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CLINICAL STUDY

Combined surgical treatment of lung cancer and heart diseases

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Abstract: *Objective:* The co-incidence of lung cancer and heart disease is increasing. This can be caused by population ageing, which has more co-morbidities and most likely due to the common etiological causes of both entities, i.e. smoking, hypertension and obesity. The aim of this study was to analyze the outcomes of simultaneously performed heart surgery and pulmonary resection in a selected group of patients.
Methods: From January 2002 to December 2011 we performed in our department 1115 pulmonary resections for lung tumor. Significant heart disease requiring surgical treatment was diagnosed in 21 patients from the whole group. In 12 patients, group A; simultaneous heart surgery and lung resection procedure were performed.
Results: Group A consisted of 8 men and 4 women with the median age of 67.8 ± 5.9 years. In this group, 10 lobectomy procedures and 2 wedge resections for pulmonary metastasis were done. Nine patients underwent coronary artery revascularization, 2 patients underwent mitral valve replacement and one patient underwent tumor removal from the left atrium. In 5 patients, extracorporeal circulation (ECC) was needed, the remaining 7 patients underwent myocardial revascularization using an off-pump technique.
Group B consisted of 7 men and 5 women with the age of 68.5 ± 7.4 years. Ten lobectomy procedures and 2 wedge resections were performed.
Conclusion: The risk of simultaneously performed lung resection and cardiac surgery is not high. Despite the certain differences in clinical indicators between group A and B, the safety of simultaneous procedure, in group A, was evident. Furthermore, earlier lung resection was enabled and the eventual complications from further surgical procedure were avoided *(Tab. 5, Ref. 33)*. Text in PDF *www.elis.sk.*
Key words: pulmonary resection, heart surgery, simultaneous heart and lung surgery, extracorporeal circulation.

In the early 19th century, lung cancer was not a frequent disease. Nowadays, it is considered as the most common neoplasm and the most cause of death among all malignant diseases with a mortality rate up to 5 %. The incidence of lung cancer has increased during the last 40 years and its incidence is similar in all continents. The increase of tumor incidence begins to be statistically important in the 4th decade of life with an incidence peak in the 6th decade. The incidence of lung cancer in men is currently stable and in women is increasing. Despite that, lung cancer is still 4 times more often in men (1). In the European Union, lung cancer accounts for 17 % of all cancers and 6 % in women (2).

The major risk factor for lung cancer is cigarette smoking (3). At the beginning of the 70s of the last century, Fingerland proved the relationship between cigarette smoking and the incidence of squamous-cell lung cancer (4).

The group of patients with lung tumors and coexisting cardiovascular disease is expanding and surgical treatment for both diseases is shifting to elder patients.

The pathophysiological base of both entities is common (5). The probability of simultaneous incidence of lung cancer and coronary artery disease in men is around 6.9 % (6).

Surgical treatment of non-small cell lung cancer is still the treatment of choice. According to Simek et al, 5-year survival rate of patients who undergo tumor resection and those who are not treated surgically, is 32–60 % and 10 % respectively (9). After a radical tumor resection, the survival rate is up to 90 % (10).

More risky groups of patients with various co-morbidities are being treated surgically for lung cancer, including patients with heart disease or those who had undergone heart surgery in the history. The appropriate timing of lung surgery in these patients is still a question (11). In the majority of these patients, heart surgery, most commonly coronary artery bypass grafting is performed in the first period and lung surgery is done in the second period. Many surgeons follow this algorithm, as they are aware of potential cardiac complications.

Materials and methods

In our department, between January 2002 and December 2011, we performed 1115 lung tumor resections. In 21 patients (1.9 %), a concomitant heart disease requiring surgical treatment was diagnosed. Thirteen patients (62 %) had ischemic heart disease, 4 patients (19 %) aortic valve disease, 3 patients (14 %) had mitral valve disease and 1 patient (4.7 %) had tumor in the left

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Table 1. Demografic characteristics of patients.

