EFFECT OF DELAYS ON SURVIVAL IN PATIENTS WITH LUNG CARCINOMA IN MONTENEGRO

Danko Živković

Brezovik Special Hospital for Lung Diseases and Tuberculosis, Medical Faculty of Podgorica, Nikšić, Montenegro

SUMMARY – Lung cancer is a global medical problem with a rising incidence and 5-year survival of 5%-10%. The aim of this study was to investigate whether waiting times and delays in diagnosis and treatment of patients with lung carcinoma have any bearing on prognosis and survival. The study was performed in the Brezovik Special Hospital for Lung Diseases and Tuberculosis. The study included all cases with the diagnosis of lung carcinoma in the Republic of Montenegro in 2009, a total of 206 patients, with follow up until the end of 2010. Median age was 66, median Karnofsky score 80, and male to female ratio 5:1. Diagnostic procedure was bronchoscopy in 89% of patients. Histologic type was small cell lung cancer in 25.7% and non small cell lung cancer in 74.3% of cases. Surgery was the main treatment for 24.4% of patients. Median delay from first symptoms to diagnosis of lung cancer was 10.35 weeks, mean 8 weeks (median patient's delay was 6.20 weeks, doctor's delay at primary health care 2.07 weeks and in pulmonology services 2.37 weeks). Median survival time for all patients was 39.27 weeks, mean 34. There was no statistically significant difference between patient's delay/doctor's delay/total delay and stage of lung carcinoma at the time of diagnosis, treatment choice and survival. Our results indicate that longer delay is not associated with poorer prognosis of lung carcinoma. The possible ways of reducing mortality of lung cancer include prevention by decreasing smoking prevalence and improved therapeutic options.

Key words: *Lung neoplasms – diagnosis; Lung neoplasms – therapy; Delayed diagnosis; Survival*

Introduction

Lung cancer is one of the most common cancers and has poor prognosis. Worldwide, an estimated 1.7 million of new cases of lung cancer were expected to be diagnosed in 2010, accounting for approximately 13 percent of total cancer diagnoses. Lung cancers are the leading cause of cancer death worldwide, with an estimated 1.4 million deaths each year. In Europe, lung cancer accounts for 20 percent of an estimate (over 350,000) of all cancer-related deaths in Europe, the highest of any cancer[1]. The decrease in the inci-

dence rates of squamous cell carcinoma and small cell lung carcinoma (SCLC) among men was probably due to a decrease in the percentage of smokers. The increase in adenocarcinoma has also been described and in the USA adenocarcinoma is now even the leading lung cancer cell type[2]. Despite recent advances in the treatment, prognosis for patients with lung carcinoma remains poor; the 5-year survival rate for patients with non small lung cell carcinoma (NSCLC) is still only about 15% in Europe[3].

According to the available data, the lung carcinoma incidence rate in Montenegro showed a steady growth between 1978 and 2005, with an average annual increase of 6%. In male population, the incidence rate rose from 19.6/100,000 to 48.5/100,000, with a mean annual growth of 5.8%. The mean standardized incidence rate was 39.2/100,000 in male population.

Correspondence to: *Assist. Prof. Danko Živković, MD, PhD*, Brezovik Special Hospital for Lung Diseases and Tuberculosis, Medical Faculty of Podgorica, Nikšić, Montenegro
E-mail: dankoz@t-com.me

Between 1976 and 2005, the lung cancer mortality rate in Montenegro increased from 19.4 to 26.3/100,000, with an average growth rate of 2%. According to our statistics, around 300 Montenegro citizens are diagnosed with this disease every year.

Nowadays, the importance of 'time factor' in the diagnosis of lung cancer is examined through new medical methods. In this respect, 'patient's delay' and/or 'health care delay' are evaluated separately. In case of lung carcinoma, the effect of 'delay' on survival remains a great mystery. Previous studies suggest that both the diagnosis and the initiation of treatment should be done as early as possible[4]. Treatment delays are a constant problem. According to some studies, delay has a negative impact on the prognosis, while other did not show such a correlation[4-7].

Time intervals between the onset of symptoms and diagnosis and beginning of treatment of a patient could be divided into 'patient's delay' and 'doctor's delay'. Patient's delay is the time between the first symptoms and the first contact with medical workers. Doctor's delay is defined as a time interval between the first examination at a health care institution and the beginning of treatment or a decision that the cancer specific treatment is not possible[8].

According to the research conducted by Moore *et al.* in the United States of America, a delay of over three months was observed in 25% of patients. The longest delay, four months on average, was noticed in the studies including patients aged <45 from the USA[9]. There are great variations in the intervals between the first contact with doctor and the established diagnosis. According to the Swedish study by Christensen *et al.*[9], the first doctor's delay was seen at the level of general practitioners and it amounted to 56 days.

