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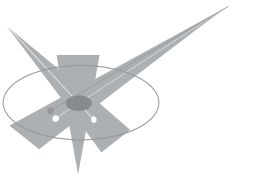

Original Paper

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Treatment of carcinoma of the oral cavity with radical and postoperative radiotherapy at the Institute of Oncology Ljubljana, 1990–1995

Primož Petrič, Primož Strojan, Marjan Budihna

Department of Radiation Oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia

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Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Aim To evaluate the treatment results of squamous cell carcinoma of the oral cavity treated with radical or postoperative radiotherapy at the Institute of Oncology Ljubljana, in the period 1990–1995.

Materials/Methods The medical records of patients were used to collect the data according to the predefined Data Acquisition Protocol. The impact of individual clinical and histopathological factors on the treatment outcome was evaluated by uni- and multivariate analysis.

Results Combined therapy was performed in 142 patients, and 93 patients had radiotherapy only. In each of the two subgroups, the performance status of patients was assessed as "poor" in 7% and 30%; the proportion of T1–2 tumours was 53.6% and 16.1%, and the proportion of cN0-stage tumours was 38% and 29%. The 5-year survival without local failure in surgically treated and irradiated only patients was 89% and 30%, without neck failure 85.7% and 50.3%, without any failure 79.1% and 27.5%, and overall survival 43.9% and 11.5%, respectively (all $P<0.0001$). In multivariate analysis, the performance status and cT-stage emerged as independent prognostic factors for all four types of survival analyzed. The type of therapy retained its independent prognostic value only in the case of survival without local failure.

Conclusions The only independent predictors of survival were performance status and cT stage, whereas the type of therapy impacted only local cure rate. The difference in survival results between the two treatments reflects primarily selection bias which occurred when patients were directed to one of the two treatment options.

Key words **oral cavity • squamous cell carcinoma • radiotherapy • surgery • survival**

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Author's address: Correspondence to: Assist. Prof. Primož Strojan, M.D, Ph.D., Department of Radiation Oncology, Institute of Oncology Ljubljana, Zaloška 2, SI-1000 Ljubljana, Slovenia, e-mail: pstrojan@onko-i.si

Background

The term *cancer of the oral cavity* (OC) denotes all types of malignancies occurring in the area extending from the vermilion border to the posterior edge of the hard palate or to the mobile tongue. The majority of patients with oral cancer are elderly males with a history of smoking and alcohol abuse [1]. In Slovenia in 2003, 87 men and 19 women contracted cancer of the OC (excluding lip carcinoma) [2].

Histologically, the most frequent type of OC cancer is squamous cell carcinoma (SCC), covering almost 90% of all cancers in this area [1]. The risk for developing carcinoma of the OC is directly proportional to the degree and length of exposure of the oral mucosa to tobacco. Alcohol additionally intensifies local carcinogenic effect of the tobacco; hence, areas that are longer exposed to alcohol will probably more frequently contract cancer. There are also other factors that influence the development of cancer, e.g. genetic susceptibility to mutagenicity of certain substances, deficiency of vitamin A in food and devices that cause chronic mechanical irritation of the mucous membrane, such as a carelessly designed dental prosthesis [1,3].

The most frequent site of SCC of the OC is the mobile tongue, usually its lateral edges, where 35–40% of all cases occur. The next most frequent site is the floor of the mouth, with the occurrence of 30–35% of all cases, while other areas in the mouth are less frequently attacked [4]. Given that these cancer sites are easily accessible and that the morbidity is rather low, the majority of patients with early stage disease are operated on, whereas patients with advanced but still operable carcinoma are treated with surgery in combination with postoperative irradiation and some particular cases also with chemotherapy. Tumours which are technically inoperable are treated with radiotherapy (RT) and concomitant chemotherapy [1].

Aim

The results of OC carcinoma treatment have not been systematically analyzed in Slovenia. Therefore, the aim of our study was to assess the results of treatment of SCC of the OC (excluding carcinoma of the lip) in patients treated with radical or postoperative RT at the Institute of Oncology Ljubljana (IOL) in the years between 1990 and 1995.

