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Radiotherapy outcomes in laryngeal cancer – a retrospective study

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Study aim. To analyze the importance of pre-treatment factors (age, sex, T, N, histological differentiation, site, Hb level, performance status) and to investigate the influence of cigarette smoking and pulmonary and cardiac diseases on treatment outcomes in laryngeal cancer patients.
Material and methods. From the year 1989 until May 1995 372 consecutive patients with cancer of the larynx were radically irradiated at the 2nd Teleradiotherapy Department of The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology in Warsaw (MSCMCC). Pt. characteristics – 88% men; 12% women, age: 29-82 years, stages: T1-20%, T2 – 34%, T3 – 30%, T4 – 16%, lymph node metastases: 27%.
Results. Complete response to treatment (CR) – 71% of cases. Loco-regional control after 2 years 52% (T1-T2 – 64%, T3-T4 – 40%). Early reactions: pain on swallowing, confluent mucositis and moist skin reaction in 69%, 48% and 41% of cases, respectively. Serious late complications – 19 patients. In a majority of these cases several forms of serious damage were observed. Patients with advanced disease (T3-T4) present a two times higher death risk as compared to patients in earlier stages of the disease (T1-T2). Patients with cervical node metastases also present a two times higher death risk as compared to N0 cases. Patients with performance status 1 or more had a respectively three or four times higher death risk than patients with performance status – 0. No significant influence of sex, histological differentiation, site, hemoglobin level and cigarette smoking, pulmonary and coronary diseases on treatment outcome has been found. The survival curves come down steeply three and more years after treatment completion due to causes other than local failure. The limited number of serious early and late reactions suggests the possibility of a total dose increase.

Wyniki radioterapii chorych na raka krtani – analiza retrospektywna

Celem pracy jest analiza wyników radykalnej radioterapii chorych na raka krtani w zależności od typowych czynników klinicznych takich jak: wiek, płeć, stopień zaawansowania choroby, stopień histopatologicznego zróżnicowania, stopień sprawności chorego, lokalizacja nowotworu, poziom hemoglobiny we krwi oraz zbadanie znaczenia potencjalnych czynników rokujących takich jak: intensywność palenia papierosów oraz występowanie choroby wieńcowej i stanów pogruźliczych w płucach. Analizowano retrospektywnie informację o 372 chorych leczonych w latach 1989-1995 samodzielnie i radykalnie promieniami w Zakładzie Teleradioterapii II Centrum Onkologii – Instytutu w Warszawie. Charakterystyka materiału: 88% mężczyzn, 12% kobiet, wiek: 29-82 lat, zaawansowanie: T1-20%, T2-34%, T3-30%, T4-16%, przerzuty do węzłów chłonnych: 27%. Całkowitą odpowiedź na leczenie (CR) uzyskano w 71% przypadków. Wyleczenia miejscowe po 2 latach wynoszą 52% (T1-T2 – 64%, T3-T4 – 40%). Wczesne reakcje: ból w przełykaniu, zlewne zapalenie błony śluzowej i złuszczanie wilgotne odnotowano odpowiednio w 69%, 48% i 41% przypadków. Ciężkie powikłania późne stwierdzono u 19 pacjentów. Stwierdzono istotny wpływ stopnia zaawansowania klinicznego T i N oraz stopnia sprawności na ryzyko zgonu. Pacjenci w późnym stopniu zaawansowania (T3-T4) mieli dwukrotnie wyższe ryzyko zgonu od pacjentów we wczesnym stopniu zaawansowania (T1-T2). Ryzyko zgonu pacjentów z przerzutami w węzłach chłonnych było również dwukrotnie wyższe od odpowiedniego ry-

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We dedicate this study to the memory of Michał Wasilewski MD, who had created the head and neck cancer radiotherapy protocols for the 2nd Radiotherapy Department of the Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology in Warsaw.

zyka dla pacjentów w stopniu N0. Pacjenci w stopniu sprawności 1 i powyżej są obciążeni trzy- i czterokrotnie wyższym ryzykiem zgonu od pacjentów w stopniu sprawności 0. Nie stwierdzono statystycznie istotnego wpływu: płci, stopnia zróżnicowania G, lokalizacji, poziomu hemoglobiny, intensywności palenia papierosów oraz występowania choroby wieńcowej i stanów pogruźliczych w płucach. Krzywe przeżycia opadają stromo trzy i więcej lat po zakończeniu leczenia z powodów innych niż miejscowe niepowodzenie. Ograniczona liczba przypadków ciężkich wczesnych i późnych powikłań skłania do rozważenia możliwości podwyższenia dawki całkowitej.

