

Urban vs. rural patients. Differences in stage and overall survival among patients treated surgically for lung cancer

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Abstract

Introduction. Besides the undoubted influence of risk factors on morbidity and survival time, there are also other environmental factors, such as awareness of the prevalence of risk factors and the availability of modern diagnosis and treatment methods.

Objective. To evaluate differences in lung cancer 5-year overall survival rates between urban and rural patients hospitalized in the Department of Thoracic Surgery of the Medical University in Lublin, Poland, and possible influence of several risk factors on these rates.

Materials and methods. The analysis was based on 125 lung cancer patients who underwent surgical procedures in years 2006-2007 and who agreed to take part in the survey.

The study aimed at recognition of the health situation and selected demographic traits of people who had been treated surgically for lung cancer. The differences were evaluated between rural and urban inhabitants in gender, age, lung function, smoking habits, exposure to risk factors at work, family history of cancer, staging of the disease, histological type of cancer, post-surgical treatment, and their possible influence on overall survival.

Results. The results showed that the only noted differences between urban and rural population were in tobacco smoking and lung function. Survival rates were very similar and did not differ from the European average.

Conclusions. The assumption that Polish rural patients are presenting with later cancer stages at the time of diagnosis, and have worse chances for survival, has become invalid in modern times.

Key words

lung cancer, overall survival, rural and urban population, inequalities in health

INTRODUCTION

Lung cancer (LC) has for years been one of the most important problems of modern civilization. Despite the advances in medical knowledge, scientists have failed to achieve significant progress in LC treatment. The main reason for this is the hidden course of lung cancer, with the result that most cases which are detected constitute patients in whom the disease is already at high levels of advancement. Since 1971, LC has remained the most frequent neoplastic disease among men. In women, the incidence of lung cancer ranks second after breast cancer, although in recent years in many developed countries, LC has become the most common cancer in women [1, 2, 3, 4, 5, 6, 7].

Currently, the number of deaths from lung cancer in Poland is close to 22,000 cases annually. Long-term studies have shown that there are about 60 different risk factors for the incidence of LC, of which 18 have a clear carcinogenic effect.

The most important etiological factor and the cause of approximately 80-90% of LC cases is tobacco smoke.

Morbidity also results from exposure to carcinogens in the workplace, local environment and diet [4, 6, 7].

Besides the undoubted influence of risk factors on morbidity and survival time, there are also other environmental factors, such as awareness of the prevalence of risk factors and the availability of modern diagnosis and treatment methods.

It became the view of the mass media that urban residents often fall ill with lung cancer due to the greater number of risk factors to which they are exposed. At the same time, it was believed that rural residents have worse access to modern diagnosis and treatment, and their lifestyle and working conditions may predispose to an increased incidence of various diseases, including LC. It should be noted, however, that in recent years the living conditions of both rural and urban populations have changed. They are influenced by migratory movements both in search for work and in search for better living conditions. Improved transportation also changed the terms of availability of many risk factors. All this makes the boundaries between village and city fade, prompting analysis in the presented study of the current situation in urban and rural areas in terms of the incidence of LC.

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OBJECTIVES

Unfortunately, formal studies of rural versus urban case-mix differences are few and inconsistent in their findings. To date, there have been only few national studies designed to assess differences in lung cancer between rural and urban patients that controls other potentially confounding variables [8, 9, 10, 11, 4, 12, 13].

The main objective of the presented study was analysis of the types, stages and survival rates of Lung Cancer among patients treated surgically in the Department of Thoracic Surgery at the Medical University in Lublin, Poland, during 2006-2007. The study aimed at recognition of the health situation and selected demographic traits of people who suffer from lung cancer. The authors' research tool – a Scientific-Research Protocol (SRP) – was applied in the study.

MATERIAL AND METHODS

The survey covered 125 lung cancer patients who in 2006-2007 underwent surgical procedures in the Department of Thoracic Surgery at the Medical University in Lublin, Poland, and who agreed to take part in the survey. Despite a larger LC population treated in the department, it was decided to narrow the number of cases only to those patients who were treated surgically in the department and granted conscious agreement for the survey. A total of 55 cases from urban and 70 from rural areas were considered in the analysis. Place of residence, age, gender, family history, and possible influence of risk factors, were collected on the basis of SRP data. Type of surgery, staging, grading, and histological type of lung cancer were provided or verified on the basis of the patients' medical records. Residence (urban – rural) was determined on the basis of the address of patients and verified by the patients themselves by the use of SRP, and according to the National Official Register of Territorial Division of the Country (TERYT) [14].

Urban population was defined as people who live in areas with a population exceeding 10,000 inhabitants. Less inhabited areas were considered as rural.