Materials and Methods

Selection of patients and data collection

Patients who were treated for SCC of the OC with curative percutaneous RT between the years 1990 and 1995 at the IOL were included. Patients with synchronous or previously treated but uncured malignancy as well as patients with incomplete or missing medical documentation were excluded from the study.

Main data sources were the database of the Cancer Registry of the Republic of Slovenia and medical records archived at the IOL, Department of Otorhinolaryngology and Cervicofacial Surgery and Department of Maxillofacial and Oral Surgery, both at the University Medical Centre Ljubljana, and the Department of Otorhinolaryngology at the Maribor Teaching Hospital. The patients' data were gathered from the medical records by following the uniform Data Acquisition Protocol, which consisted of the following data groups:

- patients' data: sex, age, performance status (due to incomplete descriptions, only a simplified two-grade scale was used, i.e. *good*, corresponding to World Health Organization [WHO, Ref. 5] grade ≤1 and *poor*, corresponding to WHO grade >1), haemoglobin concentrations before and after treatment;
- data on the disease: anatomic sub-site of the primary tumour origin, disease stage according to the International Union Against Cancer [UICC, Ref. 6] TNM staging system, differentiation grade and keratinization;
- irradiation parameters: time interval from diagnosis to the beginning of therapy, time interval from surgery to irradiation (in postoperatively irradiated patients), daily irradiation dose, a total nominal tumour dose, frequency and duration of involuntary interruptions of irradiation, intensity of RT (in terms of biologically effective dose [BED, as defined in Ref. 7]);
- date and site of the first recurrence (in the case of persisting disease after the therapy or recurring disease in less than 4 months after the completed therapy, the date of completed therapy was defined as the recurrence date);
- date and cause of a patient's death.

The follow-up of patients and recording of events were completed on June 16, 2003.

