LUNG CANCER INCIDENCE AND MORTALITY IN SPLIT-DALMATIA COUNTY, 2003–2012

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SUMMARY

Objective: The aim of the study was to analyze indicators on lung cancer (C33-C34, ICD-10) in Split-Dalmatia County in the period 2003–2012.

Methods: Data on lung cancer occurrence for the period 2003–2012 were obtained from the Croatian National Cancer Registry, while mortality data were obtained from electronic database of the Teaching Public Health Institute of Split-Dalmatia County. Croatian census 2011 and population estimates of the Central Bureau of Statistics of the Republic of Croatia were used to calculate the indicators. Results are presented as absolute numbers, shares (%), specific rates per 100,000 population, age-standardized rate (standard European population).

Results: There were 2,804 registered patients with lung cancer in the period 2003−2012 in Split-Dalmatia County – 2,179 men (77.71%) and 625 women (22.29%); 2,737 people died from lung cancer in the same period – 2,117 men (77.35%) and 620 women (22.65%). Specific rates of incidence and mortality rates were four times higher among men than among women. From 2003 to 2012, the rate of incidence among men showed a significant decrease, while among women there were no significant changes of incidence and mortality.

Conclusions: According to the indicators of incidence and mortality of lung cancer in Split-Dalmatia County, this malignant neoplasm should occupy a high place within County public health priorities measures of prevention programme, targeting risk factors responsible for their formation.

Key words: epidemiology, incidence, mortality, lung carcinoma, Split-Dalmatia County

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INTRODUCTION

Malignant diseases represent one of the world's leading public health problem and, after cardiovascular diseases, they are the most significant cause of morbidity and death in Europe (1). It is estimated that 3.45 million cases of malignancy (excluding non-melanoma skin cancer) was diagnosed in Europe during 2012, causing 1.75 million deaths (2). Despite the statistics showing reduced mortality (3) malignant diseases remain a global threat whose importance in the future will be even greater due to the increased number of residents over 65, especially those above 80 years, which will additionally challenge the health systems in order to assure adequate health care.

Lung cancer is among the most common malignant diseases, and accounts for about 12% of all newly diagnosed malignancies concerning both genders (4). Due to the poor prognosis, the lung cancer is the leading cause of death accounting for one-fifth of all the deaths that result from malignant diseases (5, 6). Most malignant lung diseases can be associated with smoking and it is estimated that smoking is responsible for about 90% of malignant lung neoplasms within male population and 83% within female population (7). Different trends in the malignant lung incidence and associated mortality in Europe mainly reflect different trends in the epidemic of smoking in European countries (8), which is why tobacco control is a priority in the European Union, geared to male and female population equally (9).

In Croatia, as well as in other developed countries, lung cancer has the highest incidence (10). The same situation is in the Split-Dalmatia County (the county with 10% of the Croatian population), the lung cancer is the most frequent malignant disease among men and it is on the 3rd place among women, with about 270 deaths per year (10).

The knowledge of a particular health problem in the community laid foundation for assessing the magnitude and addressing the problem. Therefore, the objective of this paper is to present the epidemiological indicators of lung cancer in the Split-Dalmatia County as a basis to select public health priorities and to take possible measures to control the disease and to assess the impact on the regional level.

MATERIALS AND METHODS

The descriptive epidemiological method was used in this study. Lung cancer defined as codes C33 and C34 by the 10th revision of the International Classification of Diseases (ICD-10) (11).

Data Sources

Incidence data for the period 2003–2012 were obtained from the Croatian National Cancer Registry, while mortality data were obtained from electronic database of the Teaching Public Health

Institute of Split-Dalmatia County (based on mortality data from the Croatian Bureau of Statistics).

The source of population was census of 2011, and for period in between, data were obtained from the estimates published by the Croatian Bureau of Statistics for inter-census years.

Statistics

Crude, age-standardized and age-specific incidence and mortality rates were calculated. Age-standardized rates were performed by the direct method of standardization using the European population as standard (12).