The study by Billing and Wells[15] define total delay as a period between the first visit to the general practitioner and surgery, giving further divisions into subgroups according to the reasons for delay. According to the study by Christensen *et al.*, the end-point is the date when a patient is either operated on or considered inoperable[9].

The tumor could spread considerably during the delay time. It is considered that tumor growth from Tx to T1, T2 is not just a local growth of the tumor but also an increase in its metastatic potential, mean-ing that there is more chance that N increases with an increase of T, the same as M0 in M1. In the study by O'Rourke and Edwards[12], the NSCLC patients referred for radiotherapy initially had a diagnostic computed tomography (CT) scan and later a radiotherapy planning CT scan. Delay between the two CT scans amounted to 18-131 days (median 54 days) and tumor growth in terms of percentage change in tumor cross-sectional area ranged from 0 to 373%, with a median increase of 19% in the time elapsed[12]. The studies by Porta *et al.* focused on the association between delay and survival. According to this study, a significantly better rate of survival was found in patients with longer patient's delay than in those with longer doctor's delay[13,14]. The study by Alberts *et al.* examined the causes of unnecessary doctor's delay[15-17]. According to them, one of the major reasons is the lack of comprehensive multidisciplinary approach to the treatment of patients with lung carcinoma.

Recommendations of the British Thoracic Society on the time intervals for evaluation, diagnosis and treatment are aimed at providing guidelines and good practice for treating a patient with lung carcinoma[18,19]. According to these guidelines: 1) all patients should be examined no longer than one week from referral by the home doctor; 2) diagnostic workup must be completed no later than two weeks from the date when lung carcinoma was suspected; 3) chemotherapy must start no longer than seven days of the council's decision on the type of treatment; 4) radiotherapy should start no longer than two weeks after the decision has been made for urgent cases, and no longer than four weeks after the decision has been made for complicated cases, while waiting time for palliative radiotherapy should be no longer than two weeks; and 5) surgical intervention (operation) should be completed within four to eight weeks after the treatment decision has been made[20].

Objective of the study

The main contribution of this study is to examine the correlation of delay and survival in patients with lung carcinoma. The hypothesis for this carcinoma localization is that the delay factor has a limited significance, i.e. it has no bearing on the lung carcinoma mortality. The research is expected to provide answers to the following questions:

- Do patient's delay and/or doctor's delay, as well as the total delay have any bearing on the length of survival in lung cancer patients?
- What is the real prognostic significance of delay for lung cancer?
- What recommendations could be issued in order to improve the outcome of treatment of lung cancer patients, what level should the efforts be focused on in order to raise the awareness of patients and society, and to improve coordination within health service?

Materials and Methods

The subject of the research was the effect of delay on the lung carcinoma prognosis, focusing on the total delay, patient's delay, and health service delay, including relations between the doctors of primary health care and specialist service, as well as the time interval from diagnosis to the beginning of any type of treatment of the primary malignant process in the lungs. At the Brezovik Special Hospital for Lung Diseases and Tuberculosis, the institution in charge of lung carcinoma diagnosis and treatment at the national level, approximately 200-250 new lung carcinoma patients are diagnosed every year. In the last several years, this number has seen a steady growth.

This retrospective study included all lung carcinoma patients hospitalized at the Brezovik Special Hospital for Lung Diseases and Tuberculosis in Nikšić over a 12-month period (2009), with 12-month follow up after inclusion of the last patient in the study. The study included a total of 206 lung carcinoma patients, who were diagnosed and treated between January 1 and December 31, 2009, and monitored for the next 12 months until the end of 2010.

We analyzed patient survival in relation to delay between the onset of first symptoms and the diagnosis, patient's and doctor's delay. Study patients were divided into two groups: patients diagnosed within eight weeks and patients diagnosed beyond eight weeks of the onset of first symptoms.

We performed Kaplan-Meier analysis of survival for the group of surveyed patients in relation to the period between the onset of first symptoms and the end of the study.

Results

In compliance with the methodology used, our study included 206 patients, diagnosed and treated in 2009 at the Brezovik Special Hospital for Lung Diseases and Tuberculosis in Nikšić, Montenegro. Lung carcinoma is a disease of middle-aged men, with a peak incidence in the seventh decade of life. In the last two decades, a sudden growth was seen in the number of female lung carcinoma patients, associated with an increase in the number of female smokers. According to gender analysis, most of the patients included in our study were men (n=171, 83.0%), while only 35 (17.0%) were women, yielding a male to female ratio of 5:1.

Having analyzed the group of patients according to their smoking habits, we concluded that out of 206 patients, 167 (81%) were smokers, 75% of them heavy smokers (140/206). The mean length of smoking history was 29.4 years, with a mean of 29.17 cigarettes daily.

