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Assessment of prognostic factors in radical radiotherapy for patients with non-small cell lung cancer

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Introduction. Lung cancer is still the most severe problem of oncology throughout the world. In Poland there are some 20 000 new cases per annum, among them non-small cell lung cancer accounts for about 16 000 cases. The basic method of therapy of non-small cell lung cancer is surgery; however, in Polish conditions only about 15% of patients qualify for it. Therefore, there remains a large group of patients who are potential candidates for radiotherapy.
Aim of the study. Evaluation of a group of patients qualified for radical radiotherapy according to uniform rules, treated with the same protocol and assessed by the same group of physicians. The obtained results of therapy allow to evaluate the usefulness of radical radiotherapy in patients with non-operable non-small cell lung cancer and serve as a basis of search for more effective radiotherapy protocols. The aim of the study is to attempt to define the prognostic, therapeutical, clinical- and population-related factors for survival and local control in patients with non-operable, non-small cell lung cancer.
Material and methods. Between January 1, 1990, and December 31, 1995, there were 2330 patients with non-small cell lung cancer in the Ambulatory of the Cancer Centre in Warsaw. Basing on the results of clinical examination and additional examination, 260 patients qualified for radical radiotherapy. In this group there were 31 women (12%) and 229 men (88%). In a majority of cases the stage of the disease was advanced: stage IIIA was found in 114 patients (44%), and stage IIIB in 73 patients (28%).
Statistical methods. Retrospective analysis of the results of treatment was carried out. The material covered 260 patients. The survival time and the time to local progression were the basis for the analysis. The survival probability was calculated with the Kaplan-Meier method. Multidimensional analysis of the prognostic factors (age, clinical advancement of the disease, performance status, loss of weight, LDH and haemoglobin level, tumour size, pulmonary function, prior exploratory thoracotomy, presence of selected clinical symptoms) was carried out with D.R. Cox proportional risk model.
Results. Survival probability at two years was 33% ±2% and at five years 10% ±2%. Two-year local control was obtained in 35% ±4% and five-year in 23% ±4% of cases. In the survival analysis the following parameters had significant influence on the results: stage of the primary tumour – T ($p=0.0059$), stage of the nodal involvement – N ($p=0.0128$), performance status of the patient ($p=0.0163$), LDH level ($p=0.00005$), pulmonary function of the patient qualified for radical radiotherapy ($p=0.0053$). In local control analysis, significant statistical value was demonstrated for: clinical stage of the tumour – T ($p=0.0259$), LDH level ($p=0.0002$), – pulmonary function of the patient before the treatment ($p=0.0050$).

Ocena czynników rokowniczych w radykalnej radioterapii chorych na niedrobnokomórkowego raka płuca

Wstęp. Rak płuca jest stale najpoważniejszym problemem onkologii na całym świecie. W Polsce zachorowuje na niego około 20 000 osób rocznie. Z tej grupy około 16 000 przypadków stanowi rak niedrobnokomórkowy. Podstawową metodą leczenia niedrobnokomórkowego raka płuca jest zabieg chirurgiczny, jednak w warunkach polskich może być do niego zakwalifikowanych tylko około 15% chorych. Z tych przyczyn ciągle duża grupa chorych staje się potencjalnymi kandydatami do radioterapii.
Cel pracy. Przedmiotem oceny jest grupa chorych, kwalifikowanych do radykalnej radioterapii według jednolitych zasad, leczonych z zastosowaniem tego samego protokołu i ocenianych przez tę samą grupę lekarzy. Uzyskane wyniki leczenia pozwa-