To describe incidence and mortality time trends, we carried out linear regression analysis. First, the least-squares method was used to estimate the linear trends presented in Figures. Then, correlation coefficients were calculated. A positive value indicated an increasing trend, while a negative value was indicative of falling trend. A p-value <0.05 was considered significant. Data were processed using the Statistical Package for Social Sciences, v.17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Incidence

In the Split-Dalmatia County from 2003–2012 there were registered 2,804 new cases of the lung cancer, from which were 2,179 men (77.71%) and 625 women (22.29%) (Table 1). The ratio in incidence between men and women was 3.5 : 1.

Through a ten-year study period, age-standardized rate (ASR, European standard population) incidence was 47.58/100,000 (82.22/100,000 for males and 19.43/100,000 for females). The incidence rate showed a significant decline in men ($y=-2.421x+95.538$; $B=-2.421$; 95% CI −4.55, −0,29; $R^2=0.463$; $p=0.030$), but not in women ($y=-0.152x+20.27$; $B=-0.152$; 95% CI

Table 1. *Lung cancer incidence in Split-Dalmatia County in the period 2003–2012*

Year	Male				Female			
	Population number	n	Crude rate	ASR*	Population number	n	Crude rate	ASR*
2003	214,607	200	86.99	83.12	226,994	55	22.81	18.04
2004	216,192	228	98.57	94.22	228,607	54	22.25	20.34
2005	218,135	258	110.75	102.8	230,511	81	33.14	26.17
2006	219,647	216	92.28	83.72	231,668	52	21.19	17.01
2007	220,447	242	103.11	89.78	232,385	70	28.46	20.6
2008	221,055	216	91.83	73.19	233,032	57	23.11	16.33
2009	221,353	196	83.22	69.3	233,410	53	21.46	15.85
2010	221,371	201	85.3	73.39	233,453	65	26.32	19.22
2011	221,196	215	97.16	79.66	233,487	73	31.26	22.46
2012	221,307	207	93.54	73.05	233,470	65	27.84	18.33
2003–2012	2,195,310	2,179	97.26	82.22	2,317,017	625	26.50	19.43

*ASR – age standardized rate per 100,000 (using European standard population)

Table 2. *Lung cancer mortality in Split-Dalmatia County in the period 2003–2012*

Year	Male				Female			
	Population number	n	Crude rate	ASR*	Population number	n	Crude rate	ASR*
2003	214,607	185	81.81	81.51	226,994	55	23.15	18.15
2004	216,192	210	92.87	90.86	228,607	49	20.63	17.14
2005	218,135	226	99.94	100.65	230,511	49	20.63	16.81
2006	219,647	206	91.30	90.26	231,668	67	28.35	23.13
2007	220,447	213	94.66	95.44	232,385	65	27.48	22.19
2008	221,055	231	102.54	103.94	233,032	67	28.35	22.40
2009	221,353	205	90.71	94.00	233,410	59	24.85	19.55
2010	221,371	211	93.37	96.24	233,453	53	22.31	18.20
2011	221,196	203	91.73	73.94	233,487	83	35.55	24.50
2012	221,307	227	102.58	82.33	233,470	73	31.26	21.59
2003–2012	2,195,310	2,117	94.15	90.91	2,317,017	620	26.25	20.36

*ASR – age standardized rate per 100,000 (using European standard population)

−0.986, 0.682, R^2=0.022; p=0.686) and in total population (y=−1.085x + 53.549; B=−1.085; 95% CI −2.406, 0.237, R^2=0.309; p=0.095) (Fig. 1).

Most cases of lung cancer (70.3%) occur in people over 60 years. The incidence increases with age, men markedly from the fifth, with a peak age of seventh (65–69) decade of life. In women, the distribution is similar, but without the obvious increase as in men (Fig. 2).

Mortality

From 2003–2012, in Split-Dalmatia County 2,737 persons died of lung cancer, including 2,117 men (77.35%) and 620 women (22.65%) (Table 2).

Age-standardized rate (ASR, European standard population) lung cancer mortality was 50.89/100,000 (90.91/100,000 for men and 20.36/100,000 for women).

