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SURVIVAL OF PULMONARY CANCER PATIENTS TREATED SURGICALLY

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Abstract: The aim of the study is to investigate the survival of patients treated surgically for lung cancer. 151cases treated during the years 2000–03 are reviewed. The average age was 56.6 ± 9.9 years (from 19 to 83 years old). The histological type was: 80 (53%) Squamous-cell carcinoma, 27 (17.9%) adenocarcinoma, 10 (6.6%) bronchioalveolar carcinoma, 5 (3.3%) small-cell carcinoma, and others – 29 (19.2%). The post-surgical stage was often advanced; 92 (63%) of the patients were at stage IIIA. With 5 (3.3% of total operated cases) of the patients had limited disease of SCLC. Most of the patients had lobectomy (64.9%) and pneumonectomy (16.6%) Performed. Neo-adjuvant treatment was carried out on 37 (24.5%) of the patients. Only half of the patients were alive after 1 year, and 11.9% after 2 years of the postoperative period.

Survival was highly significantly better in patients with an early stage of the disease.

Survival resulted decreasingly with the extent of the surgical intervention; lower survival resulted in the patients treated with pneumonectomy, but this was not statistically significant. Significantly better results of survival were seen in correlation with higher values of pre-surgical FEV1.

There are significant differences in survival ($p < 0.05$) in relation to diagnosis, group-age, histology, and highly significant differences ($p < 0.01$) regarding definition N, M, stage of disease, FEV1.

There were no significant differences in the survival of patients according to sex, type of intervention, site of intervention, FVC, definition T.

Key words: Pulmonary carcinoma, surgery, survival.

Introduction

Lung cancer is a major health threat in most parts of the world, and the lungs are the major site of cancer in the world today. The increase in lung cancer occurrence follows about 20–30 yrs after a parallel trend in cigarette smoking. The leading causes of death in 2030 are projected to be cancers, ischaemic heart disease, stroke, HIV/AIDS, and chronic obstructive pulmonary disease. [1]

Deaths due to neoplasm diseases occupy the second place in the structure of general mortality in Albania. [2] Cancer causes every seventh death. Elderly males have an increased risk of dying from cancer. Female cancer death rates are increasing, but they are still below the Eur-B+C average. Mortality developments for cancers of the larynx, trachea, bronchia and lungs is different for men and women. For men, the death rate remains stable, and below the declining Eur-A and Eur-B+C averages. For women, it is increasing at the same rate as the Eur-A average, and it has already passed the Eur-B+C average. These mortality patterns reflect the previous trends in smoking, which became more common in Albania between 1990 and 2000. [3]

In 2004 mortality from neoplasm was 93.1 deaths per 100 thousand inhabitants. [2]

The successful surgical treatment of lung cancer remains the best, and in the main only, chance of a cure.

However, there is substantial debate regarding the various aspects of surgical treatment. Surgery is the best option in NSCLC and if the disease is limited to one lung and has not spread beyond its confines. Furthermore a sufficient respiratory reserve needs to be present to allow resection. The art of surgery has improved with a lowering of perioperative mortality and morbidity by better selection of patients for surgery and considerable refinements in postoperative care. Both the patient and the tumour must be fit, appropriately chosen for resection, and the choice of resection, wedge, lobe or whole lung, is critical to the patient's recovery and quality of life in the future.

Aim of study

The aim of the study is to investigate long-term survival in patients who underwent surgery for lung cancer, and the relationship and predictive factors.

Material and Methods

Based on the Protocol for Lung Cancer Diseases, 151cases of pulmonary cancer patients who underwent surgical treatment during the years 2000–03 are reviewed.

The average age was 56.6 ± 9.9 years (from 19 to 83 years old). According to the histological type 80 (53 %) patients with Squamous-cell carcinoma were operated on, 27 (17.9%) with adenocarcinoma, 10 (6.6%) with bronchioalveolar carcinoma, 5 (3.3%) with small-cell carcinoma, and others – 29 (19.2%).