Data collection and analysis were in compliance with The Personal Data Protection Act of 29 August 1997 (Dz.U. 1997, No. 133, item 883, as amended), as well as with the regulations and procedures of the National Cancer Registry.

The patients were observed for a period of 5 years or up until the date of death. Date of death was updated and verified by the Office of Citizen's Affairs in Lublin, with the use of the National Identification Number (PESEL).

Statistical analysis was performed with the use of software Statistica 9.0 PL (Statsoft, Poland) and Open Source Epidemiologic Statistics for Public Health. Quantitative variables were expressed as arithmetic mean \pm standard deviation (SD), median value, interquartile range (IQR) and non-parametric U Mann Whitney test were used for analysis of differences between the two groups. Qualitative variables were analyzed with the use of Chi² test, analysis of Odds Ratio and Confidence Limits. The results were accepted as statistically significant at significance level $p \leq 0.05$.

RESULTS

125 lung cancer Caucasian patients were included in the study 56% of whom (70) were rural inhabitants, while the remaining 44% (55) were urban inhabitants. 102 patients were males (81.6%) and 23 were females (18.4%).

Among the patients from rural areas, 84.29% were males and 15.71% – females. The situation was similar in the sub-population of urban inhabitants, where the percentage of males was higher than that of females (78.18% and 21.82%, respectively).

The mean age of the rural inhabitants treated for LC was 59.41% \pm 10.27, (Median=60, IQR=13), while of urban inhabitants the mean age was 61.8% \pm 8.15 (Median=61, IQR=11).

Post-operative analysis of clinical data, intraoperative and histopathological findings allowed the application of pathomorphological staging according to VII, revised lung cancer classification recommended by the International Association for the Study of Lung Cancer (IASLC) [15, 16] (Tab. 1).

Table 1. Analysis of LC clinical stages of evaluated patients

| | Staging | | | | | | |
|-----------------------------|-----------|-------------|-----------|-------------|-------------|------------|-----------|
| | IA | IB | IIA | IIB | IIIA | IIIB | IV |
| Urban area patients [n=55] | 1 (1.82%) | 17 (30.91%) | 1 (1.82%) | 7 (12.73%) | 16 (29.09%) | 9 (16.36%) | 4 (7.27%) |
| Rural area patients [n=70] | 4 (5.71%) | 22 (31.43%) | 2 (2.86%) | 11 (15.71%) | 19 (27.14%) | 6 (8.57%) | 6 (8.57%) |
| $\chi^2 = 3.266, p = 0.775$ | | | | | | | |

In order to simplify analysis of pathomorphological types of lung cancer, all cases were divided into 5 groups (according to main histological types of cells): microcellularae, planoepithelialae, macrocellularae, adenocarcinoma and mixed type carcinoma (Tab. 2).

Table 2. LC histological types of evaluated patients

| | Histological type | | | | |
|-----------------------------|-------------------|-----------------|-----------------|-----------------|-------------|
| | Plano epitheliale | Adeno carcinoma | Macro cellulare | Micro cellulare | Mixed |
| Urban area patients [n=55] | 23 (41.82%) | 12 (21.82%) | 7 (12.73%) | 5 (9.09%) | 8 (14.55%) |
| Rural area patients [n=70] | 32 (45.71%) | 23 (32.86%) | 2 (2.86%) | 3 (4.29%) | 10 (14.29%) |
| $\chi^2 = 6.727, p = 0.151$ | | | | | |

In pathology, grading is a measure of the progress of tumours and other neoplasms. The histological tumour grade score, together with the metastatic (whole-body-level cancer-spread) staging, are used to evaluate each specific cancer patient, develop their individual treatment strategy, and to predict their prognosis. The grade of neoplasms was evaluated according to the guidelines of the American Joint Commission on Cancer [16]. Comparison of rural and urban populations did not show any significant differences ($p = 0.854$) (Tab. 3).



Table 3. LC grading of evaluated patients

| | Grading | | |
|----------------------------|-------------|-------------|-------------|
| | I | II | III |
| Urban area patients [n=55] | 9 (16.26%) | 28 (50.91%) | 18 (32.73%) |
| Rural area patients [n=70] | 11 (15.71%) | 39 (55.72%) | 20 (28.57%) |
| $\chi^2=0.316, p=0.854$ | | | |

In order to compare the risk of cancer, the patients were asked if they smoked cigarettes, how many cigarettes they smoked per day, did they have any LC patients in their families, and did they have any contact with risk factors at work (Tab. 4).