In the reported period there were no significant changes in mortality trend for males (y=−0.687x + 94.697; B=−0.687; 95% CI −3.120, 1.746; R^2=0.050; p=0.533), for females (y=0.478x + 17.736; B=0.531; 95% CI −0.145, 1.101; R^2=0.282; p=0.115), and for total population (y=−0.014x + 50.978; B=−0.014; 95% CI −0.985, 0.956; R^2=0.000; p=0.974) (Fig. 3).

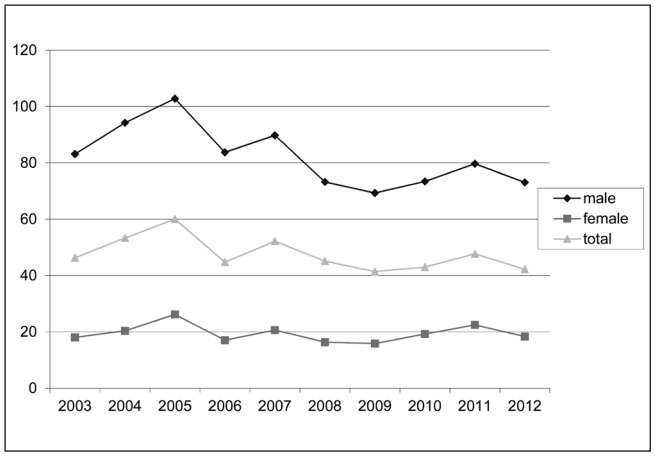

Fig. 1. *Lung cancer age-standardized (ARS – European standard population) per 100,000 incidence rates in Split-Dalmatia County by sex, 2003–2012.*

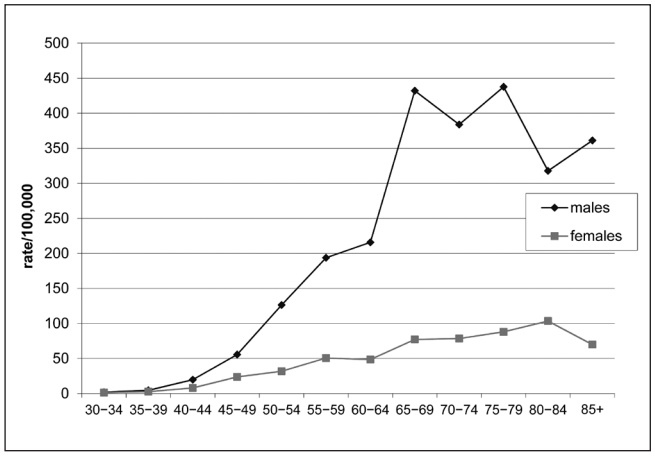

Fig. 2. *Average age-specific incidence rates for lung cancer in males and females, Split-Dalmatia County, 2003–2012.*

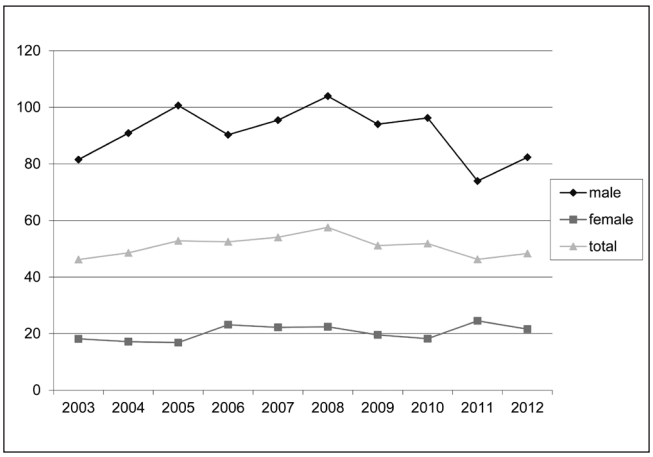

Fig. 3. *Lung cancer age-standardized (ARS – European standard population) per 100,000 mortality rates in Split-Dalmatia County by sex, 2003–2012.*