Table 1 – Табела 1

Baseline characteristics of subjects with surgically treated pulmonary carcinoma
Основни карактеристики на субјекти со хируршко третиран пулмонален карцином

Subjects n	151
Male	138 (91.4%)
Female	13 (8.6%)
Age (years)	56.6 ± 9.9 (19–83)
Cigarette/day	22 ± 13.7
Smoking years	26 ± 14.7
Pack/years	34 ± 25.8
FVC % predicted	94.8 ± 12.4
FEV_1 % predicted	85.2 ± 16.5
PaO2 mmHg	85.5 ± 11.5
PaCO2 mmHg	39.3 ± 5.3
SaO2	95.5 ± 3.6
Time from symptom onset (months)	4,9 ± 5,2 (0–30)
Survival (months)	15.6 ± 7.7

Concomitant chronic bronchopulmonary disease was observed in 48 (31.8%) of cases:

– concomitant cardiovascular diseases – 38 (25.2%) patients, Diabetes Mellitus – 4 (2.6%), gastro-intestinal diseases – 12 (7.9%), nephrologic – 4 (2.6%), others – 25 (16.6%).

Neo-adjuvant treatment was carried out on 37 (24.5%) patients.

Statistical analysis

Means and standard deviations were calculated for numerical variables and percentages and their respective 95% confidence intervals for categorical variables.

The Mann-Whitney test was used to assess the statistical significance of differences in mean values for numerical variables.

The Pearson chi-square and Fisher's exact tests were used to assess the statistical significance of differences between categorical variables.

The General Linear Model (GLM) was used to compare mean values of survival (in months) between different stages of disease.

The Kaplan-Meier survival analysis was used to plot the differences according to sex and histological type.

All statistical analysis was conducted in SPSS for Windows, version 15.0 (Chicago, Illinois).

Results

Most of patients had lobectomy (64.9%) performed and (16.6%. pneumonectomy Pneumoectomy was performed more often (specific weight was double) on the left site, meantime there are no differences for other types of interventions. (Table 2)

Table 2 – Табела 2

Patients according to the type and site of intervention
Пациенти според видот и местото на интервенција

Site of intervention			Type of intervention				Total
			Segmentectomy	Lobectomy	Bilobectomy	Pneumonectomy	
	Right	Nr.	10	63	14	12	99
		%	10,1%	63,6%	14,1%	12,1%	100,0%
	Left	Nr.	4	35		13	52
		%	7,7%	67,3%		25,0%	100,0%
Total		Nr.	14	98	14	25	151
		%	9,3%	64,9%	9,3%	16,6%	100,0%

According to the post-surgical stage (Table 3, Fig. 1) the disease was often advanced; 92 (63%) patients at stage IIIA. 5 patients (3.3% of total operated cases) had limited disease of SCLC.

Table 3 – Табела 3

Patients with NSCLC according to post-surgical stage
Пациенти со NSCLC според постхируршката фаза

Post-surgical stage NSCLC		Nr. of cases	Percent
	IA	1	.7
	IB	20	13.7
	IIA	5	3.4
	IIB	20	13.7
	IIIA	92	63.0
	IIIB	2	1.4
	IV	6	4.1
	Total	146	100.0

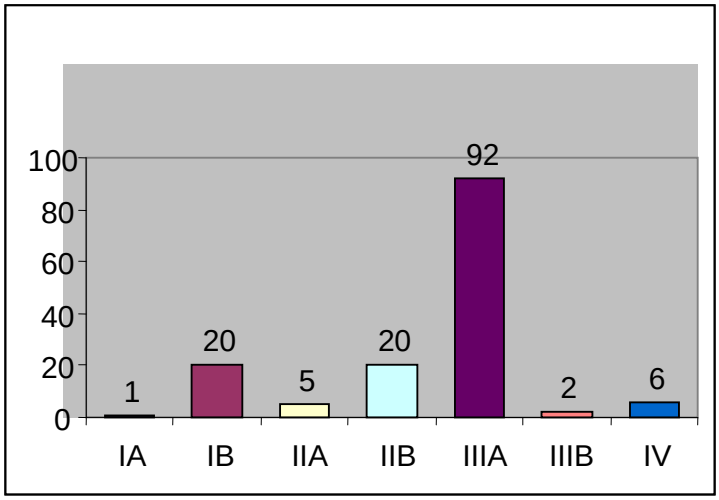

Figure 1 – Post-surgical stages of NSCLC patients
Слика 1 – Постхируршки фази на пациентите со NSCLC