Słowa kluczowe: rak krtani, radioterapia, analiza retrospektywna
Key words: cancer of the larynx, radiotherapy, retrospective study

Introduction

Our knowledge concerning radiotherapy of laryngeal cancer is mostly based on retrospective studies. The most reliable of these are studies on patients treated at the same department, irradiated by the same team of doctors and following the same treatment protocol. The results of such studies can also be the starting point for prospective and some retrospective studies [1]. In 1989 M. Wasilewski supervised the preparation of treatment protocols of the most frequent tumors for the 2nd Radiotherapy Department of the MSCMCC in Warsaw in mind [2]. Until 1995 two fractionation strategies have been employed for radiotherapy of laryngeal cancer – conventional and that of concomitant boost [3]. Altogether 372 patients with cancer of the larynx were radically irradiated until May 1995 and have become the subject of the present analysis. What is more, the present study also tackles the problem of cigarette smoking and of concomittant pulmonary and cardiac diseases, which may affect lung ventilation capacities.

Aim of the study

To analyze the importance of pre-treatment factors such as age, sex, T, N histological differentiation, site, Hb level, type of treatment, performance status and the influence of cigarette smoking on radiotherapy treatment outcomes of laryngeal cancer patients.

Materials and

372 consecutive patients with cancer of the larynx were treated radically between January 1989 and May 1995 at the 2nd Department of Radiotherapy of the MSCMCC in Warsaw. All of them – 327 men and 45 women were included in the analysis. Patient age ranged from 29 to 82 years, stage incl. T1, T2,T3, T4, N1, N2, N3, M0, histopathologically confirmed as SCC of the larynx. Disease stage was set basing on ENT examination, lateral and tomography X-ray images, CT examination (if necessary), chest X Ray and hematology. Patient characteristics are presented in Table I.

Methods

In patients with glottic cancer stage T1, T2, NO irradiation had been performed in one stage. The entire larynx was irradiated solely. In case of T3 NO glottic and T1, T2, T3, NO supraglottic cancer irradiation was performed in two stages. Stage one included irradiation of the primary tumor and, selectively, the cervical lymphatics. Stage two included irradiation of the entire larynx solely. The fraction dose of 2 Gy was estimated at the reference point ICRU 50. Total dose was 66 Gy. In patients with glottic cancer in any T stage with cervical nodes N 1,2,3 involvement irradiation was applied to the entire cervical area. In both sites boost doses with 9 or 12 MeV electron beam were applied for residual tumors. Additionally, in all N+ cases, the low cervical field was irradiated.

Fractionation schedules

Conventional irradiation: fraction dose 2 Gy, number of fractions 33, total dose 66 Gy. Total time 45 days. Concomittant boost [2]: total dose 66.2 Gy, elective dose 50,2 Gy, 19 fractions a 1.8 Gy and 10 fractions a 1.60 Gy, boost dose 16 Gy in 10 fractions. The overall treatment time 39- 41 days. The concomittant boost schedule was considered as the pilot study with special attention paid to early morbidity. There was no randomization between the schedules.

Pretreatment preparations

Pretreatment preparations included the thermoplastic mask, localization radiograms taken on simulator, delimitation of the tumor contour on the radiogram, central cross-section in T1 T2 glottic cancer and in T3 glottic and all supraglottic cases two cross-section fitting to the first and second stage of the treatment.
Time of irradiation was calculated by computer. The dose was estimated in the reference point ICRU in the middle between the two lateral portals.

