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LARYNGEAL CANCER IN FARMERS FROM LUBLIN REGION OF POLAND

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Abstract: The aim of the study was to analyse if work related risk factor had any influence on stage, localisation and histology of type of malignant tumour. Demographic and risk factors and results of treatment of farmers with patients working outside farming were compared. The group included 148 patients with primary laryngeal squamous cell carcinoma (LSCC) diagnosed and treated in our institution in the years 1999–2002. 84 (56.8%) of 148 patients were farmers and 64 (42.2%) patients worked outside farming. The univariate analysis of demographical and clinicopathological features of the farmers' group versus the other professions group with LSCC showed a statistical significance for sex, age and G stage. Nearly statistical significance was observed for the N stage (p=0.06) and for primary localisation of the tumour (p=0.05). The difference in 3 and 5-year survival rates between the group of farmers in comparison with the group of patients working outside farming and with LSCC was not significant for most of the demographical and clinicopathological features. Local, nodal or local plus nodal recurrence occurred in 15 (21.1%) of 84 farmers during 3 years follow-up. Distant metastases were observed in 7 (8.3%) of 84 farmers with LSCC, 6 to the lungs and one to the liver. Farmers with larynx cancer had different presentation pattern than other profession patients. The incidence of glottic cancer and well differented cancer was higher in farmers than in other professions. The prevalence of larynx cancer in women was significantly lower among farmers than in other professions. There were older patients in the group of farmers and relatively less women than in the group of patients with other professions.

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INTRODUCTION

Laryngeal cancer (LC) is the second most common respiratory system neoplasm, following lung cancer [6]. Laryngeal squamous cell carcinoma (LSCC) is the most common malignant tumour of the head and neck. Its incidence varies widely in different countries and increasing trends have been observed in many previous studies [28]. Smoking and alcohol abuse are well established major risk factors [10, 27]; however, occupational and environmental factors also contribute to its incidence [33]. Viral infections, nutritional deficiency and local habit of diet have also been implicated in the aetiology of laryngeal cancer [21, 24, 25, 26, 27]. Differences in the life style, labour conditions and occupational expositions to noxious agents may also affect the individual patients.

Several studies have also assessed some of the occupational exposures that might increase the risk of laryngeal cancer. Increased risk has been reported for several occupational groups, including textile workers, metal processors, coal miners, mechanics and machinists [1, 11, 35]. Agricultural activities may entail exposure to several harmful substances, including pesticides. Some pesticides appear to be mutagenic in laboratory tests [14, 19] and cytogenetic effects have been reported among exposed workers [5, 15]. These circumstances may perhaps explain some exceptional observations on an increasing the number of cases of lung [2], kidney [22], rectum [13] and larynx cancers [16].

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Differences in occupational exposures, health awareness and everyday habits may influence the presentation pattern and treatment results in farmers (I group) and patients with other occupations with laryngeal cancer (II group).

The aim of the present study was to analyse if work related risk factor had any influence on stage, localisation and histology of the type of malignant tumour. Demographic and risk factors and results of treatment of farmers with patients working outside farming were compared.

MATERIAL AND METHODS

The group included 148 consecutive patients with primary laryngeal squamous cell carcinoma (LSCC) diagnosed and treated by the first author in our institution in the years 1999–2002. The group consisted of 130 males and 18 females, aged between 32–78 years (mean 58.6 years). 84 (56.8%) of 148 patients were farmers living in the countryside and 64 (42.2%) of 148 patients lived in towns and

Table 1. Demographic and clinicopathological features of 84 farmers and 64 different professions patients with LSCC.