As seen in Table 4 and Fig. 2 all this group of patients died within 39 months of the postoperative period. Two patients died within 30 days of the postoperative period. Only half of the patients were alive after 1 year, and 11.9% after 2 years of the postoperative period. There are no significant differenrces in survival according to the sex. (P > 0.05) (Fig. 3)

Table 4 – Табела 4

Deaths of surgically treated pulmonary cancer patients
Смрти кај хируршки третирани пациенти со пулмонален карцином

Deaths (months)		Nr.	Percent	Cumulative percent
	up 1	2	1.3	1.3
	6	7	4.6	6.0
	9	23	15.2	21.2
	12	44	29.1	50.3
	15	33	21.9	72.2
	18	12	7.9	80.1
	21	10	6.6	86.8
	24	2	1.3	88.1
	27	3	2.0	90.1
	30	4	2.6	92.7
	33	3	2.0	94.7
	36	5	3.3	98.0
	39	3	2.0	100.0
Total		151	100.0	

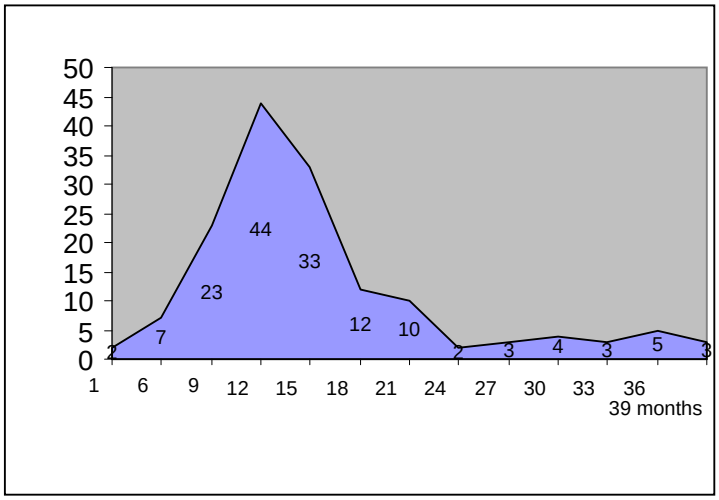

Figure 2 – Deaths of surgically treated pulmonary cancer patients
Слика 2 – Смрти кај хируршки третирани пациенти со пулмонален карцином

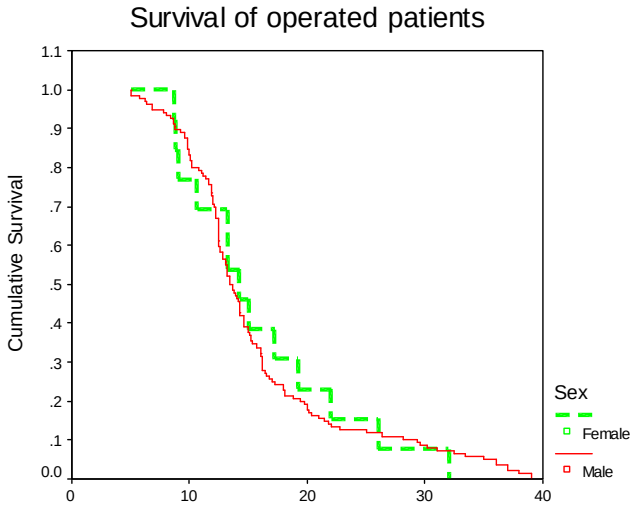

Figure 3 – Survival of operated patients according to sex
Слика 3 – Преживување на оперирани пациенти според полот

No significant differences on the survival of patients resulted according to the site of intervention. (Fig. 4)