Statistical methods

Survival time, response to the treatment, time to the loco-regional recurrence and loco-regional control probability were analyzed. The survival time and time to loco-regional recurrence was calculated from the beginning of irradiation to the last follow up information or to the event – death or loco-regional recurrence respectively. The response to treatment was defined as complete tumour regression (CR) observed three months after treatment completion. Time to loco-regional recurrence was available for CR patients. Survival probability and loco-regional recurrence-free probability were estimated using the Kaplan-Meier method [4]. Loco-regional control probability was obtained by multiplication of the CR-probability and loco-regional recurrence free probability. The prognostic factors analysis for survival and loco-regional recurrence free probability was performed by means of Cox's proportional hazard model [5]. Analysis of prognostic factors analysis for treatment response was performed using the logit regression model. The indicator of the treatment schedule (conventional / concomitant boost) was involved into the models. In the first step of the modeling process the typical prognostic factors: age, sex, stage, site, hemoglobin level, performance status and histological differentiation were included. In the modeling process the backward selection method on the p=0,1 level was applied. The models obtained were used for testing the two factors: cigarette smoking intensity and respiratory insufficiency. The statistical significance level was fixed as

α=0.05. The definitions of the analyzed factors are presented in Table I.

Table I. Patient characteristics

		N (%) 372 (100) or mean ± SE
T-stage		
	T1	74 (20)
	T2	123 (34)
	T3	112 (30)
	T4	57 (16)
	missing	6
N-stage		
	N-	270 (73)
	N+	100 (27)
	missing	2
site		
	supraglottic	197 (57)
	glottic	151 (43)
	missing	24
hemoglobin level (Hb)		13.8 ± 0.09
	missing	36
sex		
	female	45 (12)
	male	327 (88)
age		
	≤55	138 (37)
	(55, 70]	197 (53)
	>70	37 (10)
performance status (WHO)		
	0	238 (64)
	1	112 (30)
	>1	21 (6)
	missing	1
differentiation		
	G1	148 (41)
	G2	82 (22)
	G3	29 (8)
	Gx	107 (29)
	missing	6
respiratory insufficiency		
	no	311 (84)
	yes (tbc, coronary disease, hypertension)	61 (16)
smoking (cigarettes/day * years)		
	0	116 (31)
	(0, 580]	74 (19)
	(580, 875]	91 (25)
	>875	91 (25)
treatment protocol		
	conventional	251 (68)
	concomitant boost	121 (32)

Results

The overall survival and the survivals for the early (T1-T2) and late (T3-T4) stages are presented in Figures 1 and 2. Similarly, curves for loco-regional recurrence-free probability and for loco-regional control probability are shown on Figures: 3-4 and 5-6, respectively. The related probability values for 2, 5 and 8 years of follow-up time are shown in Tables II, IIIa and IIIb. In the early and late stages the patients with metastases in the lymphatic nodes

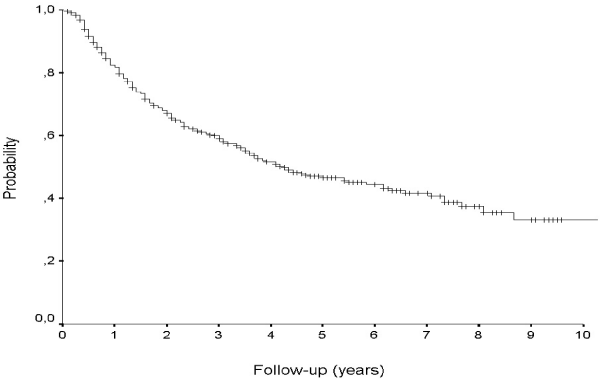

Figure 1. Survival curve (entire group)