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lają określić przydatność radykalnej radioterapii u chorych na nieoperacyjnego, niedrobnokomórkowego raka płuca i są podstawą do poszukiwań skuteczniejszych programów leczenia napromienianiem.
Celem pracy jest próba określenia czynników prognostycznych, kliniczno-populacyjnych i terapeutycznych dla przeżyć i miejscowego wyleczenia chorych na nieoperacyjnego, niedrobnokomórkowego raka płuca.
Metody statystyczne. Przeprowadzono retrospektywną analizę wyników leczenia. Materiał obejmował informacje o 260 chorych. Podstawą oceny wyników był czas przeżycia oraz czas do wystąpienia progresji miejscowej. Prawdopodobieństwo przeżycia obliczano metodą Kaplana-Meiera. Wielowymiarową analizę czynników prognostycznych (wiek, stopień klinicznego zaawansowania choroby, stopień sprawności, utrata masy ciała, poziom dehydrogenazy mleczanowej i hemoglobiny, wielkość guza, stopień wydolności oddechowej, fakt przebycia torakotomii zwiadowczej, obecność wybranych dolegliwości) przeprowadzono używając modelu proporcjonalnego ryzyka D.R. Cox'a.
Wyniki. Prawdopodobieństwo dwuletniego przeżycia chorych wyniosło 33% ±2%, a pięcioletniego 10% ±2%. Prawdopodobieństwo dwuletniego miejscowego wyleczenia wyniosło 35% ±4%, a pięcioletniego 23% ±4%. W analizie przeżyć następujące parametry miały istotny wpływ na uzyskane wyniki: stopień zaawansowania guza pierwotnego – cecha T (p=0,0059), stopień zajęcia regionalnych węzłów chłonnych – cecha N (p=0,0128), – stopień sprawności chorego (p=0,0163), poziom dehydrogenazy mleczanowej (p=0,00005), wydolność oddechowa chorego kwalifikowanego do radykalnej radioterapii (p=0,0053). W analizie miejscowej wyleczalności znamienną wartość statystyczną wykazano dla: stopnia zaawansowania klinicznego guza – cecha T (p=0,0259), poziomu dehydrogenazy mleczanowej (p=0,0002), wydolności oddechowej chorego przed leczeniem (p=0,0050).

Key words: radical radiotherapy, prognostic factors, non-small cell lung cancer
Słowa kluczowe: radykalna radioterapia, czynniki prognostyczne, niedrobnokomórkowy rak płuca

Introduction

Lung cancer is still the most severe oncological problem throughout the world. In Poland there are about 20 000 new cases diagnosed every year. In this group non-small cell lung cancer accounts for about 16 000 cases. The basic method of therapy of non-small cell lung cancer is surgery; however, in Polish conditions only about 15% of patients qualify for it [3-5]. Therefore, the group of potential candidates for radiotherapy is rather numerous.

Although, according to some authors, radical radiotherapy allows to obtain tumour regression in as much as 50% of cases, still five-year survivals constitute merely 3-6% [6-8]. The main reason for failure are dissemination of the neoplastic process and local recurrence [6, 7, 9--15]. Some hope lies in the assessment of the prognostic factors for this modality. These assessments could contribute to the selection of a group of patients for whom radiotherapy could be an acceptable form of treatment. The vast majority of papers on this subject suggest univocally that the performance status, stage of the neoplastic process and weight loss over 10% during the last six months before treatment are the most important prognostic factors in the therapy of non-operative, non-small cell lung cancer.

Aim of the study

The aim of the study was to attempt to assess both the known, classical as well as the potential prognostic factors for patients with non-operative, non-small cell lung cancer subjected to radical radiotherapy. The results were to serve as a basis for revision and rationalisation of the hitherto indications for this therapeutical modality in the considered group of patients.

Material

Between January 1, 1990 and December 31, 1995, 2330 patients with non-small cell lung cancer called in the ambulatory of the Institute of Oncology in Warsaw. After examinations 260 patients (31 women (11.9%) and 229 (88.1%) men) aged between 24 and 79 (mean 61, median 62) qualified for radical radiotherapy.

Clinical stage was assessed according to TNM classification. In the considered group there were 16 patients (6.2%) in the I stage and 57 (21.9%) in the II stage. In the majority of cases the neoplastic process was considerably advanced: stage III A was found in 114 patients (43,8%) and stage III B in 73 patients (28.1%).

Blood count and biochemical tests were made for all the patients. Haemoglobin level before treatment was between 6.2 and 17,2 g/dl (mean 13.4 g/dl, median 13.0 g/dl). Alkaline phosphatase level was assessed in 257 patients (99%). It was between 10 and 353 IU/l (mean 107.8 IU/l, median 98 IU/l). LDH level was assessed in 214 patients (82.3%) and it was between 60 and 531 IU/l (mean 194.1 IU/l, median 176 IU/l). In 200 patients chest tomography was performed to assess the tumour size, in 47 other patients the information on the size of the lesion came form the description during exploratory thoracotomy. In the remaining patients the tumour size was estimated from the chest X-ray. The largest transversal dimension of the tumour was between 10 mm and 90 mm (mean 54 mm, median 50 mm).