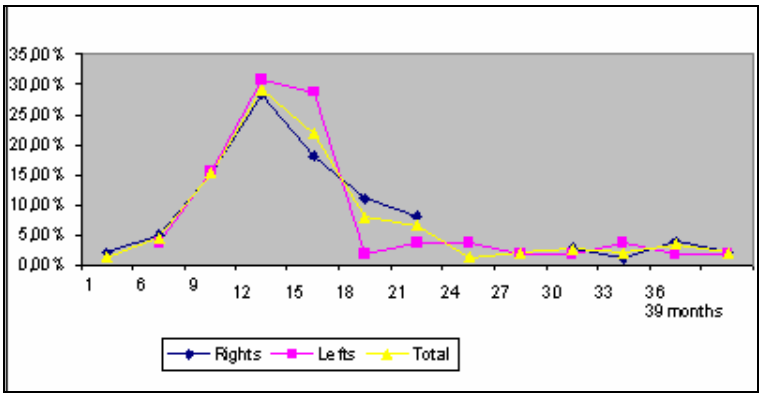

Figure 4 – Survival of patients (%) according to surgical site
Слика 4 – Преживување на пациенти (%) според местото на операцијата

Table 5 – Табела 5

Period of survival of surgically treated pulmonary cancer patients according to stage of disease
Период на преживување на хируршки третирани пациенти со пулмонален карцином според фазата на болеста

Period of death (months)		Post- operative stage of disease							Total
		IA	IB	IIA	IIB	IIIA	IIIB	IV	
Up 1	Nr.							2	2
	%							33,3%	1,4%
6	Nr.					2	1	4	7
	%					2,2%	50,0%	66,7%	4,8%
9	Nr.				1	18	1		20
	%				5,0%	19,6%	50,0%		13,7%
12	Nr.		1		4	39			44
	%		5,0%		20,0%	42,4%			30,1%
15	Nr.		1	1	5	24			31
	%		5,0%	20,0%	25,0%	26,1%			21,2%

18	Nr.			2	4	6			12
	%			40,0%	20,0%	6,5%			8,2%
21	Nr.		1		6	3			10
	%		5,0%		30,0%	3,3%			6,8%
24	Nr.		2						2
	%		10,0%						1,4%
27	Nr.		2	1					3
	%		10,0%	20,0%					2,1%
30	Nr.		3	1					4
	%		15,0%	20,0%					2,7%
33	Nr.	1	2						3
	%	100,0%	10,0%						2,1%
36	Nr.		5						5
	%		25,0%						3,4%
39	Nr.		3						3
	%		15,0%						2,1%
Total	Nr.	1	20	5	20	92	2	6	146
	%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

Pearson Chi-Square Asymp. Sig. (2-sided) 0,000
Pearson's R -0,838 (Approx. Sig. 0,000).
Spearman Correlation -0,723 (Approx. Sig 0,000)

There is a strong negative correlation between stage of cancer and survival time. (The higher the stage, the lower the survival time). Survival was highly significantly better in patients with an early stage of the disease. ($P < 0.001$) (Table 5)

Likewise the General Linear Model was used to compare mean values of survival (in months) according to the stage of the disease that showed highly significant results. (Table 6)

Table 6 – Табела 6

Survival of patients according to stage of diseases
Преживување на пациенти според фазата на болеста

Stage	Survival (in months)
IB	30.11
IIA	22.44
IIB	16.20
IIIA	12.94
IIIB	6.90
General Linear Model (GLM) was used to compare mean values of survival (in months) between different stages of disease. Age-and-sex-adjusted P < 0.001.	

In the patients studied, survival according to the histologic type was longer in cases with squamous cell carcinoma (P < 0.02), but not significantly different in other histologic types. (Fig. 5). In 5 patients with SCLC mean survival was 11.4 ± 3.4 (8.6–16.2) months, significantly lower than other types of NSCLC.