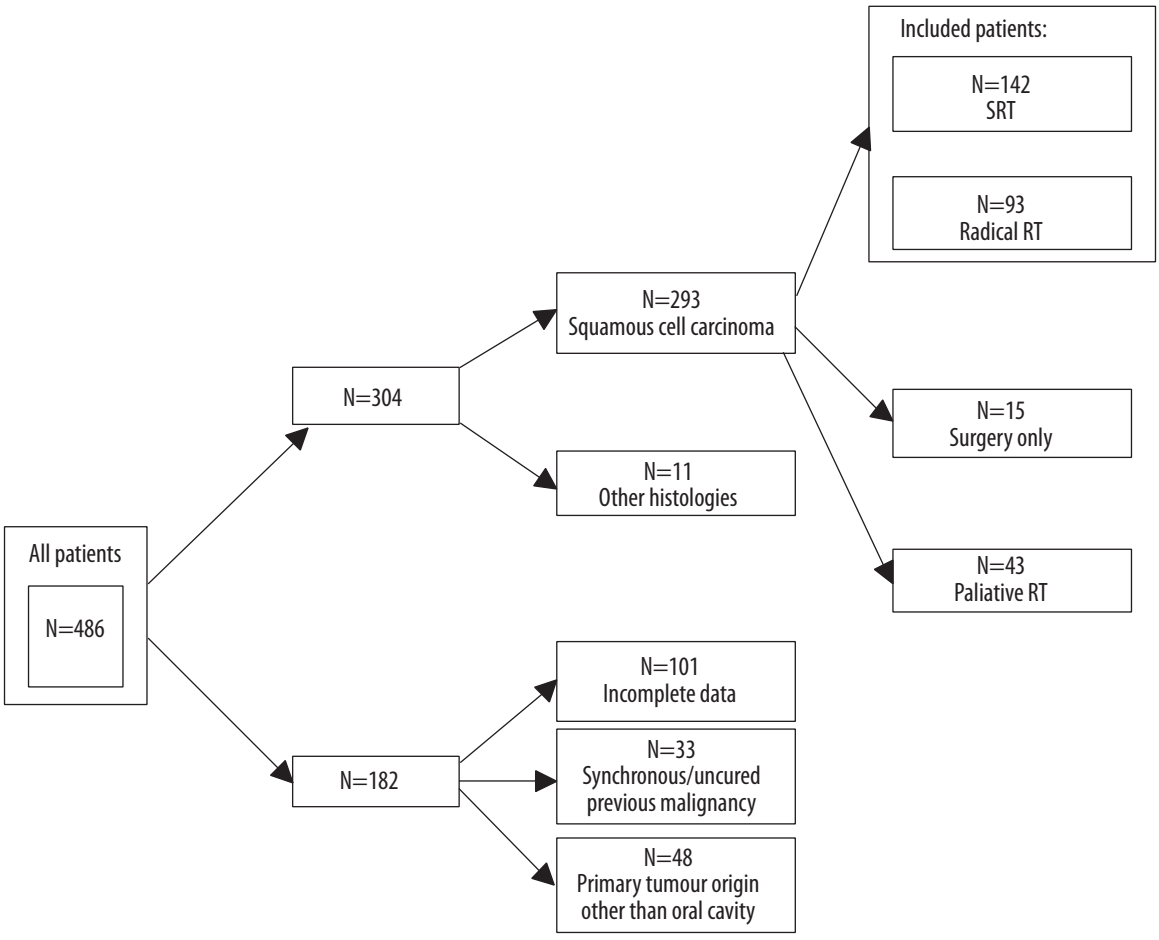

Figure 1. Selection of patients who entered the study (N – Number of patients; SRT – Surgery and postoperative radiotherapy; RT – Radiotherapy).

Statistical analysis

Data were analyzed by using the statistical program package SPSS, version 8.0 (SPSS Inc, Chicago, Illinois, USA), according to the intention-to-treat principle. All statistical tests were two-sided and a P value of <0.05 was considered statistically significant.

Continuous variables were defined by arithmetic mean, range and standard deviation, and categorical variables by the rate of occurrence. T-test for comparing two independent samples was used for continuous variables, and chi-square test or Fisher's exact test to evaluate the differences in frequency distribution of categorical variables. Univariate analysis of patients' survival was carried out using the Kaplan-Meier product-limit method [8] and log-rank comparison to evaluate the difference between the survival curves [9]. The analysis involved (*i*) survival without local failure (event: recurrence of primary tumour), (*ii*) survival without neck failure (event: recurrence on the neck), (*iii*) survival without any failure (event: recurrence on the primary site and/or in regional lymphatics, and/or distant metastases), and (*iiii*) overall survival (all deaths considered as events). The follow-up period and survival were calculated from the first day of therapy. Multivariate analysis was performed according to Cox's proportional hazard model where only variables that proved to be statistically significant by univariate analysis were introduced [10].

Results

Descriptive Data

Having examined the medical files, a list of 486 patients was created. Having taken into account the inclusion criteria, we could include only 235 patients in the final statistical analysis (Figure 1). Of these

Table 1. Basic descriptive data on patients and tumours by treatment modality.

Parameter	Treatment modality			P-value*
	All (N=235)	SRT (N=142)	RT (N=93)	
Age (years)**	57.4, 31-92	56.7, 31-82	58.6, 36-92	NS
Sex (M/F)	14.7/1	14.8/1	14.5/1	NS
Performance status				
– good	197 (83.3%)	132 (93.0%)	65 (69.9%)	<0.0001
– poor	38 (16.2%)	10 (7.0%)	28 (30.1%)	
Hb (g/L)**				
– before RT	134.0, 69-190	127.9, 107–153	137.0, 69–190	NS
– after RT	122.9, 67-153	122.4, 77–152	123.1, 67–153	NS
cT-stage				
– cT1	15 (6.4%)	13 (9.2%)	2 (2.1%)	<0.0001
– cT2	76 (32.3%)	63 (44.4%)	13 (14.0%)	(T1+T2 vs. T3+T4)
– cT3	49 (20.9%)	28 (19.7%)	21 (22.6%)	
– cT4	95 (40.4%)	38 (26.8%)	57 (61.3%)	
cN-stage				
– cN0	81 (34.5%)	54 (38.0%)	27 (29.0%)	<0.0001
– cN1	56 (23.8%)	34 (23.9%)	22 (23.7%)	(N0 vs. N+)
– cN2	90 (38.3%)	53 (37.3%)	37 (39.8%)	
– cN3	8 (3.4%)	1 (0.7%)	7 (7.5%)	
Overall UICC TNM stage				
– SI	9 (3.8%)	7 (4.9%)	2 (2.2%)	<0.001
– SII	33 (14.0%)	28 (19.5%)	5 (5.4%)	(SI+SII vs. SIII+SIV)
– SIII	56 (23.8%)	38 (26.8%)	18 (19.4%)	
– SIV	137 (58.3%)	69 (48.6%)	68 (73.1%)	
Degree of differentiation				
– G1	38 (16.2%)	26 (18.3%)	12 (12.9%)	NS
– G2	133 (56.6%)	89 (62.7%)	44 (47.3%)	(G1+G2 vs. G3)
– G3	30 (12.8%)	16 (11.3%)	14 (15.1%)	
– GX	34 (14.5%)	11 (7.7%)	23 (24.7%)	