Table 4. Analysis of LC risk factors in patients

| | Urban area [n=55] | Rural area [n=70] | p | X ² | Odds Ratio | Confidence Limits |
|----------------------|-------------------|-------------------|--------|----------------|------------|-------------------|
| Smoking | 24 (43.63%) | 35 (50.00%) | 0.4793 | 0.5005 | 0.7758 | 0.3782-1.583 |
| LC in family | 7 (12.73%) | 9 (12.86%) | 0.9828 | 0.0004 | 0.9884 | 0.3433-2.846 |
| Risk factors at work | 12 (21.82%) | 19 (27.14%) | 0.4938 | 0.4682 | 0.7491 | 0.327-1.716 |

Statistical analysis did not show any significant differences between the two evaluated populations.

To compare the amount of cigarettes smoked and their possible influence on risk of LC, the quantity of lifetime tobacco exposure as pack-years was coded according to the American National Cancer Institute [16]. One pack-year is equal to the number of cigarettes smoked per day multiplied by number of years smoked divided by 20 (one pack-year is smoking 20 cigarettes a day for one year). Analysis in the presented study showed significant differences between urban and rural inhabitants ($p=0.035$). In rural areas, people smoked more cigarettes (47.37 ± 21.65 Median = 44.5, IQR = 21) than in urban areas (39.28 ± 17.7 , Median = 39.0, IQR = 17.5).

As LC surgeries are dependent not only on neoplasm recognition itself, but also on the functional status of the lungs, the spirometry findings of both evaluated populations were assessed. Two main dynamic tests – FEV1 (Forced Expiratory Volume in one second) and FVC (Forced Vital Capacity) were compared. Statistical analysis showed significance in both tests. Rural populations had better results of FEV1 and FVC (Tab. 5).

Table 5. Differences in results of spirometry tests

| | Urban area patients [n=55] | Rural area patients [n=70] | p |
|--------------|----------------------------|----------------------------|---------|
| FEV1 [mL] | | | |
| Mean±SD | 2,388.54 ± 665.13 | 2,651.03 ± 671.23 | p=0.028 |
| Median (IQR) | 2,420.0 (780.0) | 2,645.0 (970.0) | |
| FVC [mL] | | | |
| Mean±SD | 3,271.27 ± 832.69 | 3,660.0 ± 772.73 | p=0.005 |
| Median (IQR) | 3,260.0 (1,180) | 3,675.0 (1,000.0) | |

Analysis of collected data enabled comparison of the necessity for post-surgical treatment and the number of deaths. No significant differences were found between the two evaluated groups (Tab. 6).

Table 6. Analysis of post-surgical treatment and patients' deaths

| | Urban area [n=55] | Rural area [n=70] | p | X ² | Odds Ratio | Confidence Limits |
|-------------------------|-------------------|-------------------|--------|----------------|------------|-------------------|
| Post surgical treatment | 24 (43.63%) | 28 (40.00%) | 0.6822 | 0.1676 | 1.161 | 0.5676-2.376 |
| Death | 30 (54.55%) | 34 (48.57%) | 0.5072 | 0.4399 | 1.271 | 0.6259-2.579 |

Overall survival is a term that denotes the chances of staying alive for a group of individuals suffering from cancer. It shows the percentage of individuals in the group who are likely to be alive after a particular duration of time. At a basic level, the overall survival is representative of cure rates. In LC, a 5-year survival time is considered as a measure of complete treatment. After that period of time, any other sign of LC is considered as a new case of LC. Five-year survival rates can be used to compare the effectiveness of treatments. Overall survival rates were calculated separately for the urban and rural populations, and were performed according to the pathomorphological stage (pTNM), in compliance with IASLC criteria [15, 16]. Overall survival expressed in months for urban area inhabitants was equal 35.28 ± 4.22 (Median = 36.0, IQR = 7.0), and for rural the area – 34.89 ± 3.86 (Median = 35.0, IQR = 6.5). No significant differences were found ($p=0.699$) between two evaluated populations.

DISCUSSION

The presented study highlights several demographic differences between rural and urban patients presenting with lung cancer. The study has several limitations: 1) there is no uniform way to define 'rural population' in different countries; it is possible that rural patients who seek care in rural hospitals present at later stages of disease than those who travel to urban centres for care. 2) The size of individual counties varies widely; there can be rural areas in large counties that include population centres that result in an urban or suburban classification.

In recent years there has been a steady increase in the number of initiatives designed to assess and improve the quality of medical care in Polish rural regions. These initiatives have been met with apprehension among the inhabitants of these regions. Many providers of this care argue that observed differences in outcomes of medical care might reflect case-mix differences more than the quality of care in rural and urban regions. In particular, general practitioners are often uneasy when their outcomes are compared with those of urban doctors, largely because they perceive that rural patients typically present with more serious diseases. Although there is considerable evidence in the literature indicating the impact of patients demographics, such as race and socioeconomic status on overall survival and stage of the disease at the time of diagnosis, there are no reliable results of analysis performed in novel times.

