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Comparison of Three Postoperative Follow-up Methods in Patients with Oral Cancer

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ABSTRACT

The goal of this research was to determine the existence of the significant time differences in the identification of the recurrences and neck metastases in the patients surgically treated for the oral cavity cancer by comparing three postoperative follow up methods. The study included 286 patients surgically treated for oral and pharyngeal cancer in period from 1991 to 2007 at three different institutions, divided into three groups based on the different postoperative follow up protocol. In this study we were able to show that the period of identification of recurrences and neck metastases was significantly shorter in the group of patients whose follow up included neck ultrasound, along with methods of inspection and palpation of the oral cavity and the neck. In conclusion, implementation of more contemporary methods such as the neck ultrasound is needed along with usual follow up methods, such as inspection and palpation of the oral cavity and the neck. Also, follow up of the patients surgically treated for the oral cavity cancer should be conducted systematically¹. Ultrasound examination of the neck should be recommended due to its low cost, harmlessness, possible frequent usage, high quality visual imaging and possibility of combination with the fine needle aspiration cytology (FNAC) of the suspicious lymph nodes.

Key words: oral cancer, pharyngeal cancer, follow up, ultrasound

Introduction

It is well known that management of patients with oral cancer does not end with surgical treatment. Follow up in the postoperative period after oral cancer surgery is almost as equally important as surgical treatment itself due to the high percentage of recurrences and neck metastases within that period². Percentage of recurrences depends on the initial disease stage at the time of surgery as well as on the type of surgical intervention. Namely, the radical operation during the lower stage of the disease leads to the higher percentage of recovery from oral cancer than the same radical operation performed at the higher disease stage.

Another important factor is the type of surgical intervention used for patient management which can be either local tumor excision or local excision with unilateral neck dissection or tumor excision with bilateral dissection of the neck.

Assuming we have clear criteria for the type of surgical treatment needed for the particular stage of the disease³⁻⁴, it is possible to estimate the efficacy of chosen surgical procedure, and at the same time, the efficacy of recurrences detection and neck metastases based on the specific follow up method.

It is important whether recurrences or neck metastases are discovered in the early or advanced stage of disease⁵, because this is crucial factor for the efficacy of the secondary surgical intervention as well as therapy in general⁶. If the unilateral neck metastasis is discovered after the local excision of the tumor, the neck dissection can be performed significantly earlier if the postoperative follow up is adequate^{7,8}.

Similarly, if the metastases on the contra lateral side of the neck appear after the »commando«⁹ operation, the dissection of that part of the neck can be performed sig-

nificantly earlier if the postoperative follow up is adequate.

Also, if a local recurrence is detected, a secondary surgical intervention can be performed, including tumor excision with unilateral or even bilateral dissection of the neck.

This study compares three postoperative follow-up methods used for 286 patients treated for the oral cavity and pharyngeal cancer in the period between 1991 to 2007 at Department of Oral and Maxillofacial Surgery, Rijeka University Hospital Center; Department of Otorhinolaryngology – Head and Neck Surgery, Zagreb University Hospital Center and Department of Oral and Maxillofacial Surgery, Osijek University Hospital Center.

During this period different postoperative follow up methods were used. The alterations in the follow-up protocols are the consequences of changes in the consensus recommendations regarding checkup intervals and introduction of new diagnostic tools in postoperative follow up^{10–13}.

Despite generally accepted rules there are still some significant differences among Departments regarding checkup intervals and used tools for that purpose^{14,15}.

Therefore, the main purpose of this retrospective study is to evaluate differences in the length of the time passed before the recurrences or neck metastases were discovered between three different patient groups surgically treated at different departments based on the different follow up protocols.

Patients and Methods

The study included 286 patients surgically treated for oral and pharyngeal cancer in period from 1991 to 2007, who had local recurrences and/or neck metastases within 2 years after the operation. Data were collected at Department of Oral and Maxillofacial Surgery, Rijeka University Hospital Center; Department of Otorhinolaryngology – Head and Neck Surgery, Zagreb University Hospital Center and Department of Oral and Maxillofacial Surgery, Osijek University Hospital Center. The time until the recurrence was observed is shown in months. It represents the number of months passed from the operation until the follow up examination which revealed the suspicion of a local recurrence and/or neck metastases. In all cases the diagnosis was confirmed either by lymph node biopsy, tissue biopsy or by ultrasound guided lymph node cytopunction.

