various types of approach have been distinguished throughout the evolution of VATS, among which: the multiportal approach (at least 3 ports), the biportal approach (2 ports), the uniportal approach [6–9] .

The subxiphoid approach starts from the hypothesis of pain related to the incision in the intercostal space, avoiding this access ensures a low level of pain. [10,11] .

Robotic surgery is used in centers with increased experience and unrestricted access to modern medical technologies [12,13] .

Another classification of the types of approach, which dictates the positioning of the thoracoports for minimally invasive surgery and requires the use of a specific type of instrumentation, is that related to the position of the dissection instruments in relation to the pulmonary hilum and includes: the anterior approach of the pulmonary hilum, respectively the posterior approach [14,15] .

1.3. VATS versus classic surgery

Since the beginning of minimally invasive surgery, the advantages and disadvantages of each type of approach have been studied. Thus, it is considered that the minimally invasive approach ensures a low level of pain due to a much-reduced dimensional incision and minimal pressure on the intercostal nerves thanks to the lack of use of the wound spacer. Reducing the incision and performing a dissection under video magnification seems to ensure a reduced inflammatory response in minimally invasive operated patients [16] . A

reduced inflammatory response ensures less quantitative pleural drainage, less hospitalization and faster social and professional reintegration.

2. VATS in the treatment of bronchopulmonary cancer

2.1. Overview

The treatment of bronchopulmonary cancer is a multidisciplinary one, among the therapeutic options are: surgical resection, systemic oncological therapy and radiotherapy. For a correct therapeutic management, it is necessary to discuss each case of bronchopulmonary cancer in a multidisciplinary therapeutic indication committee [17] .

2.2. Directions

According to the international guidelines in force at the time of writing this paper, bronchopulmonary cancer without lymph node invasion (N0) has an absolute first-line surgical indication. The surgical treatment of bronchopulmonary cancer must be performed by a team of surgeons with expertise in oncological pathology, in a reference center with a representative case history. Lobectomy or anatomical lung resection is the type of resection recommended by international guidelines. Sublobar resections are permitted and should be considered under certain conditions.

2.3. Contraindications

The contraindications of the minimally invasive approach usually depend on the expertise of the anesthetic-surgical team. The main contraindication for a minimally invasive approach is represented by the impossibility of creating an optimal working room. The advantages of the minimally invasive approach were presented in detail in previous chapters. The main disadvantage, however, being represented by the impossibility of palpating the mediastinal or pulmonary structures (with few exceptions), a maneuver extremely frequently used in classic surgery.

2.4. Complications

During lung resection through a minimally invasive approach, complications can occur that complicate the surgical procedure. Among these, the most feared is the vascular accident at the level of the pulmonary artery, with massive hemorrhage that most of the time requires the conversion of the minimally invasive approach to thoracotomy. [18–20] .

II. The special part

3. Contributions regarding the minimally invasive approach in relation to classical surgery for the surgical treatment of bronchopulmonary cancer

3.1. Study objectives

Bronchopulmonary cancer is one of the most common life-threatening pathologies, being among the first causes of death worldwide. The evolution of early diagnostic methods, as well as the emergence, even if sporadic, of bronchopulmonary cancer screening programs, have led to the identification of cases of malignant bronchopulmonary tumors of the NSCLC type in early stages (stages I-II) that have an absolute surgical indication.

3.2. The motivation of the study

The limitation of the use of the minimally invasive approach in the surgical treatment of bronchopulmonary cancer in Romania is the direct cause of the lack of a cost-benefit analysis related to the health system in our country, thus requiring a study to highlight the advantages of the minimally invasive approach, as well as the long-term financial impact.

3.3. Working assumptions

With this paper, I aim to: analyze the cases of patients with bronchopulmonary cancer operated in the Clinic of Thoracic Surgery of the Bucharest Oncological Institute through the classical approach, respectively minimally invasive. Establishing therapeutic indication protocols for NSCLC bronchopulmonary cancer.

3.4. Materials and methods

In this study, we retrospectively analyzed the data collected from 228 patients diagnosed with NSCLC type bronchopulmonary cancer, operated in the Thoracic Surgery Clinical Department of the Bucharest Oncological Institute during 2016-2022.

3.5. Distribution of patients by study years

Over the seven years of retrospective analysis in which data were collected to achieve a large enough sample, we can see the number of regulated lung resections for histopathologic confirmed NSCLC bronchopulmonary cancer by year in Table 3.1.