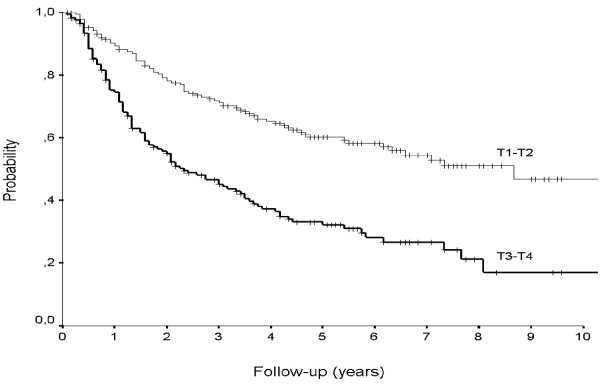

Figure 2. Survival curves in T1-T2 and T3-T4 stages

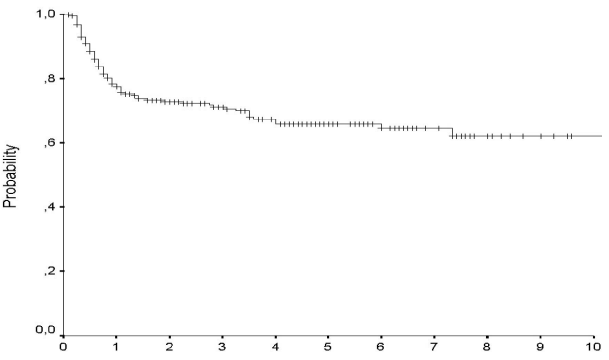

Figure 3. Loco-regional recurrence-free probability curve (patients with CR)

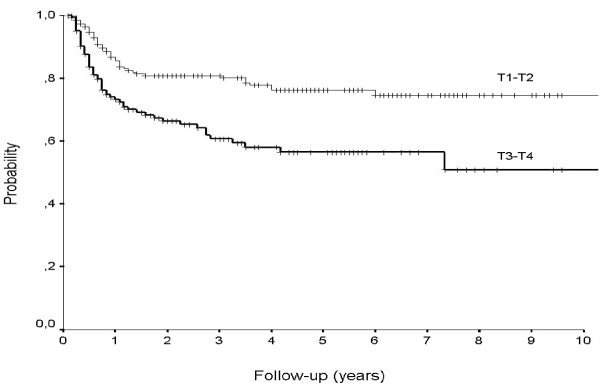

Figure 4. Loco-regional recurrence-free probability curve in T1-T2 and T3-T4 stages (patiens with CR).

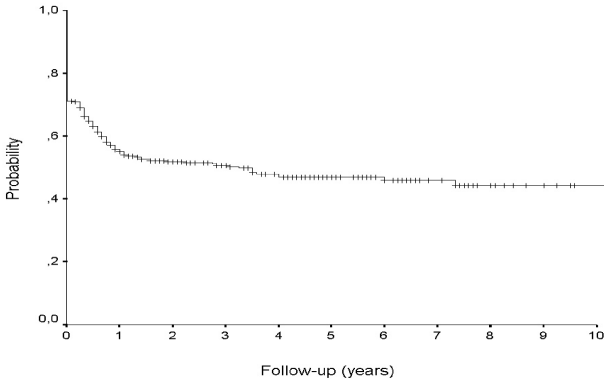

Figure 5. Loco-regional control (entire group)

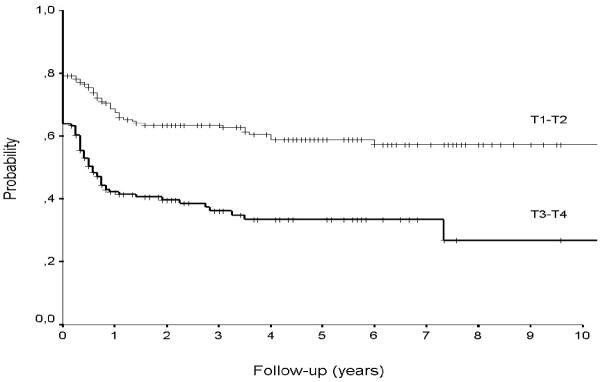

Figure 6. Loco-regional control in T1-T2 and T3-T4 stages

Table II. Survival probability in T1-T2 and T3-T4 stages

Follow-up (years)	Survival probability ± standard error		
	All patients	T1-T2	T3-T4
2	0.67 ± 0.03	0.78 ± 0.03	0.55 ± 0.04
5	0.47 ± 0.03	0.60 ± 0.04	0.32 ± 0.04
8	0.37 ± 0.03	0.51 ± 0.05	0.21 ± 0.05

Table IIIa. Loco-regional recurrence-free probability in T1-T2 and T3-T4 stages

Follow-up (years)	Probability ± standard error		
	All patients	T1-T2	T3-T4
2	0.73 ± 0.03	0.80 ± 0.03	0.67 ± 0.04
5	0.66 ± 0.03	0.76 ± 0.03	0.57 ± 0.04
8	0.62 ± 0.04	0.75 ± 0.04	0.51 ± 0.07