Demographic and clinicopathological features		Farmers (n = 84)		Other professions (n = 64)		Statistical significance	
		n	%	n	%	χ^2	p
Sex	Men	78	92.9	52	81.3	4.58	0.03
	Women	6	7.1	12	18.7		
Age	≤ 60 years	38	45.2	42	65.6	6.08	0.01
	> 60 years	46	54.8	22	34.4		
Alcohol abuse	Yes	63	78.8	47	74.6	0.34	0.56
	No	17	21.2	16	25.4		
Smoking	Yes	74	91.4	53	84.1	1.78	0.18
	No	7	8.6	10	15.9		
Localisation	Supraglottic	36	42.9	37	57.8	5.87	0.05
	Glottic	47	55.9	24	37.5		
	Subglottic	1	1.2	3	4.7		
T stage	T1	15	17.9	10	14.6	1.7	0.64
	T2	11	13.1	5	7.8		
	T3	33	39.3	25	39.1		
	T4	25	29.7	24	37.5		
N stage	N0	58	69.1	35	54.7	7.3	0.06
	N1	19	22.6	17	25.6		
	N2	7	8.3	8	12.5		
	N3	0	0	4	6.2		
Clinical stage	I stage	15	17.9	10	15.6	1.67	0.64
	II stage	10	11.9	4	6.2		
	III stage	21	25.0	17	26.6		
	IV stage	38	45.2	33	51.6		
Histology grade	G1	30	35.7	11	17.2	6.23	0.04
	G2	44	52.4	43	67.2		
	G3	10	11.9	10	15.6		
Recurrence	Yes	15	21.7	18	33.3	2.07	0.15
	No	54	78.3	36	66.7		
Type of recurrence	Local	4	26.7	11	61.1	3.93	0.14
	Nodal	6	40.0	4	22.2		
	Local + nodal	5	33.3	3	16.7		
Distant metastases	Yes	7	8.3	8	12.5	0.69	0.41
	No	77	91.7	56	87.5		

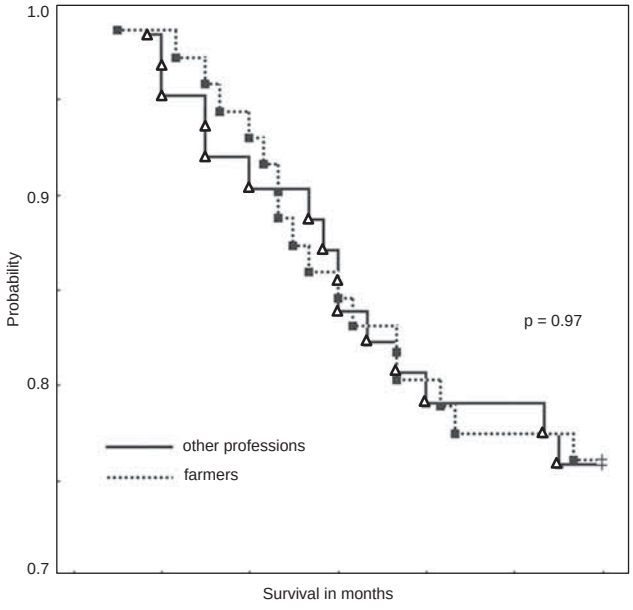

Figure 1. Kaplan-Meier curve. 3-year cumulative survival rate over time for farmers and different profession patients with LSCC.

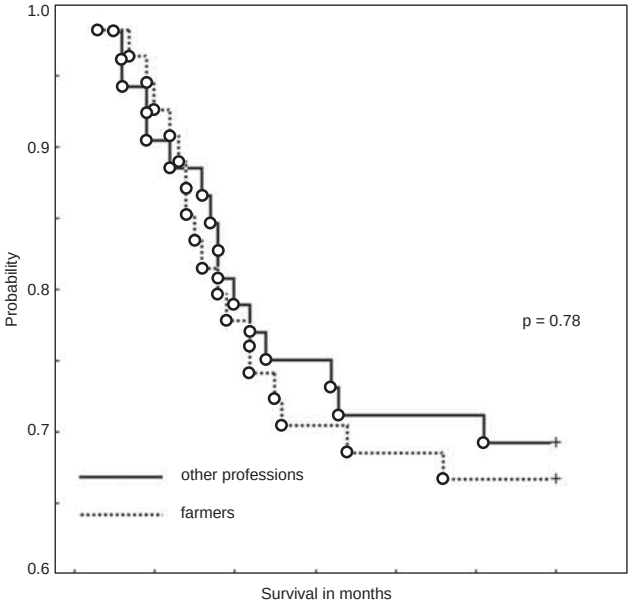

Figure 2. Kaplan-Meier curve. 5-year cumulative survival rate over time for farmers and different profession patients with LSCC.

