

Epidemiological Characteristics of Lung Carcinoma in Montenegro

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Abstract

Lung carcinoma is a disease with the highest incidence of all malignant diseases suffered by men in Montenegro. Our study includes all patients diagnosed with lung carcinoma and treated in 2009 in the Republic of Montenegro. A majority of the patients were in their seventh decade, with median age of 66. The gender ratio was 5m:1f. In 2009, the lung carcinoma incidence in Montenegro was 33/100.000 citizens. Across the municipalities, the rate was lowest in Rozaje - 13, and highest in Kolasin 100.5. Regionally, there was no statistically significant difference. In the coastal region, the rate was 38.2, in central 37.2, while it was 29.7 in the northern region. According to the smoking habit, the structure of patients was: 81% smokers/19% non-smokers. An average Karnofsky score was 80 (60/100 interval).

A definite lung carcinoma diagnosis was made by means of bronchoscopic biopsy in 89%, and using other methods in 11% of the cases. The histological type was SCLC 25.7%, NSCLC 74.3%.

Surgery was the primary treatment in 24.4% of the patients (only surgery in 13.6%, combined in 10.8%), symptomatic treatment in 14.1%, while the remaining patients were treated by HT, RT or a combination of methods.

At the end of 2009, there were 23.8% live patents included in the study. The survival time of the whole group of patients from the first symptoms until the end of the study was 39.27 weeks, median 34.

Keywords: Lung Carcinoma; Epidemiology; Montenegro

Introduction

Every period in the development of human population was accompanied by a specific disease, which sometimes had fatal consequences for human species. Previous epidemics of infectious diseases have decimated the mankind. The modern era is characterized by a growing incidence of malignant diseases [1].

Malignant tumour, neoplasm, carcinoma, cancer are the names for several hundreds of diseases. Lung carcinoma is a major social and medical problem of modern civilization, which is very difficult to solve. While it was almost unknown disease in the previous century, it has now reached "epidemic" proportions. Unfortunately, "the most horrible epidemic is the one with mortality rate approximately equal to incidence" (WHO) [2].

Lung carcinoma is a disturbing disease with a growing incidence and annual survival of 5 - 10%. Apart from the prevention, oncology pays most attention to early detection of carcinoma, which should result in better prognosis of malignant disease and better chances of getting cured. The screening for breast, PVU, colon etc. carcinoma considerably affects the curing percentage and patients' survival time. In the case of lung carcinoma, the mass screenings with periodic chest scan and cytological sputum examination have resulted in a modest increase in the number of operable patients, but not in a lower mortality rate [3]. There was no statistically significant prolongation of patients' lives either. Screening has not proved its economic viability as a mass method [4]. Bad prognosis of the lung cancer is a consequence of the aggressive biological nature of lung carcinoma and comparative inefficiency of current forms of treatment. The effect of treatment, including the latest types, on the course of this disease is marginal. In the early 20th century, this disease was very rare. After that period,

several countries of Western Europe and America saw a sudden increase in the number and frequency of male patients after sudden development of industry and tobacco processing. Several decades later, bronchogenic carcinoma has a significant incidence in female population as well. Morbidity and mortality rate of bronchogenic carcinoma is different across the globe, and it largely depends on the smoking habits of the population.

Therefore, the specific incidence values in male population range from over 100 (New Zealand indigenous population) and a little below 100 (black people in the USA, Poland, Russian, the Netherlands) to a little below 20 (Puerto Rico, India). In most countries, an average specific incidence in male population ranges between these values. In the female population, the same indicator shows that the most affected are the women from New Zealand (incidence approximately 60), followed by those from China, Scotland and white women in the USA (incidence approximately 30), while the least affected are the women of India (incidence below 4) [5]. According to incidence, lung carcinoma is in the first place in the male, and in the sixth place in the female population on the global level [1]. Apart from being the first in frequency of incidence, lung cancer is also the most frequent cause of death for men in the developed countries [5].

The lung carcinoma incidence has a steady and progressive growth in all countries of the world. At the beginning of this century, lung carcinoma was responsible for 1% of mortality rate, whereas 2 - 3% of population dies of lung carcinoma today. Bronchogenic carcinoma is the most frequent carcinoma in the world today, and it accounts for 12.3% of all new carcinoma in 2002. According to the WHO statistics for 2002, out of 1.3 million of new patients registered, 900,000 died, 200,000 of whom in Europe. In former Yugoslavia, carcinoma mortality rate rose from 26.5 per 100,000 citizens in 1981, through over 29.8 (1985) to 33.4 (1990).