	Group A	Group B	p-value
Age	67.8 ± 5.9	68.5 ± 7.4	0.81
sex (F)	4	5	1
sex (M)	8	7	..
NYHA I	0	6	0.00191
NYHA II	5	6	..
NYHA III	7	0	..
Smoking	8	9	1
Diabetes	5	5	1
Hypertension	4	4	1
Histology Staging I	3	2	0.474
Histology Staging II A	3	4	..
Histology Staging II B	2	1	..
Histology Staging III A	0	3	..
BMI ((Ø)	31.4 ± 5.0	31.8 ± 5.3	0.845

atrium, which grew from the left lower lobar bronchus via the pulmonary veins to left atrium. The first group, group A, consisted of 12 patients (57 %) where lung and heart surgical procedures were carried out simultaneously. Nine lobectomy procedures were performed for non-small cell lung carcinoma, one lobectomy was performed for Grawitz tumor metastasis to the left lower lobar bronchus, which in turn propagated through the pulmonary veins to the left atrium and thus mimicked left atrial myxoma (12). Two atypical resections were done for isolated metastasis of colon adenocarcinoma. Nine patients requested myocardial revascularization, 2 patients underwent mitral valve replacement and 1 patient required tumor extirpation from the left atrium together with left lower lobectomy.

In 10 patients, pulmonary resection was performed via a median sternotomy after the opening of the pleural cavity. The surgical technique was identical with pulmonary resection provided from a lateral thoracotomy access. Ligation and interruption of the pulmonary vessels were done to prevent hematogenous dissemination of tumor cells. Preferably, the intrapericardial approach to the confluence of the pulmonary veins in the left atrium was applied. Patients with lung carcinoma stage I–IIA were scheduled for simultaneous procedures. In these patients, isolated mediastinal nodes sampling was performed. In the case of peripheral metastatic lesion, atypical pulmonary resection using a stapler was performed considering the risk of bleeding from the pulmonary tissue after heparin administration prior the subsequent cardiac surgery.

In 2 cases (left lower lobe resection and atypical resection), the surgical procedure was performed via a left anterior short thoracotomy (LAST). Initially, cardiac revascularization was performed using minimally invasive direct coronary artery bypass (MIDCAB) technique, where the left mammary artery was anastomosed to the left descending artery. Subsequently pulmonary resection was performed.

In the remaining 9 patients with concomitant heart disease and lung tumor requiring surgical intervention, lung resection was postponed for a serious heart involvement. In the 1st stage a heart surgery was carried out and then, after an interval of 1–5 months, pulmonary resection was achieved.

Table 3. Group B – (Isolated Lung Surgical Treatment)

n	Histology / Staging	Lung Procedure
1	SCLC / II A	LLL+ MS
2	SCLC / II A	RLL + MS
3	AdenoCa / III A	LLL+ ML
4	SCLC / II A	RLL + MS
5	SCLC / III A	RUL + ML
6	SCLC / III A	RLL + ML
7	Meta AdenoCa	WR
8	Meta AdenoCa	WR
9	SCLC / II A	RLL + MS
10	SCLC / I	RUL + MS
11	SCLC / II B	RLL + MS
12	AdenoCa / I	RUL

SCLC – Squamous cell lung cancer, LLL – Left lower lobectomy, RLL – Right lower lobectomy, RUL – Right upper lobectomy, MS – Mediastinal sampling, ML – Mediastinal lymphadenectomy, WR – Wedge resection

Table 4. Surgical Procedures

	Group A	Group B	p-value
T. of operation (min.)	307.5 (280-410)	105 (75-145)	0.000034
On Pump (n)	5	0	..
Off Pump (n)	7	0	..
T. of ECC (min.)	51 (47-73)	0	..
T. of APV (min.)	19 (12-48)	8 (4-20)	0.0015
T. of ICU (hour)	37.2 ± 15.7	13.8 ± 3.8	0.000292
T. of hospital. (days)	12.4 ± 2.5	9.7 ± 1.5	0.00475

T – time, ECC – Extracoroporal circulation, APV – Arteficial pulmonary ventilation