Clinical characteristics

The overall performance status score was assessed according to Zubrod. In the group there were 19 patients with score 0 (7.3%), 216 with score 1 (83%) and 25 with score 2 (9.6%).

During the first clinical examination the presence of the following clinical symptoms was assessed: haemoptysis, hoarseness, intensive cough and chest ache necessitating pharmacological management, and dyspnoea with exertion when climbing two flights of stairs. These symptoms were treated as the analysed prognostic

factors. The time of appearance of these symptoms was not recorded.

Weight loss during the six months before the treatment was reported by 98 patients (37.7%). Losses were from 1 kg to 20 kg (mean 2.25 kg). In 67 patients (25.8%) a loss of at least 5 kg was noticed. In a group of 260 patients, in 47 (18%) before the irradiation an exploratory thoracotomy was performed. All these interventions were performed outside of the Center of Oncology.

In a majority of patients the thoracosurgeons carried out pulmonary function tests. In 63 patients disqualified from surgery the features of dyspnoea were found. These patients were treated with radical radiotherapy and underwent a detailed analysis in the present study.

Method of treatment

The patients with the following characteristics qualified for radical irradiation: good general condition, no significant dyspnoea (easily climbs two flights of stairs), without severe circulatory insufficiency resistant to treatment, with no weight loss over 10% during last six months. Patients with local advancement, with no involvement of the supraclavicular lymph nodes, with no oesophagus infiltration and with no infiltration of the entire wall of the myocardium, the chest wall and the spine (excluding the Pancoast tumour), with no presence of the neoplasmatic cells in the pleural or pericardial cavity liquid were subjected to treatment. The basic qualification criterion was the tumour size. Patients with transversal dimension of the tumour of up to 6-7 cm were treated.

The irradiation treatment was carried out according to a uniform treatment protocol, under the supervision of the same group of physicians. Treatment was carried out in two stages. In the first stage a 44-46 Gy dose was administered to the tumour site with the neighbouring mediastinum using the AP fields. In the second stage the dose to the tumour was increased up to 64-69 Gy, with the use of the oblique fields, while avoiding the spinal cord. The technique of large fields, *i.e.*, the fields including the tumour and the neighbouring mediastinum region was applied to 234 patients. A 2 cm margin of normal tissue around the tumour and the involved mediastinum lymph nodes was added. The mediastinum of the normal side was surrounded by a 1 cm margin on the left in the case of a right lung tumour and a 2 cm margin on the right in the case of a tumour in the left lung. In nine cases the supraclavicular region on the side of the tumour was included due to a tumour of lung top. In 26 patients (10%) the treatment was carried out with small fields including the tumour and the nearest lymph nodes. This was the group in which the general state or impaired pulmonary function created a risk of severe complications. For all the patients the total dose was calculated according to the ICRU recommendations in the middle of the AP dimension in the central radius for the AP fields and in the isocentre for the oblique fields.

Conventional irradiation, 2 Gy per day, 5 times per week was applied to 254 patients. Also 6 patients in whose cases the first stage of treatment was carried out with nonconventional fractionation were included in the analysis. This group initially qualified for palliative therapy. In this group after the first stage of treatment significant tumour regression was observed in the computer tomography tests and qualification was changed from palliative to radical. The equivalent dose for the first stage of treatment was recalculated with the linear-quadratic formula.

Irradiation was carried out with the Cobalt 60 gamma beams or photon X beams with energies of 4, 9 and 15 MeV obtained in linear accelerators. In the cases where the first stage of treatment was performed with Cobalt or photons of 4 MeV, the second stage was carried out with higher energy.