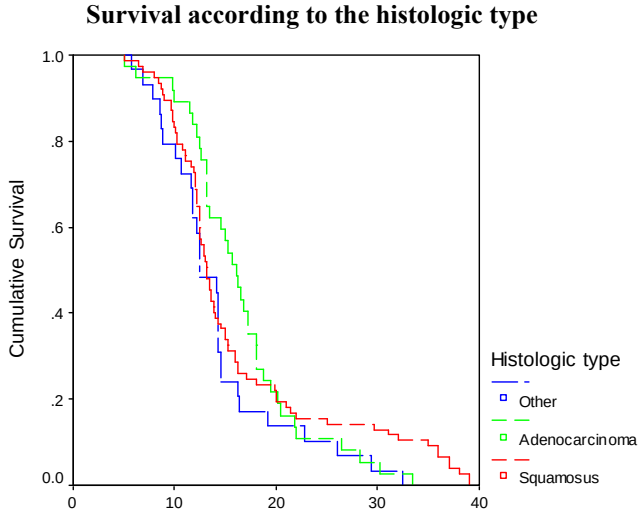

Figure 5 – Survival of patients according to histologic type
Слика 5 – Преживување на пациентите според хистолошкиот тип

According to the type of intervention (Table 7, Fig. 6) lower survival resulted in the patients treated with pneumonectomi, but the differences are not statistically significant (P > 0.5) Survival (months) resulted decreasingly: segmentectomy – 19.8 ± 10.4 (from 5 to 37), lobectomy – 16.1 ± 7.7 (5–34), bilobectomy – 15.8 ± 8.4 (8.4-39), and pneumectomy 12.2 ± 5.1 (0.3–20.4).

Table 7 – Табела 7

Period of survival of surgically treated pulmonary cancer patients according to type of intervention
Период на преживување на хируршки третираните пациенти со белодробен карцином според типот на интервенцијата

Period of death (months)		Intervention				Total
		segmentectomy	lobectomy	bilobectomy	pneumoectomi	
1	Nr.				2	2
	%				100,0%	100,0%
6	Nr.	2	4		1	7
	%	28,6%	57,1%		14,3%	100,0%
9	Nr.		16	2	5	23
	%		69,6%	8,7%	21,7%	100,0%
12	Nr.	2	29	6	7	44
	%	4,5%	65,9%	13,6%	15,9%	100,0%
15	Nr.	2	23	3	5	33
	%	6,1%	69,7%	9,1%	15,2%	100,0%
18	Nr.	2	6	1	3	12
	%	16,7%	50,0%	8,3%	25,0%	100,0%
21	Nr.	2	6		2	10
	%	20,0%	60,0%		20,0%	100,0%
24	Nr.	1	1			2
	%	50,0%	50,0%			100,0%
27	Nr.		3			3
	%		100,0%			100,0%

30	Nr.	2	1	1		4
	%	50,0%	25,0%	25,0%		100,0%
33	Nr.		3			3
	%		100,0%			100,0%
36	Nr.	1	4			5
	%	20,0%	80,0%			100,0%
39	Nr.		2	1		3
	%		66,7%	33,3%		100,0%
Total	Nr.	14	98	14	25	151
	%	9,3%	64,9%	9,3%	16,6%	100,0%

Pearson Chi-Square Asymp. Sig. (2-sided), 152

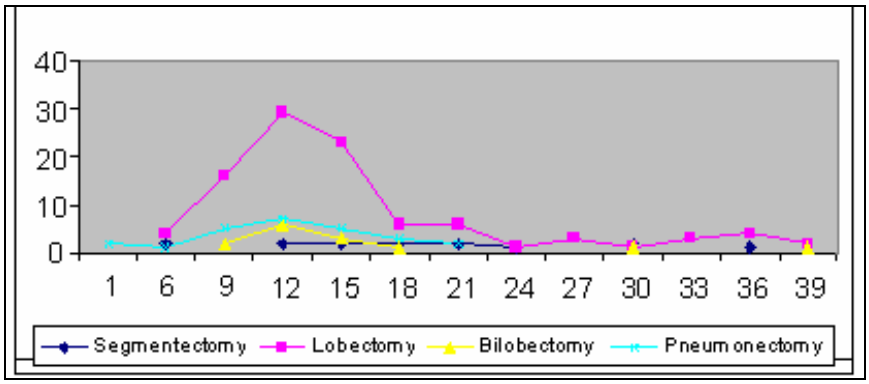

Figure 6 – Period of post-surgical survival according to type of intervention
Слика 6 – Период на постхируршко преживување според типот на интервенција