Out of the first ten carcinoma in Montenegro, lung carcinoma has No. 1 incidence rate. According to the available data, the lung carcinoma incidence rate in Montenegro saw a steady growth between 1978 and 2005, at an average annual rate of 6%. An average standardized incidence rate for this period amounts to 20.8 per 100,000 citizens.

In the same period, there were 120 male and 22 new female patients registered on average. In the male population, the incidence rate increased from 19.6/100,000 to 48.5/100,000, at an average annual rate of 5.8%. An average standardized incidence rate was 39.2/100,000 for men. For women, the corresponding rate increased in the same period from 3.7/100,000 to 11.4/100,000 at an average annual rate of 6.4%, with an average standardized incidence rate of 64/100,000 of women. The incidence analysis according to age gives low values for the ages up to 44. A significant increase is seen for the ages between 45 and 65, while a steep rise is seen after 65, especially with men [6].

Between 1976 and 2005, the lung cancer mortality rate increased in Montenegro from 19.4 to 26.3/100,000 at an average annual rate of 2% [7-26].

Methodology and Respondents

At the Public Health Institution Special Hospital for Lung Diseases and Tuberculosis in Brezovik, the institution in charge of lung carcinoma diagnostics and treatment in the republic, approximately 200 to 250 new patients are diagnosed with lung carcinoma a year. Over the last several years, this number has seen a steady growth.

With the adoption of the Law on Limited Use of Tobacco Products (2004), a comprehensive campaign was initiated, aimed at lowering the number of lung carcinoma patients. Unfortunately, according to the statistical data, there are still no results of the undertaken measures. This prospective study includes all lung carcinoma patients hospitalized at the Special Hospital for Lung Diseases and Tuberculosis "Brezovik" in Niksic, over a 12-month period (2009), with a 12-month follow-up after the inclusion of the last patient in the study.

Results

The study includes a total of 206 lung carcinoma patients, who were diagnosed and treated between 1 January and 31 December 2009, and monitored for the following 12 months until the end of 2010.

Analysis of the age structure shows that the majority of patients are of advanced age, between 60 and 70. Median age was 66. The youngest patient was a woman of 36, who suffered from the lung adenocarcinoma, while the oldest one was a patient of 86, with lung epidermoid carcinoma. According to the gender analysis, most of the patents included in our study were male, 171 (83.0%), while only 35 (17.0%) were women, meaning that the gender ratio was 5m:1f.

In Montenegro, bronchogenic carcinoma is a leading malignant disease, both in terms of morbidity and mortality. In our survey, the total bronchogenic carcinoma incidence rate was 33.20 per 100,000 (Table 1).

	Place of residence	No. of patients	Percentage	Incidence rate	Cumulative %
Coastal region	Ulcinj	8	3.9	39.42	70.4
	Bar	12	5.8	29.97	36.4
	Budva	4	1.9	25.14	30.6
	Tivat	3	1.5	22.01	100
	Kotor	9	4.4	39.16	46.6
	Herceg Novi	12	5.8	36.32	42.2
Central region	Cetinje	9	4.4	48.69	66.5
	Podgorica	59	28.6	34.88	28.6
	Danilovgrad	4	1.9	24.2	72.3
	Nikšić	32	15.5	42.5	62.1
Northern region	Pljevlja	9	4.4	22.01	76.7
	Žabljak	1	0.5	.23.58	98.5
	Kolašin	10	4.9	100.51	81.6
	Mojkovac	2	1	19.87	96.6
	Berane	13	6.3	37.1	94.2
	Bijelo Polje	13	6.3	25.85	87.9
	Rožaje	3	1.5	13.21	98.1
	Plav	3	1.5	21.73	95.6
	Total	206	100		

Table 1: Geographic distribution of lung carcinoma incidence rate in 2009 in Montenegro.

The bronchogenic carcinoma incidence rates differ according to the geographic distribution, with 38.23 in coastal, 37.22 in central and 29.69/100,000 bronchogenic carcinoma incidence in northern part of Montenegro.



Figure 1: Lung carcinoma incidence rate in 2009 in Montenegro.