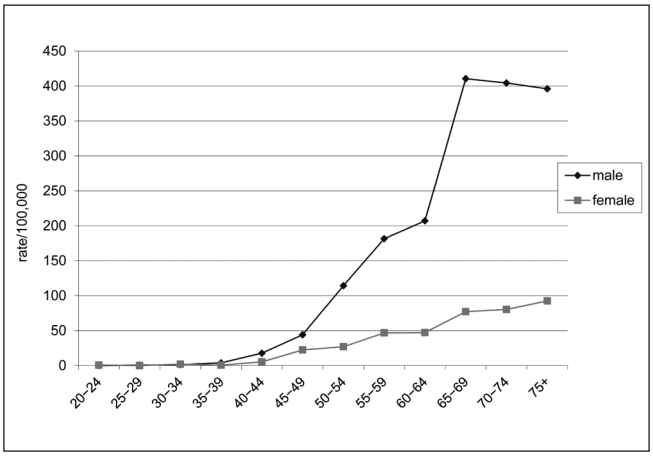

Fig. 4. *Average age-specific mortality rates for lung cancer in males and females, Split-Dalmatia County, 2003–2012.*

With aging, the age-specific mortality rates of lung cancer showed an increasing trend in both genders, although the mortality in men after 50 years of age was considerably higher than in women (Fig. 4).

DISCUSSION

According to a research conducted in Split-Dalmatia County from 2003–2012 there was a declining trend of lung cancer among men, while the incidence of lung cancer among women did not change significantly.

The occurrence of lung cancer is linked to numerous risk factors. Some of them are environmental. An association between mining and lung disease has been known in Europe for a long time. Among German and Czech mining population there are extremely high rates of lung cancers which are connected with radon exposure (13). Radon is a naturally occurring radioactive gas produced by uranium decay in the Earth's crust. It can also accumulate to unsafe levels in basements and lower building levels (14). Residential radon from soil accounts for the second most common risk factor for lung cancer, approximately 10% of cases

(14). This requires looking for resources to regulate measures in order to assess and reduce radon levels in homes, as well as exposure in underground workplaces. Except for radon, several workplace substances such as arsenic, asbestos, chloromethyl ethers, chromium, nickel refining, or polycyclic hydrocarbons have been identified as carcinogens and it is estimated that occupational exposure to them accounts for 5–10% of lung cancers (15). Among them, asbestos is the most common substance, to which occupational exposure correlates with a 5-fold excess risk of lung cancer (15). In the past century, exposure to asbestos in Croatia was as high as in other countries of the world because of large production and the use of asbestos in many industries. However, asbestos-related diseases were more commonly found in Split-Dalmatia County than in other parts of Croatia (16). The reason could be that asbestos-related industries have been developing in the region since the 1950s. In addition, the whole region was rapidly urbanized and industrialized and the process was accompanied by an increase in heavy traffic.

Pollution and air quality are also considered in the development of lung cancer. Both indoor and outdoor air quality depend on carcinogens produced by combustion of fossil fuels and particulate matter in the air (15). Various potential carcinogenic components are thought to be emitted from different sources of fossil fuel combustion products and relative risk for lung cancer is associated with exposure to combustion products. A study of large urban environments in the US found a 40% increased risk of lung cancer in six US cities with the highest levels of particulate matter (15). Indoor air pollution from the use of unprocessed fossil fuels such as soft coal and biomass fuels, which include wood, other plant-based materials and solid waste, used for heating and cooking, is implicated in lung cancer risk, primarily in the developing world (17). Studies have shown that proper ventilation of previously unvented cooking areas can reduce the risk of lung cancer by 50% (17).

Second-hand tobacco smoke, also referred to as an environmental factor, can contribute to an increased risk for lung cancer with dose-dependent relationship between the degree of exposure and the relative risk (18). It is estimated that at least 17% of lung cancers in nonsmokers are attributable to the exposure to high levels of environmental tobacco smoke during childhood and adolescence (18). A summary analysis of a large number of epidemiologic studies on the risk for lung cancer in nonsmokers found an excess risk for lung cancer of 24% in nonsmokers who lived with a smoker (18). The US Surgeon General has declared that there is no safe level of exposure to second hand tobacco smoke and the IARC Monographs Programme classified second-hand tobacco smoke as a cause of lung cancer and a possible cause of cancers of the laryngopharynx (14).