had different professions. The group of other professions consisted of 47 (73%) physical workers and 17 (27%) white collars workers. Demographical data such as sex, age, place of living and risk factors such as tobacco smoking and alcohol consumption were obtained from medical histories and compared in both groups. Clinical features of tumours were qualified according to TNM (UICC, 1992) and also evaluated histologically (G1), moderately (G2) and poorly (G3) differentiated. The data concerned also the type of operation (total laryngectomy or endoscopic laser CO_2 resection). Recurrences were classified as local, nodal, or local plus nodal. Follow-up was carried out for each patient and ranged from 36–60 months.

The demographical and clinicopathological features in relation to occupation were analysed using χ^2 test. Overall survival was estimated from the operation date to the date of the last follow-up visit. The Kaplan-Meier method and the log-rank test was applied to evaluate 3 and 5 year survival rates (Figs. 1, 2).

RESULTS

The demographical and clinicopathological features of both groups are shown in Table 1. There were 92.9% men in the farmer group and 81.3% in the group of patients working outside farming. The majority of patients from group II (65.6%) were younger then 60 years of age. In the farmers' group there were 45.2% of patients younger than 60 years. The differences in age and sex were statistically significant. Nearly statistical significance was observed for the N stage (p=0.06) (Tab. 1). 36 (42.9%) of the 84 farmers with LSCC had primary supraglottic tumours, in 47 (55.9%) cases the tumour was located in the glottis and one was localised in the subglottic region. Most tumours in patients from the non-farmer group were situated in supraglottis (57.8%). The difference in the localisation of the tumour was nearly significant (p=0.05).

25 (29.7%) of the 84 farmers with LSCC had T4 tumours, 33 (39.3%) tumours were recognized as T3, 11 (13.1%) were T2 and 15 (17.9%) were T1. 58 of 84 farmers with LSCC had no clinically evident cervical lymph nodes (N0) and 26 farmers had N1, N2 nodes. The clinical TNM stage showed that 38 (45.2%) of 84 farmers with LSCC had stage IV, 21 (25%) stage III, 10 (11.9%) stage II and 15 (17.9%) had stage I. 44 (52.4%) of 84 LSCC tumours were G2, 10 samples (11.9%) were G3 and 30 (35.7%) tumours were G1 (well differentiated). Poorly differentiated tumours were more frequently discovered in farmers than in other professions. The difference in G stage between both groups was statistically significant (p=0.04).

74 (91.4%) farmers with LSCC were habitual smokers and 78.8% frequently consumed alcohol. Alcohol and tobacco use was similar in both groups.

Local, nodal or local plus nodal recurrence occurred in 15 (21.1%) of 84 cases. Distant metastases were observed in 7 (8.3%) of 84 farmers with LSCC, 6 to the lungs and one to the liver. There were no significant differences between analysed groups in the type and incidence of recurrence.

From the whole group of 84 farmers with LSCC 54 (64.3%) were alive 3-years after initial treatment. The univariate analysis of 3 year survival and demographical and clinicopathological features is presented in Table 2. From the group of 84 farmers with LSCC 36 (42.9%) were alive 5 years after initial treatment. The univariate analysis of 5 year survival and demographical and clinicopathological features is presented in Table 3. No significant differences in type and rate of the recurrence and in survival rates were found between the groups.

Table 2. Analysis of 3-years survival in the groups of 84 farmers and 64 different profession patients with LSCC (log-rank test).