Methods of analyses

The source for the retrospective analysis of the clinical material were the case histories. Observation closed on December 31, 1999. For all the patients the information whether the patient was alive, and if not, the date of death was known. The material comprised information on 260 patients. The basic information for the assessment of results was the survival time and time to local progression. The local progression was assessed from the chest X-ray. The survival time was measured from the starting date of irradiation to the date of death or of the last information that the patient lives. Time to local progression was measured form the starting date of irradiation to the date of finding the features of progression or, if the progression was not found, the date of the last clinical examination. Survival probability was calculated with the Kaplan-Meier method [16]. Local control has been defined as the probability of non-occurrence of the local progression. Multivariant analysis of prognostic factors has been carried out with the use of the D.R. Cox proportional risk model [17]. The function of death risk and the function of local progression occurrence was modelled. The following classical prognostic factors were included in the model: age, tumour stage T, regional lymph nodes involvement stage N, Zubrod performance status, weight loss during the last six months, lactate dehydrogenase level (LDH) and haemoglobin level (HB). The significance of the following potential prognostic factors was investigated: tumour size, pulmonary function, prior exploratory thoracotomy, existence of selected clinical symptoms before treatment (cough, chest ache necessitating for management, dyspnoea with exertion). The definition of the analysed parameters is shown in Table I. The final form of the model has been obtained by stepwise elimination of variables for which the test critical level was larger than 0.1 ($p>0.1$). The statistical significance $\alpha=0,05$ was assumed. The assumptions of the model were verified with the graphic methods.

Tolerance of the treatment was assessed. Post-irradiation reaction intensity was scored with the RTOG/EORTC scale [18, 19].

Tab. I. Characteristics of the material and coding of the analysed variables

Analysed variable	Coding		N (%)
Age at the time of diagnosis	WIEK	260 (100)	
AGE ≤58	1		88 (33.8)
58 < AGE ≤66	2		97 (37.3)
AGE > 66	3	75 (28.8)	
Clinical stage T	T	260 (100)	
T1	1		14 (5.4)
T2	2		99 (38.1)
T3	3		77 (29.6)
T4	4		70 (26.9)
Clinical stage N	N	260 (100)	
N0	0		25 (9.6)
N1	1		118 (45.4)
N2	2		111 (42.7)
N3	3		6 (2.3)
Performance status according to Zubrod	ZUBROD	260 (100)	
0	0		19 (7.3)
1	1		216 (83.1)
2	2		25 (9.6)
Weight loss during last			
6 months	UW	260 (100)	
UW = 0	1		162 (62.3)
0 < UW ≤5	2		53 (20.4)
UW > 5	3		45 (17.3)
LDH level	LDH	214 (100)	
LDH (120	1		72 (33.6)
120 < LDH ≤232	2		72 (33.6)
LDH > 232	3		70 (32.8)
Haemoglobin level	HB	260 (100)	
HB 12.8	1		82 (31.6)
12.8 < HB ≤14.3	2		89 (34.2)
HB > 14.3	3		89 (34.2)
Size of the tumour	WLKG	260 (100)	
WLKG (40	1		49 (18.8)
40 < WLKG ≤60	2		157 (60.4)
WLKG > 60	3		54 (20.8)
Impaired pulmonary function	MALAWYD	2	60 (100)
NO	0		197 (75.8)
YES	1		63 (24.2)
Thoracotomy	THORACO	260 (100)	
NO	0		213 (81.9)
YES	1		47 (18.1)
Cough	KASZEL	260 (100)	
YES	1		113 (43.5)
NO	2		147 (56.5)
Ache	BOL	260 (100)	
YES	1		56 (21.5)
NO	2		204 (78.5)
Dyspnoea	DUSZ	260 (100)	
YES	1		67 (25.8)
NO	2		193 (74.2)
Haemoptysis	KRWIOPL	260 (100)	
YES	1		98 (37.7)
NO	2		162 (62.3)

Results

Survival

Observation period varied between 2 and 98 months (median 16 months). In the tested group 230 patients died. In 196 cases in the last clinical examination the features of the disease were found (75%). Among 64 patients who died without features of the disease, according to the last examination, in 15 cases the reason of death was found: in 9 cases the direct reason was myocardial infarct, in one case it was stroke without features indicating metastases (the patient had no computer tomography of the brain and the diagnosis was made on the basis of neurological examination), in two cases the reason was a car accident, in two – suicide, in one – stomach perforation. It can not be excluded that in the remaining cases the reason of death was the recurrence or the post-irradiation effect.