* Comparison between SRT and RT groups. ** Average value, range.
N – Number of patients; SRT – Surgery and postoperative radiotherapy; RT – Radiotherapy; Hb –Haemoglobin; NS – Nonsignificant (statistically) difference.

235 patients, 142 (60.4%) were treated with surgery and postoperative RT (SRT group), and 93 (39.6%) were treated with curative RT alone (RT group). Mean age of all patients was 57.4 years (range 31–92); the ratio between male and female patients was 14.7/1. Characteristics of patients and tumours and comparison of the two groups are shown in Table 1, and the differences between clinical and pathological assessments of T-, N- and overall stage in the SRT group (stage migration) are shown in Table 2. The most frequent sites of origin of the primary tumour were the floor of the mouth (45.5%) and the tongue (38.3) (Table 3).

At diagnosis, metastases in the cervical nodes were more frequently detected in patients with

Table 2. Distribution of clinical and pathological T-, N- and overall UICC TNM stages in SRT group (N=142).

Parameter	Clinical assessment	Pathological assessment
T-stage		
– T1	13 (9.2%)	10 (7.0%)
– T2	63 (44.4%)	67 (47.2%)
– T3	28 (19.7%)	26 (18.3%)
– T4	38 (26.8%)	39 (27.5%)
N-stage		
– N0	54 (38.0%)	79 (55.6%)
– N1	34 (23.9%)	31 (21.8%)
– N2	53 (37.3%)	32 (22.5%)
– N3	1 (0.7%)	0 (0.0%)
Overall UICC TNM stage		
– SI	7 (4.9%)	4 (2.8%)
– SII	28 (19.5%)	43 (30.3%)
– SIII	38 (26.8%)	37 (26.1%)
– SIV	69 (48.6%)	58 (40.8%)

locally advanced tumours (cT3–4, 72.9%) than in patients with early tumours (cT1–2, 53.8%; p=0.003). In the SRT group of patients in whom clinical examination at diagnosis detected no evidence of metastases in the regional lymph nodes (N=54), metastases were confirmed in 24% of these cases by a histopathological examination of the resected specimen following surgical treatment. Metastases were more frequent in patients with tongue carcinoma (35%) than in those with floor of the mouth tumour (20%). In patients with clinically determined neck node involvement (N=88), histopathological examination of resected tissue from the neck did not show any metastases in altogether 43.2% of cases (tongue carcinoma 44.4%; floor of the mouth carcinoma 45.7%).

Course and technique of irradiation

The mean interval from the diagnosis (in RT group) or surgery (in SRT group) to the first day of RT was 23.7 days (range 0–186) and 27.9 days (range 8–119), respectively. More than 95% of patients of both groups were irradiated by a telecobalt unit. Daily doses ranged between 1.8 and 2.0Gy in 78.5% of patients from the RT group

Table 3. Anatomic subsite of primary tumour origin in oral cavity.