Patient's delay

Conducting patient survey concerning the time elapsed between the onset and recognition of first symptoms of the disease and their consultations with doctors (patient's delay), we found that this time interval ranged from 2-3 days to 33 weeks, mean 6.2 weeks (range, 0.23-33.00 weeks, 95% confidence interval (95% CI) for 206 patients) or median of 4.00 weeks (95% CI). Medical records and patient interviews revealed that a mean of 6.52 weeks had elapsed between the onset of first symptoms and chest radiography (between 1.00 and 34.00 weeks with 95% CI).

Doctor's delay I

The mean doctor's delay in primary health care until examination by a lung disease specialist was 2.07 weeks (between 1.00 and 20.00 weeks with 95% CI). The Brezovik Special Hospital for Lung Diseases is a central institution for diagnosis and treatment of lung carcinoma in Montenegro, which means that almost all patients were treated there. Decisions on the manner of treatment of lung cancer patients are made by a council. In most cases, histopathologic findings were obtained after bronchoscopy. In few patients, malignant lung disease was diagnosed after the surgery

(video-assisted thoracoscopic surgery (VATS) wedge resection) performed at the Department of Chest Surgery, Clinical Center of Montenegro in Podgorica. The mean delay of the specialist medical service was 2.37 weeks.

Doctor's delay II

Having added together primary health care doctor's delay (I) and specialist medical service delay (II) before primary lung carcinoma was diagnosed, we concluded that the health care delay or total doctors' delay was 4.22 weeks (between 1.00 and 23.00 weeks with 95% CI).

Total delay

Adding together patient's delay and health care delay yielded a mean total delay of 10.35 weeks. For the whole group of 206 patients surveyed, median delay was 8.0 weeks (between 2.00 and 51.00 weeks with 95% CI).

According to statistical analysis based on the Kaplan-Meier method, it is evident that the cumulative survival was 12 weeks after the onset of first symptoms with 95% CI. The mean survival time was 44.17 weeks, between 40.66 and 47.68 weeks with 95% CI. Median survival was 39 weeks, between 34.32 and 43.68 weeks, with 95% CI (Fig. 1).
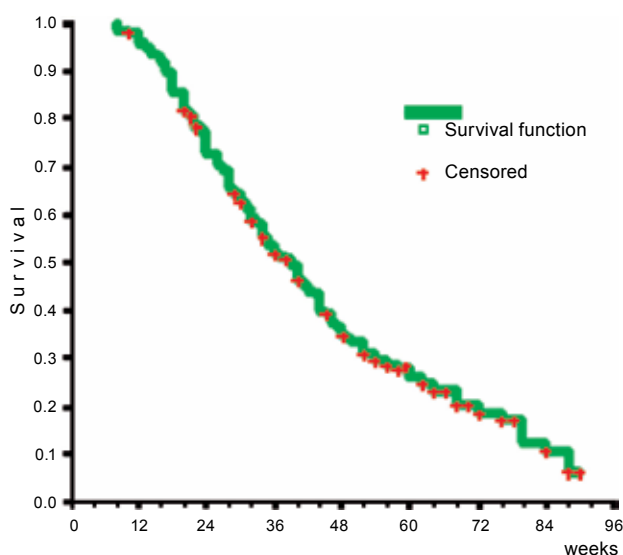

Fig. 2. Survival curve after diagnosis (Kaplan–Meier).

