

Characterization of lung cancer patients, their actual treatment and survival: experience in Slovenia

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Background. The aim of the study was to establish characteristics of lung cancer patients diagnosed at the University Clinic of Respiratory and Allergic Diseases Golnik in 1996, their selected and realized therapy, and survival.

Methods. The retrospective study comprises 345 patients aged from 37 to 90 years (mean 65), 285 males and 60 females. Performance status (Karnofsky): > 80 in 171 patients, 60-80 in 130 and <60 in 44 patients. Microscopically confirmed tumour in 97%: by bronchoscopy 281, transthoracic needle biopsy 23, peripheral lymph nodes biopsy 12, sputum cytology 7, pleural (effusion) cytology 4, distant metastases biopsy 2, mediastinoscopy 1, autopsy 4 patients. Histology and/or cytology: squamous 131, adenocarcinoma 86, large cell 63, small cell 51, non-small cell 1, unclassified 2. Clinical staging of non-small cell lung cancer (NSCLC): stage I 63, stage II 32, stage IIIA 48, stage IIIB 59, stage IV 77, undeterminable 2 patients. Staging in small cell lung cancer (SCLC): limited disease 24, extended disease 27 patients.

Results. The selected primary oncological therapy was changed in 11%. Realized primary therapy: radiotherapy 102 (30%), surgery 77 (23%), chemotherapy 47 (14%), supportive treatment 111 (33%). In resected patients staging was correct in 46%, underestimated in 44%, overestimated in 10%. The overall five-year survival was 7.8% (median 6.2 months) and the five year survival of resected patients was 41.9% (median 33 months). The median survival of irradiated patients was 5.7 months, of supportively treated patients 2.5 months. The survival was significantly different according to the performance status and stage.

Conclusions. The selected oncological therapy was actually realized in 89%. In our patients there was a low percentage of NSCLC treated by chemotherapy. Among five-year survivors there were 26 resected and one supportively treated patient, that confirms surgery as the most effective therapy in our lung cancer patients.

Key words: lung neoplasms – diagnosis – therapy; survival analysis

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Introduction

In recent years there were among 2 million inhabitants in Slovenia approximately one thousand new primary lung cancer patients per year. The data of Cancer Registry of

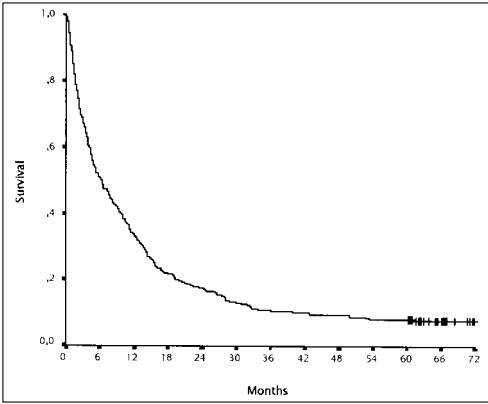


Figure 1. Overall survival of 345 patients

Slovenia presented 958 new cases in 1996, with the incidence rate of 82 per 100.000 population for men and 17 per 100.000 population for women. During that year the lung cancer was the most common cancer in men and the sixth most common cancer in women (after cancer of the breast, skin, corpus uteri, colon and cervix uteri).¹ More than a third of lung cancer patients were diagnosed at the University Clinic of Respiratory and Allergic Diseases Golnik. The study presents the evaluation of routine management and survival of 345 lung cancer patients. This number involves all lung cancer patients diagnosed in 1996, and among them some were also treated by chemotherapy at this institution. Surgery was applied at the Department of Thoracic Surgery, Clinical Centre, Ljubljana,

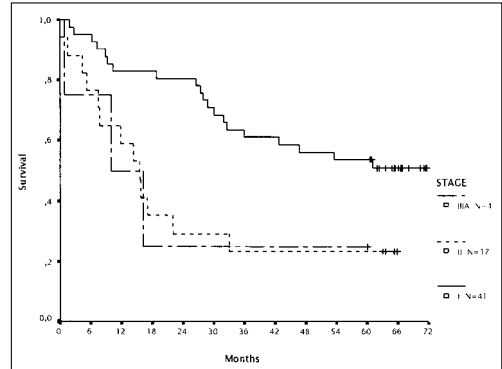


Figure 2. Survival of resected patients according to clinical stage

and radiotherapy at the Institute of Oncology, Ljubljana.