Having analysed the group of patients according to their smoking habits, we concluded that out of 206 patients, 167 were smokers (81%), 75% of whom were heavy smokers (140 out of 206)¹. An average smoking history was 29.4 years, with a daily average of 29.17 cigarettes smoked. The survey of the group showed that out of 206 patients, 125 (61%) had an associated disease, most frequently obstructive bronchitis, pneumonia or heart failure. Because of the symptoms (cough, shortness of breath and faintness), 41.3% of the patients were treated with bronchodilators, antibiotics and antitussives.

All patients were subject to clinical examination and they were divided into groups according to the principles of the Karnofsky index. According to our results, an average patient has a Karnofsky score of 80% (60 to 100 with a 95% confidence interval). In terms of a radiological localization of lung carcinoma in our study, the localization is almost equal for right and left lung (51:49), although the most dominant localization was in the upper right lobe, where tumours were diagnosed in 41% of our patients with lung carcinoma.

Discussion

Lung cancer is a major medical problem, with rising incidence and with 5-year survival of 5 - 10%. Chemotherapy was the primary choice of therapy for small-cell carcinoma, which is considered to be disseminated malignant disease. The patients who survive for over two years are considered to be the patients with long survival time.

¹Patients with smoking history of over 40 years and/or smoking over 40 cigarettes a day.

There are three times more non-small-cell lung carcinoma and the survival is longer. Around 10% of patients live for over five years. The factors affecting the disease prognosis with lung cancer (SCLC and NSCLC) are the disease stage, and performance status, while there is no global consensus on other parameters. Bad prognosis is a result of tumour's aggressive malign potential, and currently inefficient forms of treatment.

The attempts to reduce the incidence of this disease were going in two different directions, namely prevention, primarily though fight against smoking, and early detection of the disease. In the case of lung carcinoma, mass screenings, with periodic chest scan and cytological sputum examination of high-risk groups of population have resulted in an increase in the number of operable patients, but with no effect on the mortality rate. There was no statistically significant prolongation of patients' lives either. The screening has not proved its economic viability as a mass method of early lung carcinoma detection.

More recent and sophisticated diagnostic methods, including CT, fluorescent bronchoscopy, PET, were useful for better estimation of how advanced the disease was and for reaching an adequate decision on the treatment of tumour, but they had no effect on the reduction of lung carcinoma mortality rate. In the studies, using chest CT as a screening method in high-risk persons (elderly men, long-term smokers), who were asymptomatic, there was no reduction of mortality rate.

A large number of new lung carcinoma patients in the world demand new research into early detection of the disease. The possibilities of improvement of lung carcinoma prognosis are being explored with introduction of other potential screening methods of sputum cytology, molecular diagnostics, immunohistochemistry, monoclonal antibodies for antigens released by lung carcinoma cell expression, etc.

Over the last several years, the research based on the influence of "time" factor on the course and prognosis of this disease has come into focus. One of the ethical and social problems in the healthcare system is the issue of long "delays" between diagnosis and the beginning of treatment of lung carcinoma patients. It is generally accepted (supported by some publications and disputed by others) that a longer delay in the beginning of treatments of patients with carcinoma results in a shorter survival, especially for tumours with bad prognosis such as the lung carcinoma.

The initial symptoms of lung carcinoma are not specific, meaning that there are almost no "warning" symptoms. The patients with lung carcinoma could have different symptoms, the most frequent being coughing, coughing up blood, chest pain, shortness of breath, loss of appetite, weight loss, high temperature, insomnia, and bone pain. Many authors add disease stress to already wide palette of symptoms.

Very often, the lung carcinoma symptoms are "masked" and it is sometimes difficult to recognize new ones, especially in patients with associated respiratory diseases, such as the chronic obstructive bronchitis. Moreover, demographic changes, growing number of female patients, adenocarcinoma, and young patients affect the symptomatic image of patients with lung carcinoma. An onset of only one symptom is often ignored by patients, which delays both diagnosis and treatment. The reasons for such behaviour of patients should be sought in their lack of understanding and information they have about the disease.

In their work published in the *Thorax* magazine, Corner, *et al.* [27] present the findings of their retrospective study, saying that they analysed over 30 different symptoms the lung carcinoma patients identified in their interviews on the onset of the disease. The most frequently mentioned symptoms were coughing and shortness of breath (15/22), while over one half of the patients had chest pains (12/22).

Vomiting, depression, insomnia and weight loss were seen in over one half of the patients with advanced-stage disease. The authors say that all patients had at least one "new" symptom before the diagnosis.