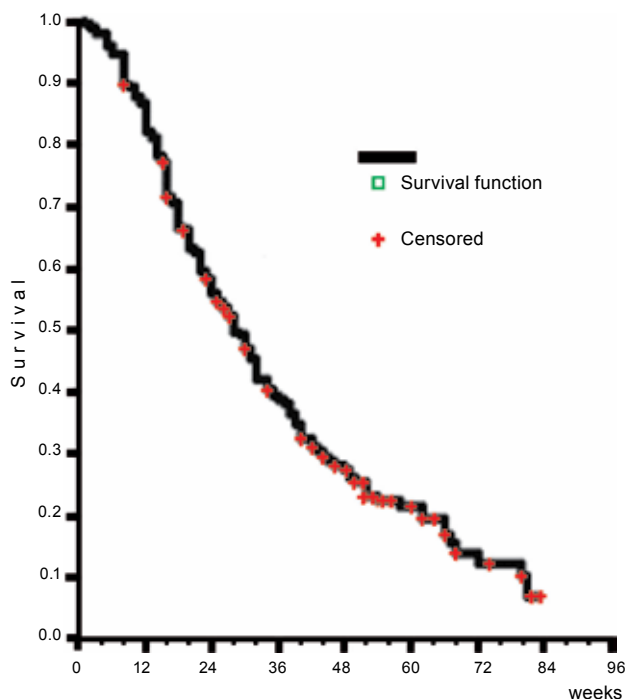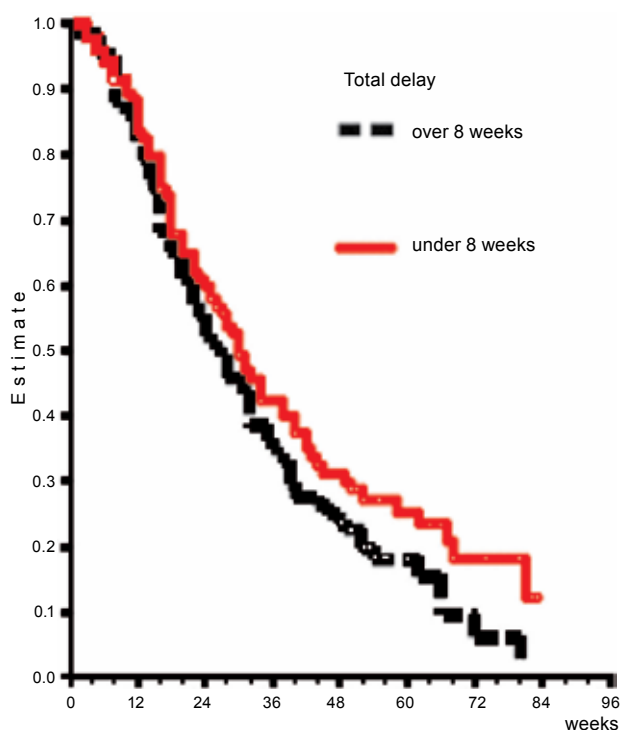Fig. 1. Survival curve after the onset of first symptoms (Kaplan–Meier).

Fig. 3. Survival curve in relation to patient's and doctor's delay (Kaplan–Meier).

According to statistical analysis based on the Kaplan-Meier method, the mean survival after the diagnosis was 35.48 weeks, between 31.94 and 39.02 weeks with 95% CI. Median survival was 28 weeks, between 24.02 and 31.98 weeks, with 95% CI (Fig. 2).

Survival in relation to patient's delay under and over 8 weeks

In compliance with the task of the study, we divided our patients into two groups: patients having recognized their symptoms and consulting doctors within 8 weeks and patients with a delay longer than 8 weeks, and analyzed their survival.

The group of patients with a delay shorter than 8 weeks included 104 of 206 patients. Median survival in the group with shorter delay was 35.00 weeks (95% CI: 29.86-40.16), while median survival in the group of patients that had recognized their symptoms and consulted doctors after 8 weeks was 40.00 (95% CI: 33.07-46.93). There was no statistically significant between-group difference in survival according to patient's delay ($p > 0.05$) under and over 8 weeks.

The group of patients diagnosed within 8 weeks included 30 of 104 live patients. Median survival in the group of patients diagnosed within 8 weeks was 30.00 weeks (95% CI: 24.82-35.18), while median survival in the group of patients diagnosed after 8 weeks was 27.00 (95% CI: 20.44-33.56). There was no statistically significant between-group difference in survival according to patient's delay ($p > 0.05$) under and over 8 weeks (Fig. 3).

According to study results, the most common type of NSCLC was squamous cell carcinoma found in 46.1%, whereas SCLC was found in 55 (26.7%) patients (Table 1).
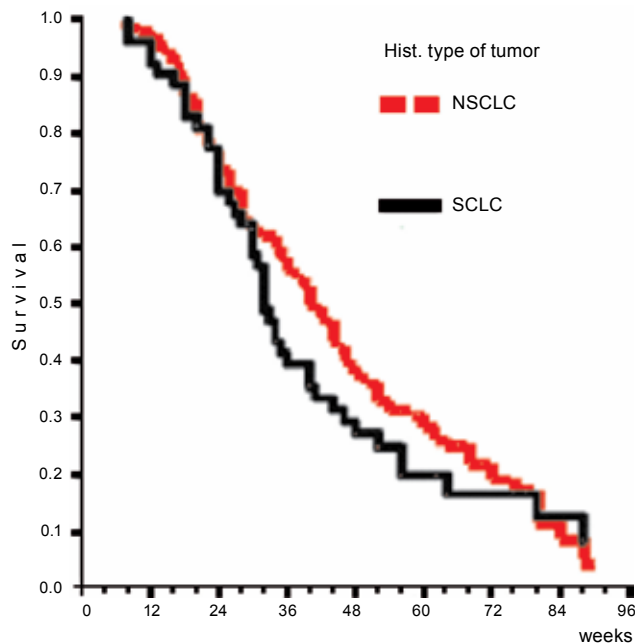

Fig. 4. Survival curve after the onset of first symptoms in relation to histopathologic type: small cell lung carcinoma (SCLC)/non small cell lung carcinoma (NSCLC) (Kaplan-Meier).