Anatomic subsite	Treatment modality		
	All (N=235)	SRT (N=142)	RT (N=93)
Floor of mouth	107 (45.5%)	71 (50.0%)	36 (38.8%)
Tongue	90 (38.3%)	47 (33.1%)	43 (46.2%)
Lower gum	20 (8.5%)	13 (9.1%)	7 (7.5%)
Retromolar trigon	15 (6.4%)	9 (6.3%)	6 (6.4%)
Upper gum	1 (0.4%)	1 (0.7%)	0
Buccal mucosa	2 (0.8%)	1 (0.7%)	1 (1.1%)
Hard palate	0	0	0

N – Number of patients; SRT – Surgery and postoperative radiotherapy; RT – Radiotherapy.

and in 96.5% of patients from the SRT group. In patients who were treated with radical RT, the applied tumour dose was more frequently lower by >4Gy from the initially planned tumour dose than in postoperatively irradiated patients (19.4% vs. 9.1%; p=0.040). In the RT group, the therapy was more frequently discontinued (55.9% vs. 26.8%, p=0.0001) and the breaks were also longer (11.7 days vs. 2.6 days, p=0.0001) compared to the SRT group. In both groups, RT was prematurely completed in 23.7% of patients and 13.4% of patients, respectively (P>0.05).

Survival of patients

Mean follow-up of all patients (regardless of treatment modality) was 42.8 months (range 2–157) and was 80.0 months (range 3–137) for those alive at the last follow-up examination.

All four types of survival in each of the two groups of patients are graphically presented in Figure 2. In all cases, the differences were statistically significant (P<0.0001), speaking in favour of postoperatively irradiated patients (Table 4). In the case of survival without local failure, the difference between the two groups of patients exceeded the threshold of statistical significance in patients with early stage tumours (cT1+2; P=0.0217) as well as in those with locally advanced tumours (cT3+4; P<0.0001). Survival without neck failure was significantly different only in the N+ subgroup (p<0.0001), whereas in cases of survival without any failure and of overall survival, the difference was significant only in patients with advanced disease (UICC TNM stage III+IV; P<0.0001) (Table 4).