If until 2019 inclusive, the number of regulated lung resections for confirmed bronchopulmonary cancer reached 50, the year 2020 represented a turning point, with a sudden drop to one third.

Table 3.1 - Distribution of enrolled patients, by study years

Study year	2016	2017	2018	2019	2020	2021	2022
Patients no.	34	37	34	47	16	24	36

3.6. Distribution of patients by gender

Analyzing Table 3.2 with the distribution of subjects enrolled in the study according to gender, a higher incidence of bronchopulmonary cancer is noted among male patients.

Table 3.2 - Distribution of patients by sex, age and smoking status

Variables	OPEN (n=102)	VATS (n=126)	p-value
Age (years)	59±23	62±25	0.621
Smokers	60 (5.40%)	56 (44.44%)	0.043
Gender			0.094
Male	64 (63.36%)	64 (50.79%)	
Female	38 (37.62%)	62 (49.20%)	

3.7. Distribution by age groups

The age of the patients included in the two study groups is between 26 and 84 years. The average age of the study participants was 61 years, males with an average age of 62 years, females 60 years

3.8. Distribution according to the environment of origin

Analyzing the distribution of patients in the two groups (OPEN and VATS) depending on the area of origin, an approximately equal distribution is found in terms of patients from the urban environment, but for those from the rural environment there is a difference of 14%, with statistical significance ($p=0.031$), as can be seen in Table 3.3.

Table 3.3 - Distribution of patients in the two groups according to the environment

		Urban (n = 170)	Rural (n = 58)	n	p	test
OPEN vs VATS, n	VATS	101 (59%)	25 (43%)	126	0.031	Chi2
	OPEN	69 (41%)	33 (57%)	102	-	-

3.9. Distribution of patients according to blood group and correlation with type of bronchopulmonary cancer

The idea of analyzing this type of distribution started from the hypothesis that a certain population with a specific blood group may develop a particular form of bronchopulmonary cancer. Observing the discrepancy between the distribution of patients in *group 0*, we can see the higher incidence of lung adenocarcinoma among patients with blood group *0*.

3.10. Distribution of patients according to associated comorbidities

Since the average age of the patients enrolled in the study is around 60 years, patients exposed in most cases to causal risk factors for bronchopulmonary cancer (smoking, respiratory ailments, alcohol), a number of comorbidities associated with the studied pathology are described. All this can be found in Table 3.4:

Table 3.4 - Distribution of comorbidities of patients enrolled in the study and their frequency

Morbidity	Hypertension	COPD	Diabetes	Ischemic heart disease	TB	Stroke	Heart failure	PAD
No. of pts.	74	24	27	14	9	6	10	11
Percent (%)	32.46	9.21	11.48	6.14	3.95	2.63	4.39	4.82

To achieve a normal distribution of the two groups (*VATS and OPEN*) in terms of comorbidities, we used *the Charlson Comorbidity Index (CCI)*.

The Charlson Comorbidity Index, which quantifies the impact of associated diseases on the patient's evolution, was similar between the two study groups, with mean values of 4.28 (min.=2, max.=8) for the classic surgery group and 4.38 (min.=2, max.=7) for the *VATS* group, with a *p-value* of 0.403.

3.11. Distribution of patients according to smoking status

Of the total of 228 enrolled patients, 76 are smokers (33.33%), 42 ex-smokers (18.42%) and 110 non-smokers (48.25%). The gender distribution of smokers is undoubtedly in favor, or better said against men, over 65% of smokers, respectively over 83% of ex-smokers being male, regardless of their background, this distribution having a statistical significance, $p < 0.001$.

3.12. Distribution according to cardiorespiratory functional status

Table 3.5 - Descriptive analysis of qualitative variables: PFT, occupational exposure, smoking status, environment, gender

		n(%)
PFT	normal	136 (60%)
	ORD	47 (21%)
	MRD	23 (10%)
	RRD	14 (6.1%)
	ODS	8 (3.5%)
Occupational respiratory exposure	NO	208 (91%)
	YES	20 (8.8%)
Smoker status	non-smoker	110 (48%)
	smoker	76 (33%)
	ex-smoker	42 (18%)
Environmental status	urban	170 (75%)
	rural	58 (25%)
Gender	male	128 (56%)
	female	100 (44%)

The distribution of patients according to the status of the respiratory function tests is not at all negligible, according to Table 3.5.