The purpose of the study was to establish characteristics of patients and their tumours, the selected and realized therapy, and the survival.

Methods

The retrospective study comprises 345 patients. The characteristics of patients and their tumours are evident in Table 1 and Table 2.

After the diagnostic procedure 337 of 345 patients were presented at a lung cancer meeting (pulmologist, surgeon, radiation oncologist, pathologist, radiologist) where a treatment modality for each patient was se-

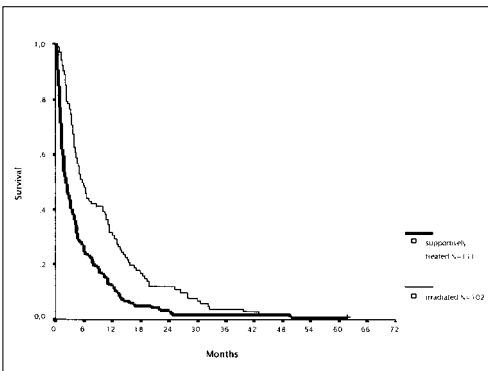


Figure 3. Survival of irradiated and supportively treated patients.

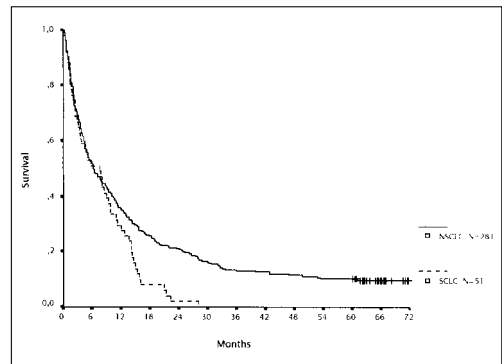


Figure 4. Survival of NSCLC and SCLC patients.

Table 1. Characteristics of patients

Number of patients	345
Gender	
male	285
female	60
Age (years)	37 – 90 (mean 65)
Predominant symptoms and signs at the time of admittance	
cough, dyspnoea, with or without hemoptysis	119
bronchitis, pneumonia	83
haemoptysis, haemophthoe	30
chest pain	30
brachialgia	11
bone pain	10
Syndrome venae cavae sup., dysphagia, paresis n. recurrentis	13
central nerve system symptoms	14
weight loss, weakness	13
digestive disorders	8
peripheral lymph nodes enlargement	4
asymptomatic	10
Performance status (Karnofsky)	
>80	171 (49%)
60 - 80	130 (38%)
<60	44 (13%)
Clinical stage (332 patients with classified tumour)	
Non-small cell cancer	
stage I	63 (22.5%)
stage II	32 (11.5%)
stage III.A	48 (17%)
stage III.B	59 (21%)
stage IV	77 (27%)
Small cell cancer	
limited disease	24 (47%)
extended disease	27 (53%)
Undeterminable	2 (1%)

lected. Thereafter it was presented to the patient. For various reasons the actual primary treatment in some patients was changed.

Staging of non-small cell lung cancer (NSCLC) was made according to TNM classification,² while the one of small cell lung cancer (SCLC) was made according to limited

Table 2. Characteristics of tumours

Microscopically confirmed tumour	334 (97%)
Not confirmed	11 (3%)
Diagnostic investigations for verification	
bronchoscopy	281
ransthoracic needle biopsy	23
peripheral lymph node needle biopsy	12
sputum cytology	7
pleural (effusion) cytology	4
distant metastases biopsy	2
mediastinoscopy	1
autopsy	4
Histology and/or cytology	
squamous cell	131 (39%)
adenocarcinoma	86 (26%)
large cell	63 (19%)
small cell	51 (15%)
non-small cell	1 (0.3%)
unclassified	2 (0.6%)

Table 3. Selected and realized primary treatment modality of patients

Primary treatment	Selected	Realized
Surgery	93 (28%)	77 (23%)
Radiotherapy	110 (32%)	102 (30%)
Chemotherapy	50 (15%)	47 (14%)
Supportive treatment	84 (25%)	111 (33%)
Total	337 (100%)	337 (100%)

No therapy (death before selection) 8 / 345

disease (LD) and extended disease (ED). The diagnostic procedure from admittance day to microscopic verification took 1 to 75 days, mean 7 days.