The two-year survival in the whole group was 33%±2%, and the five-year survival was 10%±2%. Two-year local control was estimated as 35%±4% and the five-year one as 23%±4%. The results obtained are presented in Table II and Figures 1 and 2.

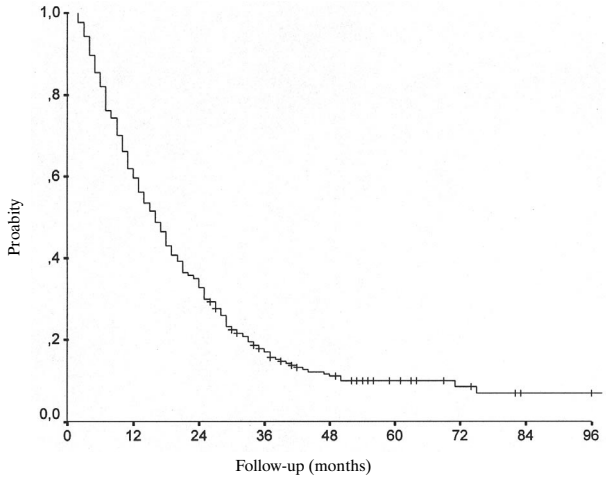

Fig. 1. Survival probability in 260 patients with non-small cell lung cancer subjected to radical radiotherapy alone

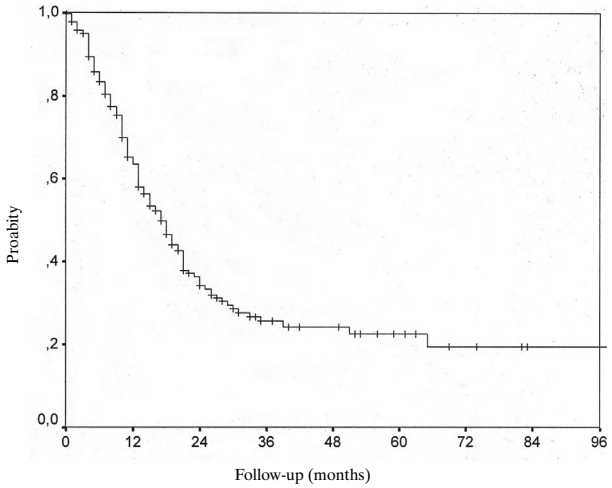

Fig. 2. Local control probability in 260 patients with non-small cell lung cancer subjected to radical radiotherapy alone

Tab. II. Survival and local control probability with the 95% confidence interval

Time of observation (months)	Survival probability (95% CI)	Local control probability (95% CI)
12	0.60 (0.54; 0.66)	0.64 (0.58; 0.70)
24	0.33 (0.29; 0.37)	0.35 (0.27; 0.43)
60	0.10 (0.06; 0.14)	0.23 (0.15; 0.31)

Prognostic factors

The influence of the following classical prognostic factors on the survival has been confirmed: tumour stage T (p=0.0059), lymph node involvement stage N (p=0.128), performance status of the patient (p=0.0163), and lactate dehydrogenase level (p<0.00005). The parameters of the chosen model of the death risk are shown in Table III. The following factors were excluded from the model (p>0.1): age, weight loss, tumour size, prior exploratory thoracotomy, clinical symptoms. In the group of potential factors the influence of only one factor on the survival was confirmed: pulmonary function (p=0.0053). Patients with impaired pulmonary function had an over 1.5 times greater death risk than those with normal pulmonary function.

Tab. III. Parameters of the assumed death risk model (Cox model)

Variable	Coefficient β	Standard error β	Critical level *p*	Relative risk
T	0.2561	0.0930	0.0059	1.2919
N	0.3121	0.1254	0.0128	1.3662
ZUBROD	0.4090	0.1703	0.0163	1.5053
LDH	0.6046	0.0947	<0.00005	1.8305
HB	-0.1598	0.0946	0.0913	0.8523
MALAWYD	0.5192	0.1862	0.0053	1.6807

In the analysis of local control a significant statistical value of the following classical factors was found: tumour advancement stage T (p=0.0259) and lactate dehydrogenase level (p=0.0002). The parameters of the assumed model of local progression risk are shown in Table IV. The following factors were excluded from the model (p>0.1): age, advancement level N, performance status of the patient, weight loss, haemoglobin level, tumour size, prior exploratory thoracotomy, other clinical symptoms. From the potential factors only the pulmonary function appeared to be statistically significant for local control (p=0.0050). The patients with reduced pulmonary function had a nearly two times larger risk of local progression. The influence of the other factors was not statistically significant.