3.13. Distribution of cases according to tumor staging

Of all patients, almost 60% were in clinical stages IIIA and IIB of the disease, only 2.2% of patients were in stage IA1, with nodules less than 1 cm and no lymph node invasion. Comparing the distributions of the clinical and pathological stages, we observe a decrease in the general stage („*downstaging* „) after the analysis of the operative part, only 24% of the patients being in the pathological stage IIIA, respectively 19% in IIB, a result that denotes the lack of invasion of some nodes that had imaging signs of adenopathy, having a short axis of more than 1 cm, respectively 1.5 cm in the case of nodes located in station 7 (subcarinal).

3.14. Distribution of patients according to approach

The central pillar of the study is the approach used to perform the surgical interventions. Thus, as we mentioned in the previous chapter, among the 228 patients, 102 benefited from the classic approach (44.73%) and were included in the "*OPEN*" group, and the other 126 were included in the "*VATS*" group (55.26%), being operated by a minimally invasive approach. It is found that among the 126 cases of VATS interventions, 37 were performed through a multiportal approach (30%), and 89 through a single port (70%); of these in 3 cases we used 4 ports, in 7 cases 3 ports and in 27 cases the biportal approach.

In Table 3.6 it is possible to observe the number of cases operated by VATS, completed by minimally invasive approach, as well as the division of those converted to thoracotomy according to the type of approach.

Table 3.6 - Conversion distribution by type of approach

Approach	complete VATS	converted VATS	converted uVATS	converted 2-port VATS	converted 3-port VATS	converted 4-port VATS
No. of pts.	107	19	13	5	0	1
%	84.92	15.07	68.42	26.32	0	5.26

3.15. Distribution according to the type of surgery

The distribution of cases according to the type of resection follows to some extent the patterns of the frequency of resections, according to the preferred localization of bronchopulmonary cancer in the lung apex, most often on the right, according to Table 3.7; in our study there is no consistent difference between the number of right and left upper lobe resections.

Table 3.7 - Distribution according to major types of resections

Variables	OPEN (n=102)	VATS (n=126)	p-value
Type of resection			
Bilobectomy	7 (6.93%)	2 (1.58%)	0.091
Lobectomy	89 (87.12%)	96 (76.19%)	0.051
Segmentectomy	6 (5.94%)	28 (22.22%)	

3.16. Results of the analysis on the type of approach and surgical intervention

After analyzing the distributions of patients in the two groups, we performed statistical tests to compare the two types of approach and identify the relationship of superiority or non-inferiority between them.

3.17. Duration of surgery

The average duration of surgery in the OPEN group was 347 minutes, compared to 299 minutes in the VATS group, $p < 0.001$.

3.18. Intraoperative blood loss

Patients operated by classical surgery had an average blood loss of 160.88 ml, while patients operated by minimally invasive approach had a bleeding amount of up to 98.68 ml, $p < 0.001$.

3.19. Air losses

Analyzing the two groups, 10% of the VATS group compared to 50% of the open surgery group experienced air loss on the second postoperative day, statistically significant difference ($p < 0.001$). When we talk about losses on day 7, only 2.4% of the VATS group still had air losses, respectively 11% in the OPEN group, with $p < 0.01$.

3.20. Duration of pleural drainage

The duration of postoperative pleural drainage maintenance was significantly shorter in the VATS group, with a mean of 5.78 days, $p < 0.001$.

3.21. Duration of hospitalization

Analyzing the duration of hospitalization, the patients operated by the classic approach had an average hospitalization of 27.7, and the patients in the VATS group had an average hospitalization duration of 12 days ($p < 0.001$).

3.22. Mediastinal lymphadenectomy associated with pulmonary resection

Complete mediastinal lymphadenectomy (CMLND) was performed in 93.13% of the cases of patients operated by classical surgery, respectively in the case of 89.68% of patients operated by the minimally invasive approach, with a *p-value* of 0.496.

3.23. Postoperative complications – Clavien-Dindo classification

The statistical analysis of the disease-free interval and postoperative complications quantified by the Clavien-Dindo classification, reported on the two groups - OPEN and VATS, respectively, showed an extension of the disease-free interval for patients in early stages of cancer (stages I-II), correlated with Clavien-Dindo complication classes 1, 2 or 3 ($p < 0.01$, respectively $p < 0.001$), but this advantage is not maintained in the case of patients in complication class 4, no statistical significance being detected ($p = 0.13$).