In our study, survival of the SCLC patients ranged between 33.83 and 47.26 weeks after the onset of first symptoms, with median survival of 32.00 weeks. In the group of NSCLC patients, survival ranged between 41.31 and 49.47 weeks, with median survival of 40.00 weeks for the log rank 1.16 and p=0.2810 (Fig. 4). There was no statistically significant difference in survival according to histopathologic type of the disease ($p > 0.05$).

In our study, survival of SCLC patients ranged between 25.73 and 37.88 weeks, with median survival of 25 weeks. In the group of NSCLC patients, survival ranged between 32.52 and 40.987 weeks, with median survival of 30.00 weeks for the log rank 1.42 and p=0.2334.

There was no statistically significant difference in survival after disease diagnosis according to histopathologic type of the disease (Mann-Whitney test u=3.667; z=0.972; p>0.05).

Table 1. Patient distribution according to histologic types of lung cancer

Histologic type of lung cancer	Number of patients	%	Total %
SCLC, small cell lung carcinoma	55	25.7	25.7
NSCLC, squamous cell lung carcinoma	93	46.1	71.8
NSCLC, adenocarcinoma	26	12.6	84.5
NSCLC, miscellaneous type	5	2.4	86.9
NSCLC, large cell carcinoma	27	13.1	100.0
Total	206	100.0	100.0

NSCLC = non small cell lung carcinoma

Discussion

In the literature, the effect of delay on survival of lung carcinoma patients has been defined as unpredictable. Most of the studies started from an assumption that shorter delay results in better survival rate. However, some research results did not confirm this assumption. The results of the study by Myrdal et al.[10] show that not even longer patient's delay and longer doctor's delay were associated with worse prognosis and shorter survival. On the contrary, the prognoses were worse in patients with shorter delay. Moreover, the results of this study showed that patients with limited disease had longer delay until they received cancer specific treatment than those with advanced disease.

According to the observations reported by Salomaa et al.[21], the growth of NSCLC is based on mathematical models, suggesting that it takes 10 to 15 years from the appearance of the first cancer cells to the possibility of detecting NSCLC by conventional chest radiograph. According to the literature, the time observed for lung tumors to double their volume ranges from 4 to 56 weeks, with median time of 17 weeks. This indicates that the growth of a tumor is comparatively slow[22,23]. Two studies monitored the growth of primary tumor with consequent CT chest scans, observing great diversity in the time of tumor growth[15,24]. The previous studies have failed to answer the question when the metastasis of lung carcinoma starts[25]. According to the study by Jung et al., in patients with T1 lung carcinoma, extra-pulmonary metastases were found in 13% of patients at diagnosis, while distant metastases were found in 24% of patients one year later[26]. If metastases have started growing years before the lung carcinoma is detected, it is difficult to expect that the delay will have any prognostic significance[27].

The age and gender distribution of patients in our study was consistent with that in other studies. Our patients were of similar age, median 66, compared with median 65 in the American and 68 in Western European studies[23]. The female to male ratio of the disease is 1:3-4 on the American continent, while in our study it was 1:5. If the number of women with lung carcinoma continues to grow, it is expected that the lung carcinoma incidence in women will have exceeded the one in men by 2030[2].

Having analyzed patient's delay, our study showed the mean delay between the onset and recognition of first symptoms and presentation to doctor to be 6.2 weeks (95% CI 0.23-33.0). The delay between the onset of first symptoms and the beginning of treatment was 9.63 weeks (95% CI: 1-35.0).

Correlating patient's delay with the histologic type of lung carcinoma yielded no statistical significance, as it was 10.6 weeks in SCLC patients and 12.00 weeks in NSCLC patients (153/206).

In comparison with the results of the Italian researchers presented in the G.I.V.I.O. study[28], which reported a mean delay of 7 days, our research indicated a little longer delay, but it could be considered as a comparatively short delay in general, in comparison with the results reported by Myrdal et al.[10] on 4.6-month delay, or by Mood et al.[29], who found a delay longer than 3 months in 25% of patients. The longest patient's delay was observed in the studies including the U.S. patients aged under 45, amounting to an average of 6 months.

Mackillop et al.[30] explain such a wide range of patients' delay by cultural and economic conditions in the places of research, as well as by the education level of the population surveyed.

In their study, Bowen and Razner[31] say that patient's delay is longer in men. Myrdal et al.[10] argue that the delay from symptoms to treatment is shorter in patients with stage IV lung carcinoma (median 3.4 months) than in stage I and II patients (median 5.5 months). They explain it by the fact that patients with advanced disease have more disease symptoms and signs making them to contact a doctor.