Protocol

Subjects were divided into three groups based on the postoperative follow up protocol. In the first group, which consisted of 92 patients, the postoperative follow up was not systematic and it was conducted upon surgeon's estimation, mainly every 2 to 3 months. The postoperative follow up included inspection and palpation of the oral cavity and neck. Diagnostic tests such as neck ul-

trasound, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) were only conducted in case of appearance of symptoms or physical examination indicating a possibility of recurrences and/or neck metastases.

The second group consisted of 105 patients who were systematically followed up, once a month during the first postoperative year, and once in 2 months during the second postoperative year. Examination methods were inspection and palpation, whereas neck ultrasound, CT and MRI were performed only when symptoms or physical examination indicated a possibility of recurrences and/or neck metastases.

The third group consisted of 89 patients, who were systematically followed up, once a month during the first postoperative year, and once in 2 months during the second postoperative year. Besides inspection and palpation every physical examination included neck ultrasound^{16,17} every 4 to 6 weeks during the first postoperative year and every 8 weeks during second postoperative year. If the suspected lymph nodes were found the neck ultrasound was followed by ultrasound-guided fine-needle aspiration cytology (USg FNAC). CT and MRI were conducted if symptoms and signs of recurrence and neck metastases could not be proven by ultrasound and USg FNAC^{18–25}.

Also, these 3 groups of patients were further divided into 4 subgroups based on 4 disease stages according to 1987 IUAC criteria²⁶. This way it was possible to compare patients that were surgically treated at the same disease stage and were checked up using different postoperative follow up protocols.

The patients divided into 3 groups, according to their postoperative follow up protocol, were also divided into 3 subgroups according to the type of surgical intervention used. The first subgroup included patients who underwent the local excision of the tumor, either intraoral or extraoral, without neck dissection (type A). In the second subgroup, beside tumor excision, unilateral neck dissection was performed (type B). In the third subgroup, beside tumor excision, bilateral neck dissection was performed (type C).

The term excision also implies marginal or segmental mandibular resection, when required, and the term neck dissection includes all types of dissection.

Thus, in the latter case, used postoperative follow up protocols were compared within patient groups that underwent same surgical interventions.

Statistical analysis

Computer program Statistica 4.3, Statsoft, Inc: 1**3, was used for all statistical calculations. Statistical analysis was performed by Student's t-test and Mann Whitney U test. Sign test was used for the comparison of follow up differences. P values of <0.05 were used as cut-off for statistical significance.

Results

Comparison of group I and group II follow up

Comparing the length of time when recurrences/metastases were discovered between group I, (follow up was conducted every 2–3 months within two years of postoperative follow up by inspection and palpation) and group II (follow up was more systematic, once a month during the first postoperative year and once in 2 months during the second postoperative year also by inspection and palpation), we found time differences for all four disease stages as well as when patients were grouped based on specific surgical procedure used.

The difference in the length of time until recurrences/metastases were observed between group I and group II, for disease stage 1 was 1 month, for disease stage 2 the difference was 1.1 month, for disease stage 3 the difference was 1.5 month, and for disease stage 4 1.6 month. However, this difference in the time passed until recurrences were observed was statistically significant only for disease stage 2 ($p=0.026$, Table 1), 3 ($p=0.048$, Table 1) and 4 ($p=0.045$, Table 1).

TABLE 1
COMPARISON OF GROUP I AND GROUP II FOLLOW UP

	Number of cases group I	Mean time of group I (months)	Number of cases group II	Mean time of group II (months)	P
St 1	14	14.3	13	13.3	0.137
St 2	28	12.6	32	11.5	0.026
St 3	30	11.7	35	10.2	0.048
St 4	20	9.6	25	8.0	0.045
OP A	22	13.0	22	12.0	0.060
OP B	53	12.2	61	10.6	0.041
OP C	17	9.6	22	8.5	0.038

St 1, St 2, St 3, St 4 – disease stages according to International Union Against Cancer, 1987, OP A – local excision of the tumor, OP B – local excision of the tumor with unilateral neck dissection, OP C – local excision of the tumor with bilateral neck dissection

When comparing the length of time until recurrences/metastases were discovered based on the type of surgical procedure used, between groups I and II, we found 1 month time difference for the type A surgery, 2.4 months for the type B surgery and 1.1 month for the type C surgery. However, statistically significant time difference, when recurrences were observed depending on surgical procedure, was observed only for type B surgery ($p=0.041$, Table 1) and type C surgery ($p=0.038$, Table 1).