Table IIIb. Loco-regional control in T1-T2 and T3-T4 stages

Follow-up (years)	Probability ± standard error		
	All patients	T1-T2	T3-T4
2	0.52 ± 0.03	0.64 ± 0.04	0.40 ± 0.04
5	0.47 ± 0.03	0.59 ± 0.04	0.34 ± 0.04
8	0.44 ± 0.03	0.57 ± 0.04	0.27 ± 0.07

(N+) made a 14% and 41% rate, respectively. CR was observed in 265 (71%) cases.

Cox's model factors for the death risk function and the loco-regional recurrence are presented in Table IV and Table VI, respectively. Table V presents the parameters of the logit regression model for CR. The frequency of the early and late reactions were presented in Tables VII, VIIIa, VIIIb. The most frequent early reactions, i.e. pain on swallowing, confluent mucositis and moist skin reaction were recorded in 69%, 48% and 41% of cases, respectively. Serious late complications were noted in 19 patients. In a majority of these cases several forms of serious damage were observed. Rescue surgery was performed in 56 patients (29%) with diagnosed recurrence. In 25 patients (7%) a second cancer was recorded during follow-up.

The prognostic value of T and N factors for survival was confirmed (Table IV). Patients with advanced stages of the disease (T3, T4) have a twice as high death risk as patients in early stages (T1, T2). The death risk of patients with the N(+) feature is also about double that of patients with N(-) feature. We also confirmed the influence of the performance status on survival. Patients with

Table IV. Cox's model factors for the death risk function

Variable	β	Standard error	p – value	Relative risk
T-stage			0.0241	
T2	0.2710	0.2522	0.2825	1.3113
T3	0.5901	0.2539	0.0201	1.8042
T4	0.7607	0.2784	0.0063	2.1398
N+	0.8136	0.1709	<0.0001	2.2560
male	0.4345	0.2627	0.0981	1.5441
age		0.0319		
(55, 70]	0.1519	0.1806	0.4004	1.1640
>70	0.7307	0.2836	0.0100	2.0765
performance status (WHO)			<0.0001	
1	1.0732	0.1625	<0.0001	2.9247
2	1.4217	0.2976	<0.0001	4.1440
respiratory insufficiency	0.1371	0.2043	0.5023	1.1469
smoking (cigarettes/day * years)			0.6292	
(0, 580]	-.2652	0.2273	0.2433	0.7670
(580, 875]	-.0401	0.2070	0.8462	0.9606
>875	-.1716	0.2137	0.4220	0.8423
Concomitant boost	0.0778	0.1701	0.6475	1.0809

Table V. Logit model factors for the probability of CR

Variable	β	Standard error	p – value	Odds ratio
T-stage		0,0057		
T2	0.0207	0.3627	0.9551	1.0209
T3	-.5757	0.3495	0.1045	0.5623
T4	-1.1098	0.3938	0.0063	0.3296
respiratory insufficiency	0.8464	0.3850	0.0279	2.3313
smoking (cigarettes/day * years)			0.9521	
(0, 580]	0.0983	0.3437	0.7749	1.1033
(580, 875]	0.0360	0.3269	0.9124	1.0366
>875	-.1062	0.3286	0.7465	0.8992
Concomitant boost	0.3040	0.2679	0.2564	1.3553
Constant	0.3969	0.3780	0.2937	

Table VI. Cox's model factors for the risk of loco-regional recurrence

Variable	β	Standard error	p – value	Relative risk
T-stage		0,0012		
T2	0.6953	0.4118	0.0914	2.0042
T3	1.4500	0.4096	0.0004	4.2630
T4	1.1184	0.4804	0.0199	3.0598
respiratory inefficiency -	.1361	0.3208	0.6713	0.8727
smoking (cigarettes/day * years)			0.1882	
(0, 580]	-.5280	0.3473	0.1284	0.5898
(580, 875]	0.0517	0.2862	0.8567	1.0530
>875	-.4739	0.3367	0.1593	0.6226
Concomitant boost	0.2888	0.2409	0.2305	1.3348