Significantly better survival results were seen in correlation with higher values of pre-surgical FEV1. ($P < 0.001$) (Table 8, Fig. 7)

Table 8 – Табела 8

Period of survival of surgically treated pulmonary cancer patients according to the presurgical FEV1
Период на преживување на хируршко третирани пациенти со пулмонален карцином според предхируршкиот FEV1

Period of survival (months)		FEV1			Total
		> 80%	80–50%	50–30%	
Up to 1	Nr.	2			2
	%	100,0%			100,0%
6	Nr.		4	3	7
	%		57,1%	42,9%	100,0%
9	Nr.		13	10	23
	%		56,5%	43,5%	100,0%
12	Nr.		29	15	44
	%		65,9%	34,1%	100,0%
15	Nr.		24	9	33
	%		72,7%	27,2%	100,0%
18	Nr.		8	4	12
	%		66,7%	33,3%	100,0%
21	Nr.		9	1	10
	%		90,0%	10,0%	100,0%
24	Nr.		1	1	2
	%		50,0%	50,0%	100,0%
27	Nr.		2	1	3
	%		66,7%	33,3%	100,0%
30	Nr.		2	2	4
	%		50,0%	50,0%	100,0%

33	Nr.		3		3
	%		100,0%		100,0%
36	Nr.		3	2	5
	%		60,0%	40,0%	100,0%
39	Nr.		2	1	3
	%		66,7%	33,3%	100,0%
Total	Nr.	2	100	49	151
	%	1,3%	66,2%	32,4%	100,0%

Pearson Chi-Square Asymp. Sig. (2-sided) 0,000

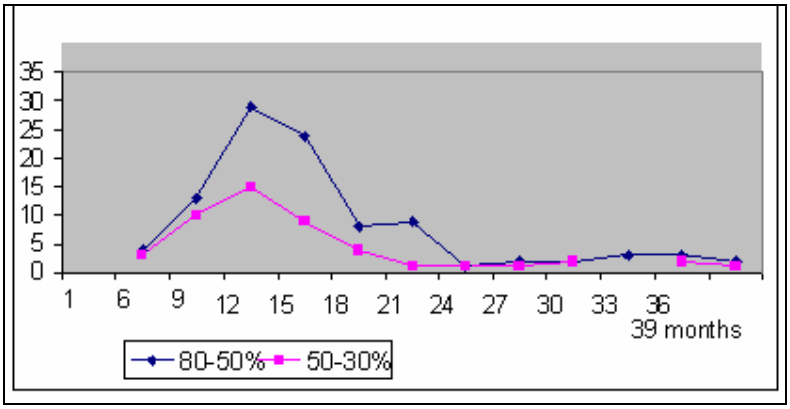

Figure 7 – Period of survival in relation to pre-surgical FEV1
Слика 7 – Период на преживување во однос на предхируршкиот FEV1

Table 9 – Табела 9

Survival in relation to clinic-pathologic and management factors
Преживување во однос на клиничко-патолошките и менаџерските фактори

Variable	Factors	Value	DF	P
Survival	Pathologic staging	320,832(a)	72	P < 0.001
Survival	Clinical staging	204,956(a)	72	P < 0.001
Survival	Definition N	99,018(a)	24	P < 0.001
Survival	Definition M	84,949(a)	12	P < 0.001
Survival	FEV1	170,381(a)	36	P < 0.001

Survival	Histology	37,957(a)	24	P < 0.02
Survival	Group – age	88,024(a)	72	P < 0.05
Survival	Sex	8,951(a)	12	P > 0.05
Survival	Definition T	37,691(a)	36	P > 0.05
Survival	Intervention	43,239(a)	36	P > 0.5
Survival	Site of intervention	13,333(a)	12	P > 0.05
Survival	FVC	17,855(a)	24	P > 0.05

There are significant differences in survival ($p < 0.05$) in relation to group-age, histology, and highly significant differences ($p < 0.01$) regarding definition N, M, stage of disease, FEV1.