The zero time for the calculation of the survival was the date of admittance to the institution until death or until the end of the follow-up period on December 31st 2001. All living patients were confirmed to have been alive at this date. The minimal follow-up time for all patients was 5 years. The survival was calculated according to Kaplan-Meier's method, differences were confirmed by the log-rank test.

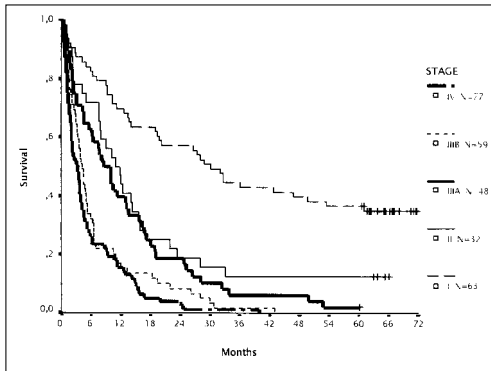


Figure 5. Survival of NSCLC patients according to stage.

Results

The selected and realized primary treatment modality is evident in Table 3. The therapy was most frequently not realized in patients selected for surgery. The overall primary oncological therapy was changed in 27 of 253 (11%) patients.

The overall survival of 345 patients is presented on Figure 1. The median survival was 6.2 months. After five years 27 (7.8%) patients were still alive.

There was no difference in survival according to gender ($p=0.127$).

Eighty-eight of 93 patients selected for surgery were admitted for thoracic surgery. Afterwards 4 patients refused the intervention while 7 patients were rejected by the surgeon. In 77 surgically treated patients 35 had lobectomy, 5 bilobectomy, 22 pneumonectomy, 9 exploratory thoracotomy, 6 mediastinoscopy (mediastinotomy). In 62 resected patients staging was correct in 46%, underestimated in 44% and overestimated in 10%. The survival of resected patients is presented on Figure 2. Their median survival was 33 months. The five-year survival of resected patients was 41.9%, stage I 51.2%, stage II and IIIA 23.5% and 25% respectively, considering the clinical TNM staging. In patients with exploratory thoracotomy the median survival was 14.1 months.

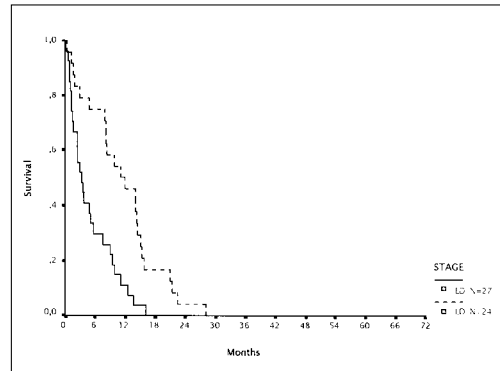


Figure 6. Survival of SCLC patients according to stage

In irradiated patients the median survival was 5.7 months and in supportively treated patients 2.5 months ($p=0.0001$), Figure 3.

In NSCLC patients the median survival was 6.3 months, in SCLC patients 7.5 months, however, the long-term survival was significantly better in NSCLC patients ($p=0.0153$), Figure 4.

The survival according to the stage was significantly different in NSCLC ($p<0.0001$), Figure 5, and in SCLC patients ($p=0.0004$), Figure 6.

The survival according to the performance status is different as well ($p<0.0001$), Figure 7.

Discussion

Of registered predominant symptoms and signs the pulmonary ones were present in two thirds of our patients. Only 3% of patients were asymptomatic. Hawson *et al.*³ reported 15% asymptomatic patients in NSCLC and 5% in SCLC among 1024 lung cancer patients. Haber⁴ established the increase of asymptomatic patients in Queensland of 7% in 1964 to 13% in 1990. Lee *et al.*⁵ established 7.2% asymptomatic in 3794 Korean lung cancer patients. The frequency of discovery of patients still at an asymptomatic stage could indicate the efficiency of detection.