Table VII. Early reactions

	N (%)
	372 (100%)
Pain at swallowing	237 (69%)
missing	30
Need for analgesics	
local	32 (11%)
general	43 (15%)
narcotic	15 (5%)
missing	80
Muccositis	
patchy	146 (44%)
confluent	158 (48%)
missing	40
Dysphagia	
light	145 (43%)
severe	58 (17%)
missing	40
Skin erythrema	169 (92%)
missing	188
Dry desquamation	196 (82%)
missing	132
Moist desquamation	73 (41%)
missing	194

Table VIIIa. Late reactions

	N (%)
Skin teleangiectasiae	
no	231 (92.4)
(0, 1] cm	13 (5.2)
[1, 4) cm	5 (2.0)
> 4cm	1 (0.4)
missing	122
Skin oedema	
no	211 (85.1)
light	22 (8.9)
medium	12 (4.8)
severe	3 (1.2)
missing	124
Skin fibrosis	
no	216 (86.4)
light	25 (10.0)
medium	9 (3.6)
missing	122

WHO=1 or WHO=2 have a respectively three or four times higher death risk than patients with WHO=0. We observed no influence of sex, histological differentiation, hemoglobin level and tumor site on survival. The negative influences of cigarette smoking and of potential respiratory insufficiency were not confirmed.

The significant influence of T-stage on the treatment response (CR) was confirmed (Table V). The CR chance of patients with T4 tumours equals 33% of the CR chance of patients with T1 tumours. The treatment response analysis of patients with expected respiratory insufficiency indicated significantly better results than in patients with no such anamnesis (!). The T-stage

Table VIIIb. Late reactions

	N	(%)
Mucosal ulceration		
no	242	(96.0)
yes	10	(4.0)
missing	120	
Mucosal teleangiectasiae		
no	237	(95.6)
(0, 1] cm	8	(3.2)
[1, 4) cm	2	(0.8)
> 4cm	1	(0.4)
missing	124	
Deep mucosal necrosis		
no	246	(96.9)
yes	8	(3.1)
missing	118	
Dysphagia		
no	228	(88.7)
light	15	(5.8)
medium	9	(3.5)
severe	5	(1.9)
missing	115	
Dryness		
no	206	(83.7)
light	21	(8.5)
medium	16	(6.5)
severe	3	(1.2)
missing	126	
Oedema		
no	200	(77.2)
yes	59	(22.8)
missing	113	
Chondritis		
no	243	(94.9)
yes	13	(5.1)
missing	116	
Chondronecrosis		
no	246	(96.9)
yes	8	(3.1)
missing	118	
Bone necrosis		
no	255	(97.7)
yes	6	(2.3)
missing	111	

was found to be the only significant risk factor of loco-regional recurrence (Table IV). Respiratory insufficiency and cigarette smoking did not influence loco-regional outcomes.

Pain on swallowing and confluent mucositis were the most frequent early reactions.

Medical remarks and considerations

In retrospective studies statistical analysis is usually performed following the typical outline of estimating the treatment outcomes and prognostic factors. This is the framework which provides the answers to the most essential questions and facilitates the comparisons with other studies. However, apart from such fundamental statistical estimations, there are several problems which require further attention and interpretation [6-12].

About 45% of patients qualified for treatment by radiotherapist – and – ENT surgeon team were in advanced stages of the disease (T3-T4), and, in 27 % of cases, presented cervical lymph node metastases. The intention of such policy was to preserve the larynx, while radical surgical treatment was considered only as salvage surgery in patients either not cured, or with recurrent cancer. In our material only 29% of these recurrence patients were operated. In 71% of such cases surgery was not performed for a number of reasons, such as lack of patient consent, highly advanced stage of disease after a very long time of awaiting admission, etc. It must also be kept in mind that in a number of uncured patients tumour growth was much more rapid after radiotherapy. In our opinion better collaboration between radiotherapists and surgeons provides a chance for considerable improvement of treatment outcomes.