There were no significant differences in the survival of patients according to sex, type of intervention, site of intervention, FVC, definition T.

Discussion

Despite performing "better treatment for lung cancer" properly, survival remains poor.

[4] According to the post-surgical stage it is shown that the disease was often advanced; 92 (63%) patients were stage IIIA. Treatment for NSCLC depends on disease staging. Patients with stage I disease are treated by surgical resection of the primary tumour. Those with stage II disease also undergo surgical resection, but they may or may not receive chemotherapy or radiation. Patients with stage III disease require chemotherapy or radiotherapy followed by surgical resection. The management of metastatic NSCLC ranges from palliative measures to chemotherapy. Surgical resection of the primary lesion or metastatic lesion is generally not done because it does not significantly improve survival. However, some oncologists propose that if only a single metastatic lesion exists, surgical resection may be appropriate. Patients with advanced NSCLC (e.g., stage IIIB or IV) are often treated with palliative care alone. [5]

Management of SCLC is different from that of NSCLC in that resection is rarely done, and treatment involves chemotherapy and radiation therapy. Surgical resection is not a good option unless the primary lesion is discovered early in the course of the disease. In our study 3.3% of total operated cases had limited SCLC disease . Patients with SCLC had a mean survival 11.4 ± 3.4 (8.6 – 16.2) months, significantly lower than other types of NSCLC. According to Ginsberg, Grewal *et al*. [4] the median survival time for patients with limited-stage disease is approximately 18 months. Small subgroups of these patients who present with a single solitary nodule are considered very early-stage limited disease and have a better prognosis. Extensive-stage disease is treated primarily with chemotherapy with a median survival time of approximately 9 months [6].

The standard treatment of choice for localized stage I through IIIA remains surgical resection with and without chemo-radiation therapy. Unfortunately, the 5-year survival for all stages of lung cancer remains at 15% [7].

Treatment is focused on surgery, radiation therapy and chemotherapy. New molecular and genetic understanding of tumour biology has led to research involving targeted therapies. There may be genes that may make certain individuals susceptible to lung cancer. [4] In our patients neo-adjuvant treatment was carried out on 37 (24.5%) patients.

Surgical resection is considered to be the single curative treatment in NSCLC, provided the procedure is radical and complete. Most of our patients had lobectomy – (64.9%) and pneumonectomy (16.6%) performed. Pneumoectomy was performed more often on the left side. Survival (months) resulted longer in patients with segmentectomy – 19.8 ± 10.4 (from 5 to 37), and declined with lobectomy – 16.1 ± 7.7 (5–34), bilobectomy – 15.8 ± 8.4 (8.4–39), and pneumectomy 12.2 ± 5.1 (0.3–20.4). According to the type of intervention lower survival resulted in the patients treated with pneumonectomy, but the differences are not statistically significant.

Unfortunately, some patients die shortly after surgery, despite intensive preoperative assessment. The percentage of patients dying within 30 days of operating is defined as "postoperative mortality" (POM). In this study there were 2 (1.3%) patients with POM. According to the literature POM resulted 4.4%; in the youngest (< 60 yrs) patients it was 2.2%, to 6.7% in the oldest group. The highest POM was seen in patients subjected to right-sided pneumonectomy, in whom it was more than double that of left-sided pneumonectomy. Multivariate analysis showed that age, extent of resection and sides of the pneumonectomy were independent prognostic factors. [8]

The prognostic value of the extent of surgery is widely known and even in patients with sufficient pulmonary reserve, (bi)lobectomy is preferred to pneumonectomy. As a long-term consequence of pneumonectomy, pulmonary hypertension and progression of emphysema may occur. Survival may appear to be poorer after pneumonectomy but this is mainly due to confounding with stage [9] Minimal operations such as wedge and segmental resections are sometimes performed in patients with limited pulmonary reserve at the risk of increasing local recurrence rates.