Demographic and clinicopathological features		Farmers (n = 84)		Other professions (n = 64)		Statistical significance	
		n	%	n	%	χ^2	p
Sex	Men	48	88.9	36	76.6	2.71	0.1
	Women	6	11.1	11	23.4		
Age	≤ 60 years	25	46.3	31	66.0	3.93	0.05
	> 60 years	29	53.7	16	34.0		
Alcohol abuse	Yes	36	72.0	34	73.9	0.04	0.83
	No	14	28.0	12	26.1		
Smoking	Yes	44	86.3	37	80.4	0.6	0.44
	No	7	13.7	9	19.6		
Localisation	Supraglottic	20	37.0	25	53.2	2.75	0.25
	Glottic	33	61.1	21	44.7		
	Subglottic	1	1.9	1	2.1		
T stage	T1	14	25.9	10	21.3	1.28	0.73
	T2	7	13.0	5	10.7		
	T3	20	37.0	16	34.0		
	T4	13	24.1	16	34.0		
N stage	N0	45	83.3	30	63.8	6.07	0.11
	N1	7	13.0	10	21.3		
	N2	2	3.7	6	12.8		
	N3	0	0	1	2.1		
Clinical stage	I stage	14	25.9	10	21.3	1.25	0.74
	II stage	7	13.0	4	8.5		
	III stage	15	27.8	13	27.7		
	IV stage	18	33.3	20	42.5		
Histology grade	G1	21	38.9	10	21.3	4.46	0.11
	G2	30	55.6	31	65.9		
	G3	3	5.5	6	12.8		
Recurrence	Yes	5	9.3	8	17.0	1.35	0.25
	No	49	90.7	39	83.0		
Type of recurrence	Local	2	40.0	5	62.5	–	–
	Nodal	3	60.0	2	25.0		
	Local + nodal	0	0	1	12.5		
Distant metastases	Yes	1	1.8	1	2.1	–	–
	No	53	98.2	46	97.9		

DISCUSSION

Farmers may be exposed to several harmful substances and cancer risk in this occupational group is considered an important public health issue. Many case-control studies considering hematolymphopoetic malignancies observed increased risk connected with the use of pesticides [23]. Settimi *et al.* [31] examined the association between cancer and farming among male agricultural workers. The cancer sites selected for the study were: lip, oral cavity and oropharynx, oesophagus, stomach, colon, rectum, lung, skin melanoma, skin non-melanoma, prostate, bladder, kidney, and non-Hodgkin's lymphoma. Increased risks of cancer associated with agricultural work were found for stomach, rectum, larynx and prostate.

Coble *et al.* [7] analysed work history information from a population-based case-control study carry out in Puerto Rico using a job exposure matrix to investigate the relationship between occupational exposures and cancers of oral cavity or pharynx. The risk of oral cavity cancer, but not

Table 3. Analysis of 5-years survival in the groups of 84 farmers and 64 different profession patients with LSCC (log-rank test).

Demographic and clinicopathological features		Farmers (n = 84)		Other professions (n = 64)		Statistical significance	
		n	%	n	%	χ^2	p
Sex	Men	32	88.9	26	72.2	2.22	0.14
	Women	4	11.1	10	27.8		
Age	≤ 60 years	18	50.0	22	61.1	0.9	0.34
	> 60 years	18	50.0	14	38.9		
Alcohol abuse	Yes	25	73.5	23	65.7	0.5	0.48
	No	9	26.5	12	34.3		
Smoking	Yes	27	79.4	26	74.3	0.25	0.61
	No	7	20.6	9	25.7		
Localisation	Supraglottic	12	33.3	16	44.4	0.95	0.62
	Glottic	23	63.9	19	52.8		
	Subglottic	1	2.8	1	2.8		
T stage	T1	12	33.3	10	27.8	0.4	0.94
	T2	5	13.9	5	13.9		
	T3	11	30.6	11	30.5		
	T4	8	22.2	10	27.8		
N stage	N0	33	91.7	25	69.4	7.6	0.05
	N1	3	8.3	5	13.9		
	N2	0	0	5	13.9		
	N3	0	0	1	2.8		
Clinical stage	I stage	12	33.3	10	27.8	0.52	0.91
	II stage	5	13.9	4	11.1		
	III stage	8	22.2	9	25.0		
	IV stage	11	30.6	13	36.1		
Histology grade	G1	16	44.4	9	25.0	3.11	0.21
	G2	19	52.8	25	69.4		
	G3	1	2.8	2	5.6		
Recurrence	Yes	2	5.6	5	13.9	1.42	0.23
	No	34	94.4	31	86.1		
Type of recurrence	Local	0	0	4	80.0	–	–
	Nodal	2	100.0	0	0		
	Local + nodal	0	0	1	20.0		
Distant metastases	Yes	0	0	1	2.8	–	–
	No	36	100.0	35	97.2		

pharynx, was significantly elevated among farm workers in the sugarcane industry. Flanders *et al.* [12] performed a case-control study to identify employment-related risk factors for laryngeal cancer. They concluded that farmers are one of the professions with higher risk of laryngeal cancer.