3.24. Costs associated with surgical treatment among patients with NSCLC

The average cost in RON of a surgical intervention for bronchopulmonary cancer is 16,200 RON. An analysis of the expenses of a surgical intervention according to the type of approach, shows higher immediate costs for the VATS group, as expected (14,111 RON for open surgery, compared to 18,781 RON for the minimally invasive approach), but without recording a statistically significant difference.

3.25. Survival of study patients at 1 year and 2 years, respectively

In the present study we obtained comparable survival results between the two groups, VATS and OPEN respectively, without a statistically significant difference. At one year, survival exceeds 58% in the VATS group, and reaches almost 50% in the OPEN group. Regarding two-year overall survival, it is less than 45%, with the VATS group having an advantage over OPEN, without statistical significance.

3.26. Discussions

The shorter duration of the surgical intervention can be explained by two aspects: first, by the complexity of certain cases operated by classical surgery, but during the realization of the two batches we tried to avoid this situation, by excluding them; the second aspect that can explain the reduction of operative time is related to mini-thoracotomy and suture which no longer require a long time to perform them, but also dissection and ligation, respectively the stapling of the structures contained in the pulmonary hilum, respectively the restoration of splits or intersegmental planes.

Total length of hospital stay was also an outcome for which video-assisted thoracic surgery demonstrated a significant advantage.

Two-year analysis of disease-free survival and Clavien-Dindo classification in the treatment of NSCLC bronchopulmonary cancer shows different results for patients who benefit from a minimally invasive approach compared to those who are operated on through the classical approach.

4. The use of the minimally invasive approach (VATS) and the classical one in the surgical treatment of patients with primary bronchopulmonary cancer, who had another cancer in the past

4.1. Introduction

Bronchopulmonary cancer can develop as a second cancer that can appear either in response to treatment for the disease in the patient's history, or secondary to exposure to causal risk factors. [21–28] .

However, a clear distinction must be made between lung metastases from a previous cancer and the development of a second primitive cancer – bronchopulmonary cancer. Pulmonary secondary determinations have an overall occurrence rate of 30% among cancer patients. Depending on the origin of the metastases, the most common primary sources are: breast, colorectal and clear cell renal cancer, each having both epidemiological and histopathological particularities [29] . In their study published in 2021, *Riggio et al* found an incidence of more than 50% of lung metastases throughout the life of breast cancer patients in advanced tumor stages [30,31] .

The focus of this study on patients with an oncological history starts from the premise that these patients may present different clinical scenarios in terms of perioperative care. Among the objectives of the study, the first was to characterize patients with bronchopulmonary cancer as a second malignancy, the second objective was to compare short-term outcomes in terms of perioperative and postoperative complications, length of hospital stay and overall survival among patients operated on by minimally invasive, respectively classic approach.

4.2. Materials and methods

The study was structured as a retrospective analysis, the data were collected between the years 2018 and 2023. An in-depth analysis of quantitative and qualitative variables such as age, sex, environment of origin, smoking status, exposure to respiratory toxins, oncological antecedents was carried out associated, the associated comorbidities transposed into the Charlson comorbidity index, the patients being subsequently divided into two groups.

4.3. Results

Of the 84 patients qualified for the study, 55 benefited from surgery for bronchopulmonary cancer through a minimally invasive approach, while 29 of the patients used the classic approach. Regarding the analysis by age groups, the average age for patients in the VATS group was 61.4 years, slightly higher than the average age of patients in the classic surgery group, which was 58.3 years. The proportion of women enrolled in the study was higher in both groups compared to men, with 58.2% percentages in the VATS group, respectively 58.6% in the classic surgery group. A significant proportion of the study population, nearly half, were current or ex-smokers. The mean smoking index (pack-years – a measure of the number of cigarettes smoked over time) was 31.5 among patients in the VATS group and a slightly higher value for patients in the classic surgery group (33.0 packs -an), without statistical significance.

Regarding tumor location (left-right), the right lung was more affected (55.8% of all cases), but the left upper lobe was the preferred site for the development of bronchopulmonary cancer as the second location, both in the VATS group (29.1%), as well as in the OPEN group (27.6%), in disagreement with the tendency of bronchopulmonary cancer localization among the general population, which develops mainly in the right upper lobe. 40% of the patients in the minimally invasive surgery group were in stage III, compared to 58.6% among those operated classically. Regarding blood loss during surgery, in the open surgery group we note a greater amount of blood lost, quantified over 200 ml, with a percentage of 37.9, in contrast to only 12.9% of patients in the group VATS. The average duration of the surgical intervention was longer among the patients operated by classical surgery (350 minutes), compared to those in the VATS group (270 minutes), a statistically significant difference, with $p=0.046$. Regarding an analysis of lymphadenectomy, 72.4% of patients in the classic surgery group underwent complete mediastinal lymphadenectomy, compared to only 65.5% in the VATS group, a difference without statistical significance.