Some chronic diseases have been associated with an increased risk for lung cancer, the strongest association being with chronic obstructive pulmonary disease (COPD). More recent studies have shown that COPD is significantly associated with an increased risk for lung cancer, especially in men (18). Interstitial fibrosis has also been associated with an increase in lung cancer risk (18). Additionally, some infections such as TBC or HIV infection are also connected with lung cancer (17). Identification of C. pneumoniae as aetiologically related to lung cancer, whether independent of tobacco smoking or as a cofactor, could have profound implications, particularly in the area of lung cancer prevention (18).

Many reports suggest that dietary factors contribute to the risk for lung cancers. Thus, the low serum concentrations of antioxidants, such as vitamin A, C, and E, have been linked with the development of lung cancer (18). In particular, β-carotene has been shown to have the greatest protective effect against lung cancer (18). Large cohort study in the Netherlands suggested that a diet rich in fruits and vegetables has been linked to decreased cancer incidence (18). Interestingly, some studies showed that vitamin supplementation did not reduce lung cancer risk and in some circumstances increased the incidence of lung cancer (18). Certain dietary items, including red meat, dairy products, saturated fats and lipids, have been suggested as increasing the risk of lung cancer (18). According to these findings, health authorities continue to recommend a balanced dietary intake of fruits and vegetables, including those containing β-carotene (18).

Genetic predisposition may also play a role in the aetiology of lung cancer. Not all tobacco users develop lung cancer. A positive family history for lung cancer has been associated with an increased risk of lung cancer development (19).

Despite all the enumerated factors, the effect of smoking is predominant (over 80%), so any significant reduction in incidence attributable to another factor is irrelevant (20, 21).

Recent data show that daily smokers present 22.4% of the total population in Split-Dalmatia County, 25.7% of men and 18.7% of women, which is very similar to data in Croatia (22). Namely in 2014, a quarter of adults in Croatia smoked tobacco every day, well above the EU average (21%) (23). The rate among 15-year-olds was almost as high. Regular smoking among 15-year-olds, at 23% in 2013–14, is the second highest rate among EU countries (after Bulgaria) and nearly 1.5 times greater than the EU average, which can be linked to generally weak anti-smoking policies (23). Also more than a half of daily smokers smoke more than 20 cigarettes a day, and there is evidence that the risk for lung cancer increases with the duration of smoking and number of cigarettes smoked per day (18). Therefore, the situation in Croatia is alarming, because there is no overall decline in the number of smokers, while the number of women who smoke is growing (23). In many countries primordial prevention attempts or prevention of an epidemic of smoking among women have not succeeded: a number of young female smokers is equal to the number of male smokers (24). A progressive incidence of lung cancer in women in the coming decades is expected, with consequently higher mortality in older age groups, as was already noted in the Scandinavian countries (25). Despite the decreasing trend of the incidence of lung cancer in men and unchanged trend of mortality, those values were among the highest in Europe. According to the 2012 data in Europe, the highest lung cancer incidence rates among men were in the countries of Central and Eastern Europe – Hungary (ASR 109/100,000), FYR of Macedonia (ASR 102/100,000), Serbia (ASR 99/100,000), Poland (ASR 90/100,000), Montenegro (ASR 86/100,000), and Croatia (ASR 85/100,000); while the lowest rate were in the northern European countries such as Finland (ASR 45/100,000) and Sweden (ASR 29/100,000). The results were reversed for women, the highest rates were estimated in the countries of Northern Europe (Denmark (ASR 55/100,000) and the Netherlands (ASR 44/100,000), and the lowest in Eastern Europe – Ukraine and Belarus (ASR 9/100,000) and the Russian Federation (ASR 10/100,000) (2). Geographical distribution by mortality was very similar to that of the incidence for both