Table 2. Group A – (Combined Surgical Treatment)

n	Histology/Staging	Cardiac Patology	Lung Procedure	Cardiac Procedure	Surgical Approach
1	SCLC / I	Myocardial infarction	LLL	CABG x 2	Sternotomy
2	SCLC / II A	Unstable angina	RLL + MS	CABG x 2	Sternotomy
3	AdenoCa / II B	Myocardial infarction	LLL+ MS	CABG x 1	LAST
4	Meta Grawitz	Tumour of left atrium	LLL	ET	Sternotomy
5	SCLC / I	Myocardial infarction	RLL	CABG x 2	Sternotomy
6	SCLC / II A	Unstable angina	RLL + MS	CABG x 2	Sternotomy
7	Meta AdenoCa	Myocardial infarction	WR	CABG x 1	LAST
8	Meta AdenoCa	Unstable angina	WR	CABG x 3	Sternotomy
9	SCLC / II A	Mitral insuffitiation	RLL	MVR	Sternotomy
10	SCLC / I	Myocardial infarction	RUL	CABG x 2	Sternotomy
11	SCLC / II B	Myocardial infarction	RUL + MS	CABG x 3	Sternotomy
12	Meta AdenoCa	Mitral insuffitiation	WR	MVR	Sternotomy

SCLC – Squamous cell lung cancer, ET – Extirpation of the tumor, LLL – Left lower lobectomy, RLL – Right lower lobectomy, RUL – Right upper lobectomy, CABG – Coronary artery bypass graft, LAST – Left Anterior Short Thoracotomy, MVR – Mitral valve replacement, ET – Extirpation of the tumor, MS – Mediastinal sampling, ML – Mediastinal lymphadenectomy, WR – Wedge resection

Retrospectively we created 2 groups, each of 12 patients. Group A, which included patients who underwent simultaneous cardiac procedure and lung resection, and group B consisting of patients, who underwent isolated lung resection.

Group B was selected from the remaining 1094 patients, who underwent isolated pulmonary resection for lung tumor. The patients were selected to group B to match, as much as possible; patients from the group A in age, gender and especially the cardiovascular co-morbidities. The histological aspect of lung tumor was also considered, so patients from both groups matched in tumor type and tumor staging. Patient who underwent neoadjuvant therapy were excluded from our study. The demographic data of both groups are shown in Table 1. The overview of procedures performed in both groups is shown in Tables 2 and 3.

In our patients, anticoagulant therapy using low molecular weight heparin in a dose between 0.3–0.6 ml was initiated up to 6 hours after the surgical procedure depending on the blood loss to the drains. In case of concomitant cardiac revascularization, antiagregation therapy by 100 mg of acetylsalicylic acid was commenced as well. The technique of drainage differed between the groups. In the Group A, pericardial and pleural drainage was performed, whereas in the group B, just pleural cavity drainage was done.

Results

Both groups didn't significantly differ in the statistical demographic data. Group A consisted of 8 men and 4 women, with the age of 67.8 ± 5.9 years. Group B consisted of 7 men and 5 women, age 68.5 ± 7.4 years. The high age of patients in the group B indicated that isolated lung resection was carried out in a group of older patients. As for the co-morbidities, there were no remarkable differences between the groups including tobacco abuse as the main risk factor for lung carcinoma and heart disease. New York Heart Association (NYHA) class showed, that patients from the Group A had a variable stage of cardiac impairment. The method of pairing succeeded to rank patients into the group B with a similar tumor type and staging.

The postoperative results (Tab. 4) showed that the operation time was longer in patients from the group A as a result of summation of two procedures time performed at one session. The duration of artificial ventilation depended on the procedure type and on the duration of anesthesia. The duration of artificial ventilation was not negatively influenced by the reduction of the pulmonary parenchyma.

Hospital stay was longer in the group A but the difference was, statistically, insignificant.

In one patient from the group A s surgical revision was indicated due to bleeding from the proximal anastomosis of the grafted vein. One patient from Group B required a surgical revision because of bleeding from a bronchial artery.