Bronchoscopic samples most commonly

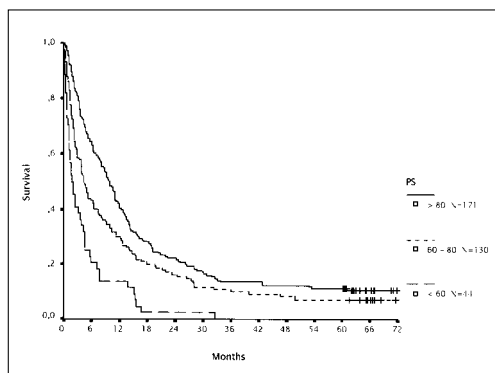


Figure 7. Survival of 345 patients according to performance status.

enabled the microscopic confirmation of tumour. In 4 patients tumour was proven by autopsy. In 11 (3%) patients tumour was microscopically not confirmed. These were patients with a low performance status, not capable for diagnostic procedures or capable for a supportive treatment only. The Cancer Registry of Slovenia in 1996 reported 92% microscopically confirmed lung cancer in male and 91% in female.¹ The percentage of unconfirmed lung cancer, named also radiological lung cancer, is rarely reported. Lung⁶ published a study of 16 Turkish centres and 3.8% radiological cancer among 11849 lung cancer patients. Juhasz *et al.*⁷ reported 11% of unconfirmed tumours in 499 NSCLC patients, so they concluded that there were no SCLC among their patients.

Squamous cell is the most common type of lung cancer, 30%⁸ to 50%⁹ of all lung cancer. The increase of adenocarcinoma in some countries over the last two decades is most likely to be attributable to the increased use of milder, filter-tip cigarette, the smoke from which is inhaled deeply, causing adenocarcinoma of the periphery of the lung.¹⁰ Small cell lung cancer is less frequent, 15%¹¹ to 30%.¹² In our patients there were 39% squamous cell and only 15% small cell, 26% adenocarcinoma and 19% large cell, meanwhile the Cancer Registry of Slovenia published 32% squamous, 17% small cell, 24% adenocar-

cinoma and no specified data for large cell carcinoma in 1996.¹

The valid TNM classification since 1997 range T3N0M0 tumours in IIB stage, it was already considered in the analysis. It was not possible to distinguish A and B in I and II stage. Based on the present data we were able to determine the clinical stage in 99% of patients. Only in resected patients it was possible to compare clinical TNM and postsurgical-pathomorphological TNM stage that has a better survival.¹³ Clinical TNM stage was correct in almost half of our patients, very similar to the published data.^{14,15,16} In our patients 13% had exploratory thoracotomy, also as a consequence of tendency to enable the resection for all patients without the proven inoperability. As exploratory thoracotomy yields no benefit to the patient in terms of survival or palliation, the goal of thoracic surgeons should be to eliminate such intervention.¹⁷ Consistent and precise staging enabled diminishing of exploratory thoracotomy from 15.1 to 2.1%.¹⁶

The duration of a diagnostic procedure in our patients was mostly about one week and did not essentially influence a therapy delay. The realization of therapy depends on the patient's motivation for therapy, confidence in the doctor, fear of therapy modality, access to the treatment and financial possibilities. The latter is not the case in Slovenia, because all citizens have health insurance that includes the whole cancer management. The difference between the selected and realized therapy was mostly the consequence of waiting for the radiotherapy up to two weeks and for the surgery about one month. During the waiting time the patient's situation can deteriorate and a primarily selected therapy may not be suitable any more. It can be also considered that the selected therapy modality was not always adequate.

All of 110 patients referred to radiotherapy came to the Institute of Oncology¹⁸ and 93% of them were irradiated, i.e. 30% of all pa-

tients. This percentage included primarily irradiated patients with curative and palliative intent, but not irradiated after thoracotomy or chemotherapy. Hawson *et al.*³ reported 40%, Skričková *et al.*¹⁹ 32.2% irradiated cancer patients, both in NSCLC only.

Of 93 patients selected for surgery 83% of them were operated (cervical mediastinoscopy and parasternal mediastinotomy as the initiation of surgical intervention included). Five percent of patients refused the surgery after coming to the thoracic surgeon, while 9% were rejected because of signs of inoperability or deterioration of a general condition.

Chemotherapy was performed in 44/47 selected SCLC and 3/3 selected NSCLC patients. That minimal use of chemotherapy in NSCLC (1%) was also due to the insufficient payment of modern expensive drugs by the health insurance. Hawson *et al.*³ reported the same use of chemotherapy in 873 NSCLC, but in 1990.

Of 337 treated patients 111 (33%) were getting a supportive care. One of them, peripheral large cell carcinoma stage I, without symptoms, unfit for the resection, survived for more than five years. A similar percentage of a supportive treatment is reported by others.^{3,19}

The presented survival figures are factual and not calculated. They do not exclude perioperative and general mortality. Almost 8% of patients survived for 5 years, all but one were resected.