In Canada, it is recommended that the interval between the examination by a selected doctor and diagnosis should be maximum 4 weeks, while the one between the diagnosis and surgery should be no longer than two weeks[32]. According to the retrospective study by Myrdal et al.[10], doctor's delay in one half of the NSCLC patients amounted to 2.5 months. The cancer specific treatment started within 6 weeks from the first consultation with a chest physician. Surgically treated patients had longer delay than those who did not undergo surgery. According to the study by Deegan et al., median doctor's delay was reduced to five weeks after the first consultation with a doctor[27].

In our study, doctor's delay included primary health care delay and secondary, i.e. tertiary health service delay (specialist services). In our case, primary health care

delay was 2.07 weeks (95% CI: 1.0-20.0) and specialist services' delay was similar, 2.37 weeks. Total delay amounted to 4.22 weeks (95% CI: 1.00-23.00).

Comparing the results of our study with those from the literature, it is concluded that doctor's delay was considerably shorter in our study. The reason for this could be sought in the centralization of health care in Montenegro and the role of councils in deciding on the treatment of patients with lung carcinoma.

The main parameter of success in the treatment of patients with malignant disease is survival. There was no statistically significant difference in patient survival after the onset of first symptoms according to the histologic type of lung carcinoma (p>0.05), or according to the time of malignant disease diagnosis (p>0.05). Analysis of survival according to patient's delay shorter than eight weeks (shorter delay) and longer than eight weeks (longer delay) yielded no statistically significant difference (p>0.05). Namely, median survival was 35.00 weeks (95% CI: 29.86-40.16) in the group with shorter delay and 40.00 (95%: 33.07-46.93) in the group with longer delay. Comparison of patient survival according to the time of lung carcinoma diagnosis using the same parameters (delay shorter and longer than eight weeks) showed no statistically significant difference either (p>0.05). Our results are consistent with those reported by Aragoneses et al.[33]. They did not observe any statistically significant difference in survival according to the lung carcinoma histology, clinical stage, and length of delay in any period, even when patients with the shortest delay of 1 to 20 days were compared with those with the longest delay of over 60 days.

We compared survival of SCLC-limited stage disease (LD) patients with a group of SCLC-extensive stage disease (ED) patients from the onset of first symptoms and found a statistically significant difference in survival (p<0.001). Median survival was 48 weeks (95% CI: 22.27-73.73) in the group with SCLC-LD and 30.00 weeks (95% CI: 24.44-35.56) in the group with SCLC-ED. There was a statistically significant difference (p<0.004) in survival of patients with SCLC from diagnosis according to the stage of disease. Median survival of patients with limited disease was 40 weeks (95% CI: 29.07-50.93), while median survival of those with advanced stage disease was 18 weeks (95% CI: 15.77-20.23).

Having analyzed survival of patients with NSCLC from the onset of first symptoms, we found longest survival in patients with stage I disease, who were all alive when the study was completed. Median survival was 88.00 weeks in stage II NSCLC patients, 62.00 weeks in stage IIIa patients, 37.00 weeks in stage IIIb patients, and 26.00 weeks in patients with stage IV NSCLC.

There was no significant difference in survival between patients with stage I and stage II NSCLC according to delay from the onset of first symptoms. A difference in survival was found in patients with stage I and II disease as compared with those with advanced stage IIIb and IV according to delay from the onset of first symptoms.

Analysis of survival in patients with NSCLC according to delay from diagnosis yielded a statistically significant difference between stage I-II patients and patients with advanced stage III b and IV disease. In compliance with the defined objectives, we analyzed survival of patients in relation to metastasis. Metastases were found in 32.5% of patients. The most frequent localization of metastases was the liver (22.5%). There was a high statistically significant difference in survival both from the onset of first symptoms and from diagnosis according to the presence of metastases (p<0.005).

The main limitations of this study were the retrospective type of the study and the number of patients included in the study. The number of study patients was not big enough to make strong conclusions from the results of statistical analysis. The number of patients probably determined great variations in statistical analysis and the results obtained. That is the reason why we did not get statistical significance in examined delays and survival of patients with lung carcinoma.

The specificity of the study population lies in its structure, also in a centralized and accessible specialist care (all patients were treated at the same institution). Unlike all younger age structures, increasing the proportion of women among patients and the predominance of adenocarcinoma in most developed countries of the West, the Montenegrin population consists mainly of older men with a high risk of cigarette smoking and the most common diagnosis of squamous cell carcinoma, stage III and IV disease. These results represent the current situation with lung carcinoma in Montenegro

and could be useful for further steps in making health care decisions and strategies.