Longer time of thoracic cavity drainage and more significant waste to the chest tubes in patients from group B correlated with a high serous production, which can be explained by the performed mediastinal lymphadenectomy.

Table 5. Postoperative outcome of complications and mortality

	Group A	Group B	p-value
Thorax drain (days)	26.9 ± 2.2	49.8 ± 17.8	0.00096
Blood loss (ml)	800 (700-2050)	1125 (750-2500)	0.104
Bleeding (n)	1	1	..
Atrial fibrilation (n)	4	2	0.64
Atrial flutter (n)	2	0	0.478
Pneumothorax (n)	0	1	1
Other complications (n)	2	1	1
30-days mortality (n)	0	0	..

No serious cardiac event occurred. In 4 patients (33.3 %) from the group A (2 after mitral valve replacement and 2 after cardiac revascularization), atrial fibrillation occurred in the post-op period, in 2 of them cardioversion was done. In the group B, 2 patients (16.7 %) developed atrial fibrillation. In these patients, lung hilus preparation was performed. The atrial fibrillation was managed successfully using amiodarone. One patient (8.3 %) from the Group B, who underwent right upper lobe resection, required a chest redrainage due to pneumothorax. Other complications occurred in 2 patients (16.7 %) from the Group A including an acute renal insufficiency and an early sternotomy infection after mitral valve replacement. One patient (8.3 %) from the group B had atelectasis in the post-op period, which was managed by bronchoscopic airway lavage and antibiotic therapy. The summary of postoperative complications is shown in the Table 5. In both groups, the 30-days mortality was null.

Discussion

Lung cancer and cardiovascular diseases have several common etiological causes. The purpose of contemporary medicine is to treat the patients using the best and the most effective modalities. The optimal timing of various surgical procedures is still a controversial topic. Each workplace has its own algorithm reflecting its relevant experience. There is no doubt that early surgical treatment of lung cancer, if indicated, is the treatment of choice (13).

Surgical treatment of obstructive coronary disease, despite the advanced recent progress in invasive therapeutic techniques, is still the most effective option for many patients, especially those with a diffuse coronary artery involvement.

In case of patients with symptomatic ischemic heart disease and concomitant lung cancer, many centers prefer a tow- staged procedure, where cardiac revascularization is carried out first, and in the second period, lung resection is done. Otherwise, the severe coronary artery impairment can cause fatal complications (14).

Although this regimen is safe and its efficacy is proven, the appropriate time for performing the subsequent lung surgery is not clearly verified. Furthermore, from the routine practice, it is difficult sometimes to persuade the patient to undergo further surgical procedure in a relatively short period. Significant can be the role of immune system attenuation, caused by the use of ECC in patients with a proliferative tumor disease (15).

The use of ECC may negatively influence many parameters of the immune system including leukocyte chemotaxis and cell-mediated immunity, particularly T-lymphocytes (16). The use of

ECC increases the concentration of free oxygen radicals, which in turn have a negative impact on the cell membrane by increasing its permeability and thus leads to cell damage (17). The decreased "vigilance" of the immune system induced after the use of ECC can enhance tumor growth and accelerate its dissemination via the lymphatic system (18).

It would be optimal to perform cardio-surgical procedures in patients with simultaneous lung cancer without the need of ECC, but that is possible in some patients who are scheduled for coronary surgery (19). Theoretically, the optimal solution, after taking in consideration the above mentioned, is to perform lung resection and subsequently cardiac surgery in the second period. However, this solution can be applicable in case of patients with insignificant heart impairment after a careful assessment of their status and ruling out the potential cardiac and circulatory complications that may accompany lung resection procedure. The need of neoadjuvant chemotherapy may delay the heart surgery. In case of an isolated coronary artery stenosis, a hybrid approach where coronary artery stenosis is intervened using percutaneous coronary angioplasty (PTCA), then lung surgery can be carried out. The question is when it is possible to perform lung resection after a stent insertion? It is recommended to wait at least 3–4 weeks and according to Hirose et al, the risk of perioperative myocardial ischemia an infarction remains significant up to 3 months after stent placement (20).