According to the data by the Main Statistical Office for 2006, 51% of the population in the Lublin Region lived in rural areas, and 49% were urban inhabitants [14]. With respect to these data, among the patients in the study we noticed a significant deficit of urban inhabitants (44) and an excess of rural dwellers (56%). This is in contrast with some European analyses. Pearce et al. demonstrated in their paper that in Scottish population, LC patients were more

often inhabitants of urban regions [17]. Similar results were obtained by Pozeta et al. in the French population [11].

According to the data by the Main Statistical Office for 2006, among the inhabitants of the Lublin Region the percentages of males and females were close to the value of 50%. Thus, with respect to the population in the region, among patients with LC the percentage of males was significantly higher, compared to females. When comparing the gender of rural and urban populations, no significant differences were found. There were notably more male patients in both populations, although this difference was higher among rural inhabitants. Similar results have been presented by other European and American authors [12, 13, 18, 19, 20, 21, 22].

When comparing the different types of LC between rural and urban inhabitants, no statistically significant differences were observed. Nevertheless, a higher percentage of adenocarcinoma cases were noted in rural areas, and more macrocellularae patients in urban areas. Recently, there have been some indications that the higher percentage of adenocarcinoma cases all over the world may be connected with changes in cigarettes content [1, 3, 7]. Analysis in the presented study revealed that more LC patients who smoked cigarettes lived in rural regions, which could be a consequence of worse awareness of smoking harmfulness. Rural inhabitants also pointed out more risk factors at their work, which seems to be quite obvious when one looks at modern agriculture where technology has made an enormous leap, but conditions of occupational health and safety have not changed a lot. On the other hand, other authors showed contrary results in which people in urban regions were more exposed to LC risk factors at work [18, 19, 21, 23]. The reason for such differences is probably the poorer development of rural regions in Poland, especially worse health and safety conditions at work.

In the presented study, patients in urban regions presented worse results in lung function tests, which can be probably explained by worse pollution in the cities.

Even though there were no significant differences in the overall survival rates between the two assessed populations, a higher percentage of deaths was noted in the urban group of patients. This is in contrast with the findings of Smaylite and Kurtinaitis in Lithuania [24] where they observed rather a decreasing of mortality in urban areas, and stable trends in rural inhabitants.

Van der Heyden et al. pointed out that these inequalities in mortality are not dependent on place of residence itself, but on smoking habit trends which seem to decrease among urban male inhabitants, but increase among young urban women [13]. In rural areas, smoking constantly remains on a high level. Rachtan et al. showed in their study a significant increase in the risk of lung cancer associated with a family history of lung cancer in first-degree relatives among women in Poland [25]. Their results confirmed the synergistic influence of cigarette smoking and family history of lung cancer in first degree relatives, which may have an influence on rural versus urban patterns. Philips et al. stress that poverty rather than place of residence is a risk factor which can be found equally in both rural and urban regions [22]. McLafferty and Wang showed that there is little indication of rural disadvantage [20]. They found that the likelihood of late-stage diagnosis was highest among patients living in the most densely populated areas of the city of Chicago. Their findings, similar to those of the presented study, provided support for Paquette and Finlayson's observations that risk

of late stage presentation of some cancers is higher among urban residents [26]. The findings of the presented study, that the rural population has better results of FEV1 and FVC, may be supported by O'Reilly et al. who demonstrated that urban areas appear less healthy than the rural areas when considering deaths by both respiratory diseases and lung cancer. They suggested that pollution may be the factor [27].

It seems that changes that have taken place in recent years in towns and villages in terms of accessibility to health care and the civilization changes of these two regions contributed to the total change in the demographic picture of lung cancer. The assumption that Polish rural patients are presenting with later cancer stages at the time of diagnosis, and have worse chances for survival, is based largely on anecdotal evidence.

CONCLUSIONS

The smoking habit which is considered as the main risk factor of lung cancer is more often observed among rural inhabitants.

Although the amount of risk factors at work and pack-years were higher among rural inhabitants, the results of functional lung tests were worse among urban patients ($p=0.028$).

Even though there were no significant differences in overall survival rates between the two assessed populations, a higher percentage of deaths was noted in the urban group of patients.

The findings of the presented study have implications for the effectiveness of screening programmes for lung cancer. It is interesting to note that although there was a higher proportion of patients from rural areas, later stages of disease were more often presented by urban inhabitants. This observation raises questions about how well screening is implemented in urban versus rural areas, and the overall effectiveness of cancer screening to prevent late-stage presentation. The concentration of health disadvantage in highly urbanized places emphasizes the need for more extensive cancer screening and education programmes, especially among the inhabitants of poorer districts.

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