genders (2). According to estimates for 2018, variation in lung cancer incidence rates across European countries shows smoking is likely to remain the top ranked cancer cause for several years to come, with the incidence in men ranging from 111.6 (Hungary), 100.9 (Serbia), 99.0 (Greece), and 65.2 (European average) to 25.6 (Sweden), 37.8 (Finland), and 40.0 (Switzerland) per 100,000 per year (26). The respective figures for women were from 58.7 (Hungary), 53.8 (Denmark), and 48.1 (Iceland) to 26.4 (European average), 8.2 (Belarus), 9.2 (Ukraine), and 10.5 (Albania). While incidence and mortality rates in men are decreasing in many European countries, particularly in Northern and Western Europe, rates in Central and Eastern Europe remain high but they are showing signs of stabilization or decline (26). However, rates in women, who acquired the smoking habit later than men, are still rising in Europe (e.g. France, Spain), although rates are beginning to stabilize, notably in the high-risk countries of Northern Europe (26). Since the therapeutic measures are more or less unchanged (27), this reduction is attributed to effective preventive measures mainly aimed against smoking (28). Primary prevention, through efforts to deter the initiation of smoking and raise cessation rates through higher taxes, regulations on smoking and information to the public, should have a major impact on incidence and mortality from lung and other tobacco-related cancers (26).

Looking at more specific causes of death in Croatia, the ranking of the top five causes has not changed since 2000. Lung cancer is the most frequent cause of death from cancer among Croatian. The preventable mortality rate from lung cancer is the third highest in the EU at 49 per 100,000 people in 2016, exceeding the EU average of 37. Moreover, smoking rates are higher than in many other EU Member States (23).

Since joining the EU, Croatia has strengthened anti-smoking policies in line with EU directives. Increasing taxes on tobacco products is one of the most effective ways of reducing the prevalence of smoking and, therefore, almost all EU countries have raised taxes on tobacco products for years, including Croatia, where this measure is one of the most important. New anti-smoking legislation has been in effect since May 2017, extending smoke-free places and health warnings on cigarette packaging. Due to the modest results of the measures carried out so far, Croatia needs to adopt additional policies on tobacco control. Certainly, one of the measures would be to ban smoking in public places, which could, among other things, have a significant impact on denormalizing smoking in the community. Besides, there is scope to set up media campaigns against tobacco use (23). Then, the cost of treatment and pharmacological therapy should be covered for those people who wish to stop smoking; these procedures already exist in a number of EU countries.

Besides, reduction in incidence and mortality is attributed to effective preventive measures mainly aimed against smoking; great efforts are being made in the early detection and treatment of lung cancer. Most patients are diagnosed with advanced lung cancer, so early detection could have a profound effect on survival. Recent large randomized trials on low-dose CT screening, including the American National Cancer Institute sponsored National Lung Screening Trial (NLST) as well as the Dutch/Belgian NELSON (Nederlands-Leuvens Longkanker Screenings Onderzoek) trial, have shown significant reductions in lung cancer mortality (20–26%) and have triggered international efforts to implement lung screening, so Croatia plans to start with national screening for lung cancer (29). Immunotherapy, which is a revolutionary therapy for many malignancies, is also highly anticipated (30). However, the costs of immunotherapy are very high, which can be a barrier to their implementation in many countries with limited budgets.

CONCLUSIONS

Despite the significant reduction in the incidence of lung cancer among males in Split-Dalmatia County within the ten-year observation period, the lung cancer is still among dominant malignancy in the County, as well as in the rest of Croatia. Therefore, a high place among the public health priorities of the County should belong to prevention programmes targeting the leading risk factor – smoking. The present patterns of smoking do not necessarily reflect the current rates of lung cancer, since it takes several decades between smoking history changes and resulting changes in lung cancer developing rates. However, if the Croatian population does not change the smoking-related behaviour, we cannot expect any significant changes related to the reduction of lung cancer morbidity and mortality rate. The success of the implemented measures is observed through the changes at the local level indicating the need for further research.

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Conflict of Interests

None declared

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