Comparison of group I and group III follow up

The comparison of group I and group III (follow up included clinical examination and neck ultrasound every 4–6 weeks during the first year and every 8 weeks during

the second year) revealed the difference in the length of time until recurrences/metastases were discovered in all four disease stages. For disease stage 1 the difference in the length of time when recurrences/metastases were observed between group I and group III was 4.7 months ($p=0.013$, Table 2), for disease stage 2 time difference was 4.6 months ($p=0.00005$, Table 2), for disease stage 3 time difference was 4.7 months ($p=0.00002$, Table 2) and for disease stage 4 the time difference was 4.6 months ($p=0.0068$, Table 2). All differences were statistically significant ($p<0.05$).

TABLE 2
COMPARISON OF GROUP I AND GROUP III FOLLOW UP

	Number of cases group I	Mean time of group I (months)	Number of cases group III	Mean time of group III (months)	P
St 1	14	14.3	12	9.6	0.013
St 2	28	12.6	26	8.0	0.00005
St 3	30	11.7	32	7.0	0.00002
St 4	20	9.6	19	6.0	0.0068
OP A	22	13.0	18	9.2	0.0000476
OP B	53	12.2	51	7.0	0.0000033
OP C	17	9.6	20	6.9	0.0074

St 1, St 2, St 3, St 4 – disease stages according to International Union Against Cancer, 1987, OP A – local excision of the tumor, OP B – local excision of the tumor with unilateral neck dissection, OP C – local excision of the tumor with bilateral neck dissection

When comparing the length of time until recurrences/metastases were observed depending on the type of surgical procedure used, between groups I and III, we found statistically significant differences between groups, which were, 3.8 months for type A surgery ($p=0.00004$, Table 2), 5.2 months for type B surgery ($p=0.000003$, Table 2) and 3.7 months for type C surgery ($p=0.0074$, Table 2).

Comparison of group II and group III follow up

Comparing the length of time when recurrences/metastases were discovered between group II and group III revealed the statistically significant time difference in the identification of recurrences and neck metastases in all four disease stages. For disease stage 1 the time difference was 3.7 months ($p=0.0091$, Table 3), for disease stage 2 the time difference was 3.5 months ($p=0.0032$, Table 3), for disease stage 3 the time difference was 3.2 months ($p=0.00025$, Table 3) and for disease stage 4 the time difference was 2 months ($p=0.0065$, Table 3).

Comparing the length of time until recurrences/metastases were observed depending on the type of surgical procedure used, between groups II and III, we found statistically significant time differences in the identification of recurrences and neck metastases for all three surgical procedures. The time difference for the type A surgery was 2.8 months ($p=0.01$, Table 3), for the type B surgery

TABLE 3
COMPARISON OF GROUP II AND GROUP III FOLLOW UP

	Number of cases group II	Mean time of group II (months)	Number of cases group III	Mean time of group III (months)	P
St 1	13	13.3	12	9.6	0.0091
St 2	32	11.5	26	8.0	0.0032
St 3	35	10.2	32	7.0	0.00025
St 4	25	8.0	19	6.0	0.0065
OP A	22	12.0	18	9.2	0.010
OP B	61	10.6	51	7.0	0.00017
OP C	22	8.5	20	6.9	0.019

St 1, St 2, St 3, St 4 – disease stages according to International Union Against Cancer, 1987, OP A – local excision of the tumor, OP B – local excision of the tumor with unilateral neck dissection, OP C – local excision of the tumor with bilateral neck dissection

3.6 months ($p=0.00017$, Table 3) and for the type C surgery 1.6 month ($p=0.019$, Table 3).