Conclusion

Our study included 206 patients diagnosed with malignant lung carcinoma in 2009. It included all lung carcinoma patients in Montenegro that year. According to our research, lung carcinoma is a disease of middle-aged men, with a peak incidence in the seventh decade of life, most frequently found in heavy smokers. According to gender structure, 83% of patients were men and 17% women, yielding a 5:1 male to female ratio. Ten percent of patients were younger than 50, while 20% were aged over 70.

The main parameter of success in the treatment of patients with malignant disease is survival. There was no statistically significant difference in survival according to patient's or doctor's delay (p>0.05), probably due to the limitations of the study such as retrospective design and small number of patients. On the other hand, these results represent current situation of the specific Montenegrin population with lung carcinoma.

Lung carcinoma is still a great medical challenge all over the world. In view of the research conducted so far, there are four possible ways to reduce the respective death rate:

– prevention (reduction) of smoking;
– early diagnosis by means of new screening technologies;
– appropriate approach to patients in a more efficient health system; and
– improvement of treatment options.

Fatalistic attitude of doctors towards this disease has changed and great efforts and funding are now invested in clinical practice in order to improve diagnostic procedures for this disease. These efforts are in part focused on the reduction of health service delay. Better coordination among doctors and team approach to treatment are the basis for a more efficient treatment of patients with lung carcinoma. If time intervals are reduced to minimum, the possibility of early detection of this disease will be higher, as well as the chances to 'prolong' survival of these patients.

References

1. International Agency for Research on Cancer, World Health Organization, GLOBACON 2008.

2. MARYSKA LG, JANSSEN H, WILLEM J. The changing epidemiology of lung cancer in Europe. Lung Cancer 2003;41:245-58.

3. JANSSEN HEIJNEN ML, GATTA G, FORMAN D, CAPOCACCIA R, COEBERGH JW. Variations in survival of patients with lung cancer in Europe. Eur J Cancer 1998;34:2191-6.

4. HAMILTON W, PETERS TJ, ROUND A, SHARP D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. Thorax 2005;60:1059-65.

5. SINGH H, HIRANI K, KADIYALA H, RUDOMIOTOV O, DAVIS T, KHAN MM, et al. Characteristics and predictors of missed opportunities in lung cancer diagnosis: an electronic health record-based study. J Clin Oncol 2010;28:3307-15.

6. KOYI H, HILLERDAL G, BRANDÉN E. Patient's and doctors' delays in the diagnosis of chest tumors. Lung Cancer 2002;35:53-7.

7. ELLIS PM, VANDERMEER R. Delays in the diagnosis of lung cancer. J Thorac Dis 2011;3(3):183-8.

8. BAUGHAN P, O'NEILL B, FLETCHER E. Auditing the diagnosis of cancer in primary care: the experience in Scotland. Br J Cancer 2009;101:S87-91.

9. CHRISTENSEN ED, HARVALD T, JENDRESEN M, et al. The impact of delayed diagnosis of lung cancer on the stage at the time of operation. Eur J Cardiothorac Surg 1997;12:880-4.

10. MYRDAL G, LAMBE M, HILLERDAL G, LAMBERG K, AGUSTSSON Th, STAHLE E. Effect of delays on prognosis in patients with non-small cell lung cancer. Thorax 2004;59:45-9.

11. BECKLES MA, SPIRO SG, COLICE GL, et al. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. Chest 2003;123:978-1048.

12. O'ROURKE N, EDWARDS R. Lung cancer treatment waiting times and tumour growth. Clin Oncol (R Coll Radiol) 2000;12:141-4.

13. JENSEN RA, MAINZ J, OVERGAARD J. Impact of delay on diagnosis and treatment of primary lung cancer. Acta Oncol 2002;41:147-52.

14. PORTA M, GALLEN M, MALATS N, PLANAS J. Influence of "diagnostic delay" upon cancer survival: an analysis of five tumour sites. J Epidemiol Community Health 1991;45:225-30.

15. BILLING JS, WELLS FC. Delays in the diagnosis and surgical treatment of the lung cancer (see comments). Thorax 1996;51:903-6.

16. ALBERTS WM, BEPLER G, HAZELTON T, RUCK-DESCHEL CJ, WILLIAMS H. Practice organization. Chest 2003;123;332-7.

17. BARRETT J, HAMILTON W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. BMC Fam Pract 2008;9:31.

18. The Royal College of Radiologists' Clinical Oncology Information Network. Guidelines on the non-surgical management of lung cancer. Clin Oncol 1999;11:S1-S53.

19. British Thoracic Society. BTS Recommendations to respiratory physicians for organizing the care of patients with lung cancer. Thorax 1998;53 (Suppl 1):1-8.

20. GINSBERG R, ROTH J, FERGUSSON M. Lung cancer surgical practice guidelines. Oncology 1997;11:889-95.

21. SALOMAA ER, SALLIENEN S, HIEKKANEN H, LIIPPO K. Delays in the diagnosis and treatment of lung cancer. Chest 2005;128;2282-8.