According to studies [9] the increased operative mortality associated with pneumonectomy has stimulated the use of lung-sparing operations. Whether pneumonectomy adversely affects long-term outcome after lung resection is unknown. They have not detected a significant long-term adverse influence of pneumonectomy on survival after adjusting for other prognostic factors, but randomized clinical trials aree needed to definitively address this issue.

In the last decade, the outcome following pulmonary resection has improved greatly with changes in surgical technique and perioperative care [10]. However, peri-operative mortality and morbidity associated with pneumonectomy remains high with a mortality of 6.8% to 23%, and major morbidity of 40% of patients [11, 12]

The survival of treated patients was limited to 39 months of the postoperative period. Only half of the patients were alive after 1 year, and 11.9% after 2 years of the postoperative period.

Survival was highly significantly better in patients with an early stage of disease. The data are poorer than in published studies such as [13] with five year post-treatment survival: IA – 67%, IB – 41%, IIA – 34%, IIB – 26%, IIIA – 14%, IIIB – 6%, IV – 2%. This is related to the advanced stage of the patients treated.

Many reports are available on the survival of patients with lung cancer. Recently, efforts have been made to collect cancer survival data from population-based cancer registries in Europe in order to make reliable comparisons of survival among different European populations by performing standardized analysis of survival on all available data sets (the EUROCARE studies). Survival analysis was carried out on 173,448 lung cancer patients diagnosed in 1985–89. The overall 1-, 3- and 5-yr relative survival for European males was 31, 12 and 10%, respectively, and for females 29, 13, and 11% respectively. [14].

Conclusion

Survival was highly significantly better in patients with an early stage of disease.

Survival resulted decreasingly with the extension of surgical intervention; a lower survival resulted in the patients treated with pneumonectomy, but was not statistically significant. Significantly better results of survival were seen in correlation with higher values of pre-surgical FEV1.

There are significant differences in survival ($p < 0.05$) in relation to group-age and histology, and highly significant differences ($p < 0.01$) with definition N, M, stage of disease, FEV1.

There were no significant differences in the survival of patients according to sex, type of intervention, site of intervention, FVC, definition T.

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Резиме

ПРЕЖИВУВАЊЕ НА ПАЦИЕНТИ СО ПУЛМОНАРЕН КАНЦЕР ШТО БИЛЕ ХИРУРШКИ ТРЕТИРАНИ

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Целта на студијата е да се испита преживувањето на пациентите што се хируршки третирани од канцер на белите дробови. Разгледани се 151 случај третирани во периодот 2000–2003 г. Просечната возраст беше 56.6 ± 9.9 години (од 19 до 83 години). Хистолошкиот тип беше: 80 (53%) карцином на сквамозни ќелии, 27 (17.9%) аденокарцином, 10 (6.6%) бронхоалвеоларен карцином, 5 (3.3%) карцином на мали ќелии, и други – 29 (19.2%). Постхируршката фаза често беше напредна; 92 (63%) од пациентите беа во фаза IIIA. 5 (3.3% од вкупно оперираните случаи) од пациентите имаа ограничена болест на SCLC. Повеќето од пациентите имаа лобектомија (64,9%) и пневмонектомија (16,6%). Неоадјувантски третман беше извршен на 37 (24.5%) од пациентите. Само половина од пациентите беа живи по 1 година, а 11,9% по 2 години од постоперативниот период.

Преживувањето беше значително подобро кај пациенти со рана фаза на болеста.

Преживувањето се намалуваше со должината на хируршката интервенција; помалото преживување беше кај пациенти третирани со пневмонектомија, но тоа не беше статистички важно. Значително подобри резултати на преживување имаше во корелација со високите вредности на предхируршки FEV1.

Има значителни разлики во преживувањето ($p < 0.05$) во однос на дијагнозата, староста на групата, хистологијата и високо значителни разлики ($p < 0.01$) во врска со дефиницијата на N, M, фазата на болеста, FEV1.

Немаше значителни разлики во преживувањето на пациентите според полот, типот на интервенцијата, местото на интервенцијата, FVC, дефиницијата T.

Клучни зборови: пулмонарен карцином, операција, преживување.

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