Postoperatively, the VATS group notes a mean value of pleural drainage of 245.9 ml in 24 hours, which was significantly lower compared to the classic surgery group of 301.4 ml, with p value <0.001 . Analysis of postoperative complications indicates a higher frequency of air leaks in the first 24 hours in the open surgery group (48.3%), compared to the VATS group (12.7%, with the value of $p<0.001$).

4.4. Discussions

The minimally invasive approach is associated with a shorter duration of the surgical intervention, a reduced hospitalization, fewer complications, lower costs in the long term, without influencing the oncological results, thus supporting the non-inferiority of this type of approach in relation to classic surgery.

4.5. Conclusions

This study demonstrates the lack of a significant long-term difference in the approach used in the surgical intervention of patients with bronchopulmonary cancer arising in patients with a history of oncology.

5. Minimally invasive surgical treatment of primitive bronchopulmonary cancer – primary and secondary – surgical results and cost discrepancy

5.1. Introduction

Corroborating the results of the first two studies in this thesis, the purpose of this study is to compare the results and costs between patients with primary lung cancer ("*primary lung cancer - PLC*"), respectively those with secondary primary lung cancer ("*second primary lung cancer - SPLC*") operated by a minimally invasive approach [27,28,32–44] . Since it is known that the prognosis of patients with bronchopulmonary cancer is relatively unfavorable, with an average survival at 5 years of approximately 20%, depending of course on the stage of the disease, and the use of the minimally invasive approach can influence the evolution of patients in the medium or long term, we issued the hypothesis of obtaining different results regarding the minimally invasive surgical treatment of patients with bronchopulmonary cancer appearing as the first or second neoplasia.

5.2. Materials and methods

The study was structured as an analysis, the inclusion criteria: patients over 18 years old, with primary bronchopulmonary cancer demonstrated histopathological and immunohistochemically, who benefited from minimally invasive surgical treatment (VATS). Exclusion criteria included patients with incomplete medical records and those who did not provide consent as evidenced by medical records. After fulfilling the selection criteria, the whole group was divided into two groups: patients with primary bronchopulmonary cancer (PLC) and patients with secondary primary bronchopulmonary cancer (SPLC).

5.3. Results

From a total of 124 patients eligible to be included in the study, the two groups, PLC and SPLC, contained an equal number of patients, operated by video-assisted thoracic surgery, namely 62. The average age of patients with lung cancer primary was 62.1 years, compared to 63.7 years, the average of those in the group with secondary primary lung cancer. About half of the patients in the two groups were exposed to cigarette smoke, the Charlson Index had a value greater than 3 in 62.9% of the patients in the PLC group, compared to 80.6% of the patients in the SPLC group, having a *p* value of 0.028.

If we analyze the parameters related to the surgical intervention, the intraoperative blood loss is significantly higher in the SPLC group, the duration of the surgical intervention is significantly longer in the SPLC group with a mean value of 300 minutes. The length of hospital stay was significantly longer among patients in the SPLC group, specifically 6.1 days, compared to 4.2 days in the postoperative period. Total expenditure was significantly higher in patients in the SPLC group.

5.4. Discussions

The results of the present study support the advantages of the minimally invasive approach in the surgical treatment of bronchopulmonary cancer, but tilt the balance in terms of benefits for patients who develop a primitive bronchopulmonary cancer, compared to those who encounter such a pathology during their evolution as patients with an oncological history.

5.5. Conclusions

In conclusion, this study supports the favorable results of the minimally invasive approach comparable between the two patient populations, those with primary bronchopulmonary cancer and secondary primary bronchopulmonary cancer, respectively, with higher operative times, length of hospital stays and costs for patients in the SPLC group, respectively favorable survival rates for those in the PLC group. These findings may have major impact in the management of patients with bronchopulmonary cancer. Further studies in larger groups of patients are needed to confirm these results and to analyze the factors contributing to the major difference in costs between the two groups.