Tab. IV. Parameters of the assumed local progression risk model (Cox model)

Variable	Coefficient β	Standard error β	Critical level *p*	Relative risk
T	0.2604	0.1168	0.0259	1.2974
LDH	0.4468	0.1190	0.0002	1.5633
MALAWYD	0.6527	0.2327	0.0050	1.9207

It should be pointed out that the advancement stage T, lactate dehydrogenase level and pulmonary function had significant influence on the long-term survival as well as on the local control.

Tolerance of treatment

During radiotherapy acute postirradiation reaction appeared in 70 patients (27%), mainly oesophagitis, shortness of breath and leukopoenia and thrombocytopoenia, including 11 patients (4.6%) in which it was assessed as damage III°. Late sequelae were found in 9 patients (3.7%). In 5 patients it was prolonged shortness of breath while walking on the level, necessitating for pharmacotherapy (II°). In 3 patients (1.1%) there was dysphagia as a result of postirradiation oesophagus obstruction, necessitating for surgical intervention (III°). In one patient (0.3%) postirradiation damage of the spinal cord in the form of paraparesis (IV°) appeared. This patient rece-

ived the total dose of 47.3 Gy administered to 11 cm of spinal cord.

Discussion

An assessment of prognostic factors in radical radiotherapy administered alone has been carried out for a group of 260 patients with non-operative, non-small cell lung cancer.

The results of the analysis make it possible to state that radical radiotherapy applied as the only method of treatment in the group of patients with non-small cell nonoperative lung cancer is the most profitable for patients with good general performance status – Zubrod 0 or 1, with good pulmonary function and with a non-advanced tumour. Biochemical tests planned in diagnostic and qualification process should include the lactate dehydrogenase level. Most of the authors concentrate on the pulmonary function. According to them radical radiotherapy can be safely performed only for patients with proper pulmonary function [6, 20-24]. However, the assessment of proper pulmonary function with the exertion test of climbing two flights of stairs is not precise.

Many authors point out that age, performance status and weight loss over 10% during last 3-6 months before the treatment are significant prospective factors [10, 25--28]. It has been demonstrated that age over 60 and in other studies – 65 is an unfavourable prognostic factor. Wigren did not demonstrate a significant dependence of the results on the age of patients [15]. In Bauer's study [25] high statistical significance of the general performance status was shown ($p=0.001$). In the investigation by Sause et al. [29] mean survival of patients with performance status less or equal to 70 points according to Karnofsky (KPS) was 5.9 months, and with over 70 points – 9.9 months. According to most of the authors, radical radiotherapy can be applied in patients without weight loss over 10% during last 6 months [21, 25, 27].

In the present study the performance status scored according to Zubrod appeared to be a significant parameter in the analysis of long-term survival ($p=0.016$), while it was found to be insignificant in the assessment of local recurrences ($p=0.8$). The age and weight loss was not found to be statistically significant.

In the studies published in the 90's a vast majority of authors underline a significant prognostic value of the stage of the disease [10, 14, 15, 26, 27, 29]. Emami *et al.* reported that in the studies carried out in the 70's and 80's this parameter had an ambiguous value [30].

In the analysed group of patients this factor appeared to be statistically significant both for the death risk function and the local recurrence function.