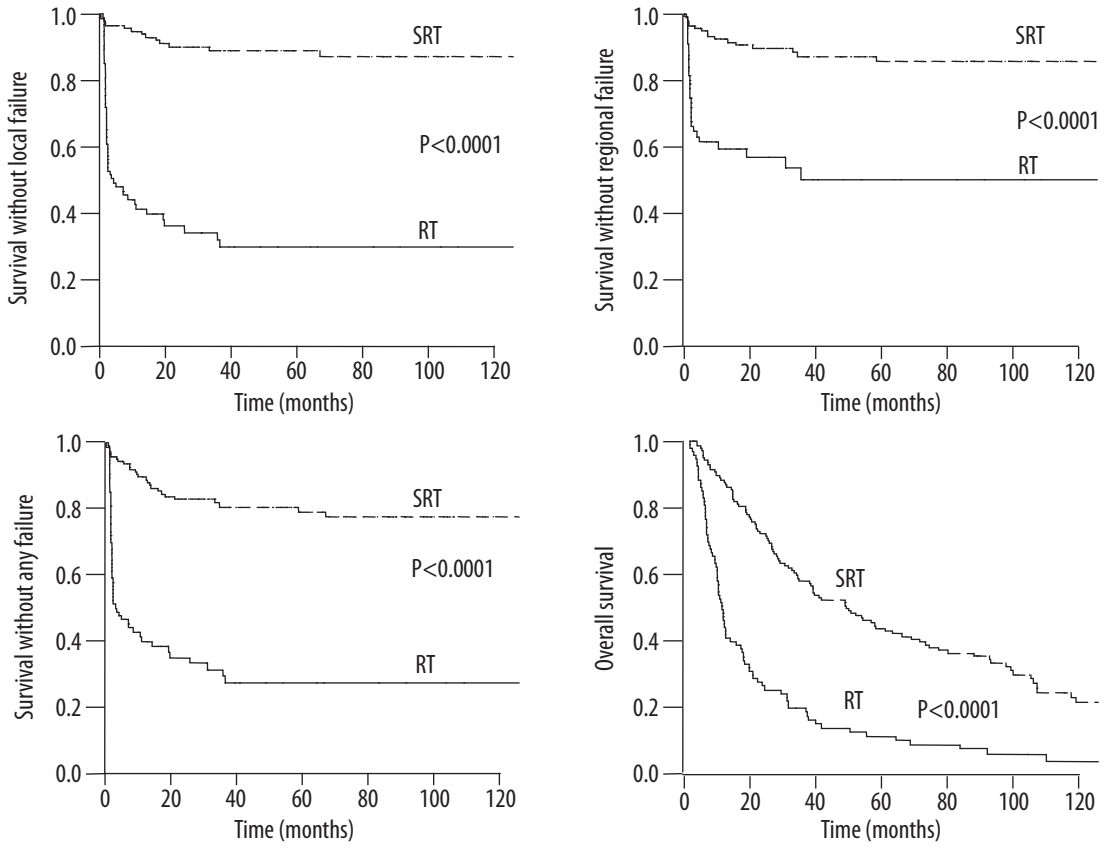

Figure 2. Survival of patients by treatment modality (SRT – Surgery and postoperative; RT – Radiotherapy).

Higher cure rate in the SRT group was observed in patients whose performance status was assessed as *good* than in those in *poor* general condition. At five years, survival without local and regional failure was 83% vs. 64%, respectively (P=0.040), survival without any failure 81% vs. 53%, respectively (P=0.007), and overall survival 43% vs. 22%, respectively (P=0.031). In patients with no unfavourable histopathological prognostic factors (e.g. extracapsular tumour spread, tumour emboli in the lymphatic or blood vessels, perineural tumour spread), 5-year survival without local and regional failure was 86%, whereas in patients with adverse prognosticators (single or in combination) it was 72% (P=0.018). Improved survival with local and regional failure was noted also in patients younger than 53 years compared to older ones (87% vs. 70%, P=0.038); differences in survival without any failure and overall survival were not statistically significant.

A more detailed univariate analysis of survival in the RT group indicated the vital role of the patient's performance status and of therapy intensity. Patients who were in better general condition had longer survival than patients in poorer general condition; this was valid for all types of survival analyzed (P<0.05). Higher RT intensity, expressed in terms of BED, was a key factor, prognosticating a longer survival, but only in good performance status patients. At five years, survival without local and regional failure of these patients was 60%, whereas in the group treated with less intensive therapy it was only 33% (P=0.024). The same was observed in the case of survival without any failure, but not in the case of overall survival (19% vs. 12%, P>0.05).

Treatment results of the second half of the observation period (1993–1995) were significantly superior to those from the first period (1990–1993). Hence, survival without local and regional failure at five years in the SRT group was 77% in the first half-term of the observation period, and in the second, 87%. Accordingly, median survival without local and regional failure in the RT group was also extended from 6 to 29 months.

The results of multivariate analysis are presented in Table 5. Performance status and cT-stage of the disease proved to be the key independent prognostic factors. The poor performance status pa-

Table 4. Survival of patients after five years of follow-up by treatment modality.

Survival	Treatment modality				P-value**
	SRT (N=142)		RT (N=93)		
	N	Survival*	N	Survival*	
Without local failure					
– cT1+T2	76	93.3%	15	70.5%	0.0217
– cT3+T4	66	82.5%	78	22.5%	<0.0001
– all	142	89.0%	93	30.0%	<0.0001
Without neck failure					
– cN0	54	91.2%	27	85.0%	NS
– cN+	88	74.1%	66	22.6%	<0.0001
– all	142	85.7%	93	50.3%	<0.0001
Without any failure					
– stage I–II	35	93.1%	7	85.7%	NS
– stage III–IV	107	74.1%	86	22.6%	<0.0001
– all	142	79.1%	93	27.5%	<0.0001
Overall					
– stage I–II	35	59.9%	7	28.6%	NS
– stage III–IV	107	38.3%	86	10.1%	<0.0001
– all	142	43.9%	93	11.5%	<0.0001

*At five years of follow-up; ** Comparison between SRT and RT groups.
N – Number of patients; SRT – Surgery and postoperative radiotherapy; RT – Radiotherapy.

tients and those with locally advanced disease of clinical stages T3–4 did worse with respect to all types of survival analyzed than patients in good general condition and with early stage (cT1–2) tumours. Mode of therapy reached the threshold of statistical significance only in the case of survival without local failure.