22. MUERS MF, HOLMES WF, LITTLEWOOD C. The challenge of improving the delivery of lung cancer care.Thorax 1999;54;540-3.

23. NHS Executive. The National Cancer Plan. A plan for investment, a plan for reform. London: Department of Health, 2000.

24. STRAUSS GM, GLEASON RE, SUGABAKER DJ. Screening for lung cancer re-examined. A reinterpretation of the Mayo Lung Project randomized trial on lung cancer screening. Chest 1993;103 (Suppl 4):337S-41.

25. ZANG EA, WYNDER EL. Differences in lung cancer risk between men and women: examination of the evidence. J Natl Cancer Inst 1996;88:133-42.

26. JUNG KJ, LEE KS, KIM H, et al. T1 lung cancer on CT: frequency of extrathoracic metastases. J Comput Assist Tomogr 2000;24:711-8.

27. DEEGAN PC, HEATH L, BRUNSKILL J, et al. Reducing waiting times in lung cancer. Thorax 1998;53:445-9.

28. Interdisciplinary Group for Cancer Evaluation. Diagnosis and first line treatment of patients with lung cancer in Italian general hospitals. G.I.V.I.O. (Interdisciplinary Group for Cancer Evaluation). Tumori 1989;75:163-7.

29. MOODY A, MUERS M., FORMAN D. Delays in managing lung cancer. Thorax 2004;59:1-3.

30. MACKILLOP WJ, ZHOU Y,QUIRT CF. A comparasion of delays in the treatment of cancer with radiation in Canada and the United States (see comments). Int J Radiat Oncol Biol Phys 1995;32:531-9.

31. BOWEN EF, RAZNER CF. Patient and GP led delays in the recognition of symptoms suggestive of lung cancer. Acta Oncol 2002;41:147-52.

32. SIMUNOVIĆ M, GAGLIARDI A, Mc CREADY D, et al. A snapshot of waiting times for cancer surgery provided by surgeons affiliated with regional cancer centres in Ontario. Can Med Assoc J 2001;165: 421-5.

33. ARAGONESES GF, MORENO N, LEON P, GARCIA-FONTAN E, FOLQUE E. Influence of delays on survival in the surgical treatment of bronchogenic carcinoma. Lung Cancer 2002;36:59-63.

Sažetak

UČINAK ZAKAŠNJELE DIJAGNOZE NA PREŽIVLJENJE KOD BOLESNIKA S PLUĆNIM TUMORIMA U CRNOJ GORI

D. Živković

Karcinom pluća je globalni medicinski problem s rastućom incidencijom i 5-godišnjim preživljavanjem od 5%-10%. Cilj ovoga rada bio je istražiti utječe li izgubljeno vrijeme (kašnjenje) u dijagnozi i liječenju bolesnika s karcinomom pluća na prognozu i preživljavanje oboljelih. Istraživanje je provedeno u Specijalnoj bolnici za plućne bolesti i tuberkulozu Brezovik. U studiju su bili uključeni svi slučajevi s dijagnozom raka pluća u 2009. godini u Republici Crnoj Gori, ukupno 206 bolesnika, s praćenjem do kraja 2010. godine. Srednja životna dob je bila 66 godina, srednji Karnofski skor 80, odnos prema spolu 5 M:1 Ž. Histološki tip je bio mikrocelularni karcinom (SCLC) u 25,7% i nemikrocelularni karcinom (NSCLC) u 74,3% slučajeva. Kirurgija je bila osnovno liječenje za 24,4% bolesnika. Srednje "izgubljeno vrijeme" od prvih simptoma bolesti do dijagnoze raka pluća je bilo 10,35 tjedana, medijan 8 tjedana (srednje izgubljeno vrijeme bolesnika je bilo 6,20 tjedana, liječnika u primarnoj zdravstvenoj zaštiti 2,07 tjedana i liječnika pulmologa 2,37 tjedana). Srednje vrijeme preživljavanja za sve bolesnike je bilo 39,27 tjedana, medijan 34. Nije nađena statistički značajna razlika između izgubljenog vremena bolesnika, liječnika i ukupno izgubljenog vremena u odnosu na stadij bolesti u trenutku postavljanja dijagnoze, terapijski izbor i preživljavanje bolesnika. Naši rezultati ukazuju na to da duže izgubljeno vrijeme nije praćeno lošijom prognozom karcinoma pluća. Mogući putovi u smanjenju smrtnosti od raka pluća su prevencija borbom protiv pušenja i poboljšanje terapijskih mogućnosti.

Ključne riječi: *Plućni tumori – dijagnostika; Plućni tumori – terapija; Kasna dijagnoza; Preživljavanje*