6. Conclusions of the thesis

1. Men are more prone to the occurrence of bronchopulmonary cancer, especially with increasing age.
2. The minimally invasive approach offers elderly patients the opportunity to benefit from surgical treatment of lung resection, from the perspective of the reduced complications it associates.
3. Most patients who develop bronchopulmonary cancer have associated comorbidities, the minimally invasive approach reducing their translation into postoperative complications.
4. Most smokers who have developed bronchopulmonary cancer associate a ventilatory dysfunction.
5. Most of the patients operated by the minimally invasive approach benefited from the uniportal approach.
6. Most surgeries performed by VATS were lobectomies.
7. Right upper lobectomy was the most common resection performed in both groups, VATS and OPEN, respectively.
8. The minimally invasive approach used in surgery for bronchopulmonary cancer is associated with low intraoperative bleeding.
9. Early air losses are much less in the group of patients operated by video-assisted thoracic surgery.
10. Drain tubes are removed earlier in the case of patients benefiting from the minimally invasive approach.
11. The length of hospital stay is significantly shorter among patients operated by VATS.
12. Patients in the VATS group had a lower number of postoperative complications.
13. The immediate costs of the minimally invasive surgical intervention are higher than those of the classical approach.
14. Bronchopulmonary cancer can occur as a second malignancy in cancer patients.
15. A greater number of women developed bronchopulmonary cancer as a second malignancy.
16. The duration of the surgical intervention in the group of patients with primary bronchopulmonary cancer developed in patients with neoplastic history, operated by VATS is significantly shorter than in the OPEN group.

17. The amount of pleural drainage in the VATS group is lower than that calculated in patients in the OPEN group, when we analyze the situation of patients with bronchopulmonary cancer developed as a second neoplasia.
18. Hospitalization of patients in the VATS group is considerably less, compared to patients with a second neoplasia operated on by the classic approach.
19. Patients with second neoplasia bronchopulmonary cancer operated by classical surgery associated a higher rate of postoperative complications.
20. From the analysis of patients with primary bronchopulmonary cancer developed as the first, respectively the second neoplasia, operated by minimally-invasive approach, it is counted that those in the SPLC group have a higher rate of associated comorbidities.
21. Patients in the SPLC group had higher intraoperative blood loss than those in the PLC group.
22. The duration of the surgical intervention is significantly longer in the SPLC patient group, over 300 minutes, compared to the PLC group patients, who registered an average value of 260 minutes.
23. The duration of hospitalization is significantly shorter in the PLC group compared to the SPLC group.
24. Expenditures are also higher among patients in the SPLC group than in the other group.
25. Patients in the PLC group had a lower rate of disease recurrence than those in the SPLC group.
26. Two-year survival was significantly better for patients in the PLC group compared with those in the SPLC group.

7. Personal contributions

In the present work, we analyzed the cases with bronchopulmonary cancer operated on in the Thoracic Surgery clinic of the Bucharest Oncological Institute, comparing the two groups created - the patients operated by the minimally invasive approach, respectively those operated by the classic approach. As can be seen from chapter 3, we carried out a thorough analysis of the variables with an impact on the evolution of patients, noting in subchapters 3.17 – 3.26 the multiple advantages of the minimally invasive approach in relation to classical surgery, supporting the data from the specialized literature.

By analyzing the two types of approach, I was able to establish as normal a standardization of surgical treatment among patients with bronchopulmonary cancer in stages I-II, in the sense of using the minimally invasive approach, with all the benefits that this type of approach brings with him. The sub-chapters that contain the results of the first study, emphasize the advantages of the approach through video-assisted thoracic surgery, in front of the approach through thoracotomy, thus through this study I can support my contribution to the alignment of the way to practice thoracic surgery in Romania, to international standards, by promoting thoracic surgery video-assisted.

From the analysis of the costs related to the type of approach through which the surgical resection of bronchopulmonary cancer is performed, even if the data obtained demonstrate a higher immediate expense for the minimally invasive approach, the analysis of all variables supports lower costs in the medium and long term.

Given the membership of the Department of Thoracic Surgery at the Bucharest Oncological Institute, part of the case history has important particularities, the one that caught my attention was the history of neoplasia among some of the patients with bronchopulmonary cancer. In this way, we laid the foundations of a statistical analysis among patients with bronchopulmonary cancer appearing as a second neoplasia, the results being consistent with the specialized literature, thus supporting the practice of the minimally invasive approach among these patients, in centers with experience in oncological surgery and expertise in the field of minimally invasive surgery.

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