Conclusions

The selected oncological therapy was actually realized in 89%. In our patients there was a low percentage of NSCLC treated by chemotherapy. Among five-year survivors there were 26 resected and one supportively treated patient, that confirms the surgery as the most effective therapy in our lung cancer patients.

References

1. Institute of Oncology Ljubljana, Cancer Registry of Slovenia. *Cancer Incidence in Slovenia 1996*. Report No.38. Ljubljana: Institute of Oncology; 1998.
2. UICC International Union Against Cancer. *TNM classification of malignant tumours*. Sobin LH, Wittekind Ch, editors. Sixth edition. New York: Wiley-Liss; 2002. p. 99-103.
3. Hawson G, Zimmerman PV, Ford CA, Johnston NG, Firouz-Abadi A. Primary lung cancer: characterization and survival of 1024 patients treated in a single institution. *Med J Aust* 1990; **152**: 230-4.
4. Haber RW. Primary lung cancer in Queensland. [Comment]. *Med J Aust* 1991; **154**: 429.
5. Lee C, Kang KH, Koh Y, Chang J, Chung HS, Park SK, et al. Characteristics of lung cancer in Korea, 1997. *Lung Cancer* 2000; **30**: 15-22.
6. Lung T. The retrospective analysis of lung cancer patients in Turkey, a country where smoking is highly prevalent. [Abstract]. *Lung Cancer* 2000; **29 (Suppl 1)**: S235.
7. Juhasz E, Temesi G, Myhali E, Maroti A. Analysis of survival data in non small cell lung cancer 1992-1997. *Lung Cancer* 1999; **25 (Suppl 1)**: S33-4.
8. Ginsberg RJ, Vokes EE, Raben A. Non-small cell lung cancer. In: DeVita VTJ, Hellman S, Rosenberg SA, editors. *Cancer: principles and practice of oncology*. 5th ed. Philadelphia: Lippincott - Raven; 1997. p. 858-911.
9. Neal AJ, Hoskin PJ. *Clinical oncology: basic principles and practice*. London: Arnold; 1997. p. 42-55.
10. Thun MJ, Lally CA, Flannery JT, Calle EE, Flanders WD, Heath CW Jr. Cigarette smoking and changes in the histopathology of lung cancer. *J Natl Cancer Inst* 1997; **89**: 1580-6.
11. Ihde D, Pass H, Glatstein E. Small cell lung cancer. In: DeVita VTJ, Hellman S, Rosenberg SA, editors. *Cancer: principles and practice of oncology*. 5th ed. Philadelphia: Lippincott - Raven; 1997. p. 911-49.
12. Hansen HH, Pappot H. Primary malignant tumours of the lung and pleura. In: Cavalli F, Hansen HH, Kaye SB, editors. *Textbook of medical oncology*. London: Dunitz; 2000. p. 245-69.
13. Mountain CF. Lung cancer staging. When the rules don't fit and other considerations. In: Motta G, editor. *Lung cancer. Frontiers in science and treatment*. Genoa: Grafica; 1994, 99-116.

14. Marel M, Melinova L, Stastny B, Skacel Z, Cermak S, Demes R, et al. The results of surgical treatment of non-small cell lung cancer at the Pneumological Clinic in Prague, Czech Republic 1985-1990. *Lung Cancer* 1994; **11**: 293-8.
15. Vidmar S. Accordance of clinical versus pathological stage (pTNM) in patients with surgically treated non-small cell lung cancer. *Radiol Oncol* 1994; **28**: 337-40.
16. Neef H. Clinical experience in staging of lung cancer at Martin-Luther University Halle-Wittenberg. *Ann Ital Chir* 1999; **70**: 909-12.
17. Steinbaum SS, Uretzky ID, McAdams HP, Torrington KG, Cohen AJ. Exploratory thoracotomy for nonresectable lung cancer. *Chest* 1995; **107**: 1058-61.
18. Debevec M. The role of radiotherapy in lung cancer treatment. Report from Slovenia. *Radiol Oncol* 1994; **28**: 376-81.
19. Skričkova J, Špelda S, Svobodnik A, Kaplanova J, Palkova J, Babičkova L, et al. A realistic view of the treatment of non-small cell lung cancer (NSCLC): an analysis of 348 consecutive patients. [Abstract]. *Lung Cancer* 2001; **32 (Suppl 1)**: S47.