In many studies haemoglobin and lactate dehydrogenase level were taken into account as prognostic factors [15, 26, 27, 31, 32]. Haemoglobin concentration is a parameter which influences the radiosensitivity of tissues and makes it possible to assess their oxygenation factor. Together with better oxygenation, larger local control has been observed. The relation of the radiotherapy results and the oxygenation factor of tissues has been demonstrated in many studies, mainly those on head and neck neoplasms [33-35]. Lactate dehydrogenase increase in the blood serum indicates the presence of foci of necrosis in the organism, increased permeability of cell membrane or the presence of quickly growing tissues. Neoplasmatic cells have increased permeability for lactate dehydrogenase and a significant growth of its level suggests the presence of a large neoplasmatic mass [31]. Because of this, indirectly, the lactate dehydrogenase level in the blood serum can be a sign of presence of a large neoplasmatic mass and presence of subclinical cancer foci. In this analysis the haemoglobin level appeared not to be significant for local recurrence risk ($p=0.4$) as well as for long--term survival ($p=0.09$). Difficulties in assessment of this parameter result from the fact that the majority of patients had proper haemoglobin level. In the analysis of lung cancer therapy studies it should be taken into account that the majority of patients are long-term smokers in whom a chronic, obturative lung disease develops. This disease is the reason for impairment of pulmonary function, which stimulates the marrow reaction in form of poliglobulia. As a result, the haemoglobin level can be high, as found in the analysed group of patients, while the oxygenation of tissues is low. The lactate dehydrogenase level appeared to be strongly significant for the results of treatment of the analysed group of patients.

In the analysis of the potential factors the tumour size was investigated. This parameter was the basic subject of assessment in the RTOG 73-01 study, the results of which were published for the first time by Perez et al. [36]. In this four-arm study comprising 378 patients the dependence of treatment results on the administered total dose and tumour size was prospectively assessed. The largest cure percentages were obtained in the case of tumours smaller than 3 cm, and the smallest percentages – when the transversal dimension of the lesion was larger than 6 cm. Katz [37] and Martel [38] published similar results. In the latter experiment the tumour size was assessed in three dimensions. In the cases when the tumour volume was smaller than 200 cm^3 the statistically longer survivals were demonstrated ($p=0.047$). In that study the statistical significance of this parameter was not demonstrated.

An important parameter in the group of the potential parameters tested in the present analysis was the pulmonary function level. Usually much worse tolerance of treatment is observed in patients with pulmonary dysfunction. According to the majority of the authors radical radiotherapy can be safely carried out only in patients with proper pulmonary function [6, 20, 22, 24]. Unfortunately, in none of these studies the diffusion ability of lungs or the partial pressure of oxygen and carbon dioxide was tested. A good pulmonary function was scored in relation to easily climbing two flights of stairs. In the present analysis a statistically significant influence of this factor on the long-term survival ($p=0.0053$) as well as on the local recurrence risk ($p=0.0050$) was demonstrated.

In the analysis of the prognostic factors it has also been attempted to assess the influence of the presence of

selected clinical symptoms, reported by the patients before the therapy, on the results of the treatment. Shortage of breath while climbing two flights of stairs, cough and chest ache necessitating for pharmacological management, and haemoptysis have been analysed. The influence of the above parameters was studied by Wigren [15]. He has also analysed the performance status of the patients, stage of the disease and haemoglobin level. Wigren has demonstrated that each of these factors, including the symptoms, reduces the probability of 24 months survival by 13%. In the present work the influence of the clinical symptoms on the results of treatment has not been confirmed.

In the analysis of the prognostic factors also the prior exploratory thoracotomy has been taken into account. Surgery reduces the oxygenation of tissues in the region of the operation, hence having a potentially negative influence on treatment results. The value of this factor appeared not to be significant in the analysis, either for the long-term survival ($p=0.3$) or for the local recurrence risk ($p=0.3$).

In spite of the fact that age and weight loss did not appear to have a significant influence on the results of treatment, it seems that these parameters should be properly taken into account in the assessment of the performance status of a patient qualified for radical radiotherapy.

The still unsatisfactory results of treatment of patients with non-small cell lung cancer are a constant challenge for oncologists and constitute an incentive for a future search of more efficient methods of therapy.

Conclusion

1. Multivariant statistical analysis has demonstrated that the independent prognostic factors in a group of patients with nonoperative, non-small cell lung cancer subjected to radical radiotherapy are:
   - for survival: clinical stages T and N, pulmonary function, performance status of the patient and lactate dehydrogenase level assessed before treatment;
   - for local control: clinical stage T, lactate dehydrogenase level assessed before treatment and pulmonary function.
2. Patients with impaired pulmonary function have a 1.5 times larger death risk and a nearly two times larger risk of local recurrence.

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Results

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