The radiotherapists are chiefly interested in local curability, estimated at least three years after treatment. Local control is the fundamental criterion of treatment efficacy, while in the studies on the outcomes of radiotherapy statistical analysis must give a clear and univocal answer to this question. Complete regression (CR), often applied in clinical elaboration, is very important in evaluating the efficiency of chemotherapy, where local curability is seldom the subject of the main interest and treatment efficicacy is usually presented as overall survival. However, CR estimation can give quite reliable information and allow to compare the significance of the studied clinical factors. This first estimation of outcome is also important because a majority of local failures are diagnosed at that moment. Patients with recurrence should be immediately referred for surgery. Another reason for follow up examinations to be held immediately after the end of treatment is to estimate the intensity of postirradiation reactions – an indicator of treatment tolerance.

The survival curves (Figure 1, 2) come down steeply not only during the first two years, but also three and more years after treatment completion. When confronted with the curve illustrating the local regional outcomes, it may indicates that after three years mortality is not brought on by primary cancer, but rather by other causes, such as distant metastases, second primary cancer – chiefly of the lung – or other diseases. The problem of this "over-mortality" is the subject of a separate study.

The influence of overall treatment time on local control in head and neck cancer was the subject of many papers [6, 12, 13]. The prolongation of total treatment time is considered to be one of the most important factors negatively influencing treatment outcomes. This problem is the subject of separate study.

The local regional outcomes of treatment – 62% of cure in early cases and 36% in patients with stage T3-T4 – are less satisfactory then expected, especially in non-advanced cases. The limited number of serious reactions and late complications suggests the possibility of increasing the total dose or shortening the total time of treatment within the limits of admissible morbidity.

Literature data indicates worse radiotherapy outcomes in patients not refraining from tobacco smoking during the course of irradiation. This observation was not proven by our study material.

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References

1. Hliniak A., Michalski W, Szutkowski Z. Cancer of the larynx. The outcomes of conventionality fractionated radiotherapy in prospective and retrospective studies. Is the meaning of conventionality the same? *Nowotwory J Onc* 2001; 51: 381-385.
2. Bulski W, Hliniak A, Piętak R et al. A comprehensive data-base system for radiotherapy patients records (in Impact of Personal Computer on Radio Oncology Departments), *European Association of Radiology, 4th Workshop*, Geneva, 1991
3. Bujko K, Skoczylas J, Bentzen SM, Hliniak A et al. A feasibility study of concomitant boost radiotherapy for patients with cancer of the supraglottic larynx, *Acta Oncologica* 1993; 00: 1-4.
4. Kaplan EL, Meier P. Non-parametric estimation from incomplete observations. *J Am Stat Soc C* 1958; 53: 457-487.
5. Cox DR. Regression models and life tables (with discussion) *J Roy Stat Soc B* 1972; 34: 187-220.
6. Fowler JF, Linstrom M.J. Loss of local control with prolongation in radiotherapy. Int J Rad Onc Biol Phys 1992; 23: 457-.
7. Lindstrom MJ, Fowler JF. Re-analysis of the time factor in local control by radiotherapy of T3T4 squamous cell carcinoma of the larynx. *Int J Rad Onc Biol Phys* 1991; 21: 813-
8. Hliniak A, Maciejewski B. Back from the ranch to "bed side". Dyskusja o praktycznej aplikacji badań nad niekonwencjonalną radioterapią chorych na raka regionu głowy i szyi. *Nowotwory J Onc* 2001; 51: 49-59.
9. Maciejewski B, WithersHR, Taylor JMG. Dose fractionation and regeneration in radiotherapy for cancer of the oral cavity and oropharynx: Tumor dose-response and repopulation. *Int J Rad Onc Biol Phys* 1989; 16: 831-.
10. Millon RR. The larynx... so to speak: Everything I wanted to know about laryngeal cancer I learned in the last 32 years. *Int J Rad Oncol Biol Phys* 1992; 23: 691-703.
11. Overgard J, Hansen HS, Jorgensen K. Primary radiotherapy of larynx and pharynx carcinoma – an analysis of some factors infuencing local control and survival. *Int J Rad Oncol Biol Phys* 1986; 12: 515-.
12. Quynh-Thu X.LE, Karen FFU, Kroll S. Infuence of fractionation size, total dose and overall time on local control of T1-T2 glottic carcinoma. *Int J Rad Onc Biol Phys* 1997; 39: 115-.

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