In our study, the most frequent symptoms were: chest pain in 79%, coughing in 84.7%, and weight loss in 82% of patients. The earliest sign that "made" patients consult a doctor, was coughing up blood, with median 2 weeks (95% CI: 1- 12). An average duration of chest pain before consultation with doctor was 4 weeks (95% CI: 2- 33).

According to Beckles., *et al.* [28], in a smaller percentage of cases, initial radiography of patients with haemoptysis gave completely negative result. However, the authors recommend additional diagnostics suspecting a malign process, for all patients with haemoptysis younger than 40, regardless of their negative radiographic results. According to the literature, haemoptysis as a symptom is seen at presentation in 6 - 35% of patients. According to Beckles., *et al.* 6% of patients were asymptomatic at diagnosis, 27% of patients had respiratory symptoms, while 27% and 32% of patients had general symptoms and symptoms as a result of distant metastases respectively [28].

In our study, the disease was discovered by chance in 7 (3.4%) of the cases, since they were respiratory asymptomatic. There were 15 (7.3%) patients with one symptom, while 50 - 55 (approximately 25%) patients most frequently had 3 - 4 symptoms. In our study, haemoptysis was an initial sign of disease in 15% of patients. Median Karnofsky index was 80%.

The references include the articles with the results of the research based on smaller series of patients, analysing the issue of delay in diagnostics and treatment in correlation with the stage of disease at diagnosis, progression of tumour from diagnosis to treatment, and the time for tumours to double their volume in relation to their histological type, both in SCLC and NSCLC. According to the observations of Salomaa E-R., *et al.* [29] the growth of NSCLC is based on the mathematical models, suggesting that it takes 10 to 15 years from the appearance of the first cancer cells to the possibility of detecting a NSCLC by conventional chest radiograph.

According to the literature, the time observed for lung tumours to double their volume ranges from 4 to 56 weeks, with a median time of 17 weeks. This indicates that the growth of a tumour is comparatively slow [30,31]. Two studies monitored the growth of primary tumour with consequent CT chest scans, observing a great diversity in the time of tumour growth.

The previous studies have failed to answer the question when the metastasis of lung carcinoma starts [32]. According to the study by Jung KJ., *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 [33]. If metastases start growing years before the lung carcinoma has been detected, it is difficult to expect that the delay will have any prognostic significance [34].

Our study included 206 patients diagnosed with malign lung carcinoma in 2009. It included all lung carcinoma patients in Montenegro that year. In our research, lung carcinoma is a disease of elderly 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, with the gender ratio of 5(M):1(F). The youngest patient was a woman of 36 and the oldest one was 86, with median age of 66. Ten percent of patients were younger than 50, while 20% of them were over 70.

The distribution of patients in our study, according to gender and age, corresponds to the research of other authors. Our patients were of similar age, median 66, compared with median 65 in the American and 68 in Western European studies [31]. The gender ratio of disease is 1:3-4 on the American continent.

There is no malignant lung disease register in Montenegro, which is why we use the estimate by the International Agency for Research on Cancer (IARC). According to the estimate for 2008, the incidence for our country was approximately 53/100,000, which is a little more compared with the results of our study. If we look at the neighbouring countries, including Serbia (66), Croatia (64), Bosnia and Herzegovina (40), our country belongs to the group with medium incidence rate for this malignant disease.

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 [32]. In terms of prognostic significance of radiographic localization of lung carcinoma, there was no consensus, with different results depending on the series [31].

In our study, the localization of primary tumour is almost equal for right and left lung (51:49), although the most dominant localization was in the upper right lobe, where tumours were diagnosed in 41% of our patients with lung carcinoma.

Conclusions

Lung carcinoma is a disease with the highest incidence of all malignant diseases suffered by men of Montenegro. In 2009, the lung carcinoma incidence in Montenegro was 33/100.000 citizens. Across the municipalities, the rate was lowest in Rozaje - 13, and highest in Kolasin 100.5. Regionally, there was no statistically significant difference. In the coastal region, the rate was 38.2, in central 37.2, while it was 29.7 in the northern region. At the end of 2009, there were 23.8% live patents included in the study. The survival time of the whole group of patients from first symptoms until the end of the study was 39.27 weeks, median 34.

Lung carcinoma belongs to a group of malignant diseases with bad prognosis. There are four possible ways to reduce mortality rate: prevention (lowering smoking incidence); early detection through new screening technologies; adequate attitude towards patients in a more efficient healthcare system, and improvement treatment options.

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