Comparison of group I, group II and group III follow up

Comparing the average length of time until recurrences/metastases were discovered between group I, group II and group III, using one of the three follow up protocols we found statistically significant difference in the length of recurrences/metastases free period between group I and II ($p=0.0027$, Table 4), group I and III ($p=0.2 \times 10^{-7}$, Table 4), and group II and III ($p=1.66 \times 10^{-5}$, Table 4).

TABLE 4
COMPARISON OF FOLLOW UP BETWEEN GROUPS I, II AND III

Group 1 (mean)	Group 2 (mean)	Group 3 (mean)	P
11.91	10.45		0.0027
11.91		7.42	0.00000002
	10.45	7.42	0.0000166

Discussion

This study shows statistically significant difference in the length of time until recurrences and neck metastases were discovered, in group of patients whose postoperative follow up was systematical, once a month during first postoperative year, and once in two months during second postoperative year (group II) comparing to the group of patients whose follow up was not systematical, and it was conducted according to the surgeon's evaluation, mainly every 2 to 3 months, over period of two years (group I). When comparing the length of time until recurrences and neck metastases were discovered in the

different stages of disease, between these two groups of patients (group I and group II) recurrences/metastases were discovered significantly earlier within disease stages 2, 3, and 4 in group II. Similarly, when comparing the length of time when recurrences and neck metastases were discovered between groups I and II, depending on the type of surgical procedure used (type A, type B, type C), recurrences/metastases were discovered significantly earlier when type B and type C surgical protocol was used in group II.

Furthermore, the comparison between groups II and III (group III consisted of patients, who's follow up was systematical and included, besides inspection and palpation, neck ultrasound every 4 to 6 weeks during first postoperative year and every 8 weeks during second postoperative year) showed significantly shorter period of time until recurrences and neck metastases were discovered in patient's group III.

This observation, that period of time until recurrences/metastases were discovered was much shorter in group III, was statistically significant for all four disease stages as well as for all three types of surgical procedures performed. Comparison between groups I, II and III based on the type of surgical procedure was performed in order to show that differences in the length of time passed until recurrences and neck metastases were discovered are result of efficacy of used postoperative follow up methods, and not a result of different surgical treatments since all three types of surgical procedures were performed on almost equal proportions of the patients in all three groups.

Thus, this study showed the importance of a systematical follow up, as opposed to a follow up based upon physician's estimate. Follow up periods varying from once a month during the first postoperative year to once in two months during the second postoperative year are consistent with the data which show that majority of recurrences and neck metastases are discovered by the end of the first postoperative year, and almost all recurrences/metastases by the end of the second postoperative year^{27–29}.

The results are even better if the usual, above mentioned methods are supplemented with regular ultrasound examinations^{30–33} combined with ultrasound guided fine needle aspiration cytology^{34–37}. This study showed that combination of the classic follow up methods and ultrasound examination are superior over classical check up methods alone.

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USPOREDBA TRI NAČINA POSTOPERACIJSKOG PRAĆENJA PACIJENATA SA KARCINOMOM USNE ŠUPLJINE

SAŽETAK

Cilj rada bio je utvrditi da li postoji značajno odstupanje u vremenu proteklom do otkrivanja recidiva i metastaza vrata kod pacijenata operiranih od karcinoma usne šupljine uspoređujući tri načina njihovog postoperacijskog praćenja. U studiju je uključeno 286 pacijenata operiranih od karcinoma usne šupljine i ždrijela u periodu od 1991. godine do 2007. godine u tri ustanove. Pacijenti su podijeljeni u tri skupine po osnovi različitog postoperacijskog načina praćenja. U ovoj studiji dokazano je da je vrijeme potrebno za utvrđivanje recidiva i metastaza vrata značajno kraće u grupi gdje je uz metode inspekcije i palpacije usne šupljine i vrata korištena i ultrazvučna pretraga vrata. Zaključak je da je primjena neke od suvremenijih metoda kao što je ultrazvučna pretraga vrata nužna uz primjenu uobičajenih metoda kao što su inspekcija i palpacija te da bi praćenje pacijenata operiranih od karcinoma usne šupljine trebalo biti sustavno. Ultrazvučna pretraga vrata se preporuča zbog niskih troškova, neškodljivosti, mogućnosti učestale primjene, visoke kvalitete prikaza i mogućnosti kombinacije sa citološkom punkcijom sumnjivih limfnih čvorova.