Many studies analysed the demographic and clinical factors in patients with laryngeal cancer, however to our knowledge no report comparing those factors in farmers and other professions is available. The demographic characteristics of the patients and the clinical factors in farmers with LSCC have been the subject of the present research. According to the majority of the studies, demographic data such as age and sex of the patients have not been implicated with poor prognosis [4, 8]. Our study demonstrated significant differences between both groups (farmers and patients working out of farming) in age and sex. There were older patients in the group of farmers and relatively less women than in the group of patients with other professions. The advanced age of patients [17] and the male sex [9] are factors that could be unfavourable for the prognosis.

Our study demonstrated that difference concerning age of subjects at presentation, the site of the primary tumour and N status in both groups (farmers and compared group of patients with LSCC) were significant in univariate analysis.

The supraglottic localisation of the tumour [8, 20], and the subglottic extension or localisation of the tumour [34] have presumed unfavourable prognosis in most patients with LSCC. In our study tumours of supraglottic localisation were very frequent present in the group of patients with different professions, while in the group of farmers the most frequent localisation was glottis.

Advanced T-stage of the laryngeal cancer and lymph nodes involvement carry poor prognosis for the patient [8, 9, 18, 32] Our study demonstrate that the difference in the lymph node status in both groups was nearly significance in univariate analysis. Farmers presented with generally lower status of lymph node involvement. Comparison of the histological finding revealed that well differentiated tumours more often encountered in farmers than patients with other professions and that the difference was statistically significant.

Semanycz [29] reported a group of patients with laryngeal cancer and found that the most numerous occupational group among men consisted of farmers, foresters and workers employed in industry. He found that in 60.3% of cases the tumour was situated in epiglottic region, in 38.3% the glottis, and in 1.2% subglottis. Supraglottic localisation of the tumour was preponderant in patients who abused alcohol, performed their work under pollution environment and derived from rural population. In 64.6% of patients the local advancement of the tumour was diagnosed as T3 or T4. In 35.4% of reported patients the tumour was diagnosed as T1 or T2 mainly involving the glottis. The analysis of clinical and demographic factors in study performed by Semanycz [29] comprised all the patients with laryngeal cancer without analysis of particular profession groups.

Bień *et al.* [3] reported in a group of 940 patients with LSCC that 3-year survival rate was achieved in 77.8% and 5-year survival in 61.7% of the whole group. The analysis of survival rates had proved the significant relation to localisation of primary tumour and clinical stage of the disease. In our study groups the 3-year survival rate was achieved in 64.3% of farmers and in 73.4% of patients with different professions with LSCC. 5-year survival rate in farmers was 42.9% and 56.3% in other patients with LSCC. The difference in survival rates between both groups was not statistically significant. Semczuk *et al.* [30] reported a group of 579 patients with laryngeal cancer treated surgically in four university departments of otolaryngology in Poland. In this study 72% of patients survived 3 years without recurrence and 59% survived 5 years. Survival analysis in most studies took into consideration all treated patients with laryngeal cancer. Comparison of our results is therefore difficult. However presented significant differences in presentation pattern and survival rates in farmers and other professions suggest different exposure factors and progress of the disease.

CONCLUSIONS

Farmers with larynx cancer had different presentation pattern than other profession patients. The incidence of glottic cancer and well diversified histological cancer was higher in farmers than in other professions. The prevalence of larynx cancer in women was significantly lower among farmers than in other professions. There were older patients in the group of farmers and relatively less women than in the second group of patients.

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