Discussion

The presented results give an insight into the efficacy of radical treatment for SCC of the OC performed at the IOL in the period 1990–1995, provide an estimate of the prognostic significance of some patient-, tumour- and treatment-related factors and allow a comparison with the treatment results obtained at other institutions. However, the inherent drawbacks of the retrospective nature of our study should be taken into account.

Patients' characteristics

Demographic characteristics of our patients were similar to those from comparable studies performed elsewhere [11–13]. The only exceptions were a more pronounced difference between the sexes in our patient group with a male-to-female ratio of 14.7/1 and an unusually high percentage (83.3%) of patients with the performance status defined as *good*. The latter is mainly due to the selective criteria applied in the recruitment of patients eligible for surgery: in the SRT group, the percentage of patients in good performance status was as high as 93%, whereas in the RT group it was statistically significantly lower, amounting to only 69.9%

Tumour characteristics

In view of the frequency distribution of primary tumour origin in the OC and distribution of cT-, cN- and overall UICC stages, our data are consistent with the data from the literature [4,14]. Some digressions were observed in tumours of the cheek (only 2 cases were detected), and in tumours of the hard palate (not found in our patients). In the SRT group, the distribution of patients with cT1–2 and cT3–4 disease stages appeared to be fairly even (53.5% and 46.5%,

Table 5. Multivariate analysis of survival.

Parameter	Survival							
	Without local failure		Without neck failure		Without any failure		Overall	
	P-value	HR	P-value	HR	P-value	HR	P-value	HR
Treatment modality								
– SRT								
– RT	<0.0001	0.15	NS	–	NS	–	NS	–
Performance status								
– good								
– poor	0.0236	0.53	0.0006	0.31	<0.0001	0.32	<0.0001	0.41
cT-stage								
– cT1–2								
– cT3–4	0.0346	0.37	0.057	0.283	0.0001	0.23	0.0001	0.44

SRT – Surgery and postoperative radiotherapy; RT – Radiotherapy; HR – Hazard ratio; NS – Nonsignificant (statistically) difference.

respectively), while in the RT group the distribution was less favourable, being biased toward advanced tumours (16.2% and 83.9%, respectively). The comparison in the frame of overall UICC stages III and IV also showed that, in the SRT group, the incidence of cT4 tumours was lower (35%) than in the RT group (84%). These differences between the groups are statistically significant and are due to a selection bias – referring patients with prognostically less favourable disease to treatment with RT alone.

According to the data from the Cancer Registry of Slovenia, in the period 1983–1997, the percentage of patients with SCC of the OC without regional lymph node involvement was 29.5% [15], whereas this percentage among the patients from our study was 34.5% (SRT 38%, RT 29%). In reports comparable to ours, the percentage of cN0 stage ranged from 23% to 89%, which reflects the differences in the distributions of cT stages and of primary tumour origin in the OC between individual studies (4, 16). The incidence rate of cN+ stage increased with cT stage and was statistically significantly higher in patients with cT3–4 tumours than in those with cT1–2 tumours (72.9% vs. 53.85, P=0.003). This difference was observed in both patients with carcinoma of the floor of the mouth and patients with carcinoma of the tongue. Due to the small number of patients, the analysis of other anatomic subsites did not seem reasonable.

In 38% of patients from the SRT group who were without regional lymph node involvement (cN0) at diagnosis, metastases were diagnosed after surgery. A similar share of patients with false negative cN0 stage was also reported by other authors, ranging between 15% and 40% [4,16]. On the other hand, the percentage of patients with false positive cN+ stage was as high as 43.2%.

Treatment results

From the evidence it may be concluded that RT has a curative potential in early stage (T1–2) tumours comparable to surgery. Treatment results with irradiation in more advanced stages (T3–4) are less favourable. Local control of T1–T2 tumours at five years after RT ranges between 43% and 98%, whereas in patients with locally advanced disease it is only 17–54%. Corresponding overall survival rates at five years are 36–85% and 5–39%, respectively [12,13,17–24]. In the advanced stages of the disease, the combination of surgery and postoperative irradiation yields better local and regional control of the disease and better survival of patients [11,13,19,21]. So far, no randomized studies have been performed to compare combined treatment with RT alone. This may only be proved indirectly, by retrospective studies such as ours which are subject to all the drawbacks of such analyses, including the selection bias which seems to be the most critical of all.