The early surgery indication after a stent placement presents a high risk of bleeding in patients using dual antiplatelet therapy, which a significantly increased blood loss in case that pleurectomy or pleural decortication is necessary (21).

In sight of these facts, many cardiothoracic centers tend to perform heart and lung surgery simultaneously (22).

The surgical approach in these procedures can be variable. The less mutilating approach for patients is isolated median sternotomy, despite the fact that it could be a less comfortable approach for the surgeon (23), especially in case that mediastinal lympfadenectomy is indicated, as the access to the posterior mediastinum can be troublesome.

Therefore, sternotomy access for simultaneous procedures can be chosen in patients with lung tumor stage I–II, when there is no evidence of lymphatic nodes involvement proved by the use of positron emission tomography.

Evaluation of postoperative pain according to the visual analogue scale of pain Scott-Huskisson, in relation to the operational approach, showed that median sternotomy is less painful than posterolateral thoracotomy (24).

In case of median sternotomy, the risk of sternal osteomyelitis was around 1% (25).

The median sternotomy approach for left lower lobe resection is considered as inappropriate (26, 27), whereas performing right lower lobe resection from a median sternotomy in case of patients scheduled for simultaneous procedure from median sternotomy is not frustrating (28).

A high incidence of perioperative cardiac complications is observed in case of patients who have aortic valve stenosis scheduled for simultaneous lung resection (29).

During simultaneous procedures, lung resection is done before the initiation of ECC. Performing lung resection using the ECC seems to be comfortable for the surgeon. However, prolonged ECC related complications might overwhelm this potential comfort (18).

The use of more than one surgical approach, e.g., medial sternotomy and posterolateral or lateral thoracotomy with the opening of both pleural cavities during simultaneuous procedures does not seem to be beneficial for the significant postoperative discomfort, more pain and a higher incidence of early postoperative complications.

In patients, who are indicated for surgical arterial grafting using the left mammary artery (most commonly anastamosed to the left descending artery), the LAST approach can be used as well for providing left sided lung resection.

The advantages of one-stage procedure are medical and economical. The main medical benefit is the earlier enabled tumor resection. The psychological aspect of the earlier performed lung resection is considerable for patients with tumor disease. The psychological aspect of the earlier enabled tumor resection. The negative impact of the ECC on the immune system, which can enhance tumor proliferation, is eliminated in case of simultaneous procedures (16, 17). A certain benefit of one-stage procedure performed via a median sternotomy is the ability to perform bilateral mediastinal lymphadenectomy, which has an important prognostic value.

Many controversial opinions exist regarding lung resection performed from a median sternotomy. These opinions are influenced by the technical difficulties associated with the surgical approach itself (30). This access is not appropriate in case of removal of the lymphatic nodes around the tracheal bifurcation (31). More important is the fact that after the lung resection, heart procedure is commenced after heparin administration, and if the result of rapid periprocedural biopsy is not satisfactory, an extended pulmonary resection could not be provided or at least can be considered as a high-risk procedure (32).

In the previous group of our patients, lung resection was performed in an interval of 2–8 months following cardiac surgery (33).

Conclusion

From our experience, which arises from a relatively small group of patients, it can be said that simultaneous procedures performed in a selected group of patients can be safe with a certain benefit for patients. This statement is in accord with similar results from literature. On the other hand, this experience cannot be considered as a standard approach for patients with concomitant heart involvement and lung cancer requiring surgical treatment. Each patient must be evaluated individually.

Using the modern therapeutic modalities, the risk of simultaneous procedures is acceptable, and in spite of a significant difference in the clinical parameters observed after simultaneous procedures in our patients, (compared to those patients who underwent tow-stage procedures), patients still profit from the earlier-provided tumor resection.

Patients in whom the use of ECC can be avoided or in whom mediastinal lymphadenectomy is not necessary could be considered for simultaneous procedure.

One-stage extensive procedure after all brings more comfort for the patient, who is exposed to only one psychical injury associated with the operation procedure and hospitalization. Considering the patient's safety, simultaneous procedure has an important economical impact caused by the reduction of hospitalizations number.

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