In the studied period, the results of combined treatment of our patients were similar to the treatment results obtained elsewhere. Moreover, the pattern and time frame of disease recurrence

were also comparable to the literature data, whereas the results of treatment with radical RT were worse than those reported from other institutions [12,13,16–19]. However, in both cases the treatment results in the period 1993–1995 were statistically significantly better than in the period 1990–1992.

The reasons for the worse outcome in the RT group may lie in the recruitment of patients for RT and its characteristics:

1. The distribution of cT stages in the RT group was biased toward advanced tumour stages (T1–2 tumours 16.1%, T3–4 tumours 83.9%), whereas the distribution in the SRT group and in comparable studies performed by other institutions [12,13,17–20] was more favourable. In the multivariate analysis of survival, the cT stage of the disease, besides the performance status, proved to be the next most important prognostic factor.
2. In the majority of comprehensive retrospective studies, at least part of the irradiation in patients with smaller tumours was delivered using brachytherapy, which definitely can improve the results [17,18,29]. All the patients in our study were treated exclusively with percutaneous irradiation.
3. In as many as 17% of patients, surgery was contraindicated due to poor medical condition, and another 17% of patients refused the proposed operation (possibility of lower motivation for therapy cannot be ruled out). Therefore, the performance status of patients in the RT group was assessed as *poor* in as many as 30% of cases (in the SRT group 7%, P<0.0001). This resulted in frequent interruptions (55.9%) of RT of long duration (mean 11.7 days), and in the applied tumour dose, which was >4 Gy lower than the prescribed tumour dose in one fifth (19.4%) of patients from the RT group.
4. It is well recognized that treatment intensity depends on the performance status of a patient: those in poor general condition are not fit to tolerate aggressive RT schedules. Given the high percentage of such patients, it was expected that the treatment results in the RT group would be less favourable. On the other hand, in a selected group of irradiated patients with good performance status it was proved that more intensive treatment (i.e. higher BED) prognosticated longer survival without local, regional or any failure. The survival of these patients was by all means comparable to the survival of patients from other comparable studies [11–13,17–19]. Treatment intensity, however, did not affect overall survival because of competitive (non-malignant) risks of death.

The results of univariate and multivariate analyses of the prognostic value of individual clinical and histopathological factors are congruent with the published results [11–13,17–21]. The performance status of patients and cT stage of disease proved to be two major independent prognosticators. Irrespective of the applied treatment modality, the performance status has kept its independent prognostic value for all types of survival analyzed. The same holds true also for cT stage. As expected, after correcting the influence of performance status and primary tumour stage, treatment modality became of lesser importance. Combined treatment with surgery and postoperative RT was found to be a statistically significant and independent prognosticator only for survival without local failure, whereas in all other analyzed survival types no statistically significant differences were observed between the two treatment modalities. It may therefore be assumed that, for regional control of the disease, irradiation alone may be as effective as the combination of surgery and postoperative RT, provided that both groups of patients are comparable in performance status of patients and cT stage of disease. Furthermore, the length of overall survival is far more dependent on the lifestyle of patients and their habits than on the treatment modality.

Conclusions

There are several possibilities to compensate the negative influence of adverse prognosticators and to improve the rather poor presented results in the radical RT group, both obviously originating from the selection bias when referring patients to different treatment programmes (i.e. patients with less advanced tumours and/or better performance status are usually directed to surgery). The most reliable seems to be to upgrade the therapeutic regimes with additional chemotherapy or brachytherapy and to improve RT planning and delivery by means of intensity-modulated RT (IMRT). The foreign experience is favourable in all three cases. In this context, the most interesting would be a comparison of results obtained so far with the treatment results obtained in the next five-year period, which was marked specifically by the introduction of chemotherapy into the majority of RT regimes, i.e. postoperative RT as well as radical RT of inoperable tumours [22–24]. Unfortunately, the treatment results of brachytherapy and IMRT are not yet available at the IOL because of insuffi-

cient technical capacities that do not allow their application in routine clinical practice.

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