SURGICAL TREATMENT OF EARLY ORAL CARCINOMA—RESULTS OF A PROSPECTIVE CONTROLLED MULTICENTER STUDY

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Abstract: *Purpose of the study.* To assess whether early stage (pT1–2,pN0–1) oral cavity carcinoma is adequately treated by radical surgical resection alone.

Material and Methods. Prospective multicenter study. Of 105 patients with cT1–2 cN0–1 oral carcinoma treated in conformity with the study design, 12 had to be excluded because of tumor-positive margins or pN stage >N1. The remaining 93 patients were monitored for at least 2 years.

Results. Seventeen patients had local or regional recurrence develop. In 12 of the 17 patients locoregional control was achieved by second treatment. Overall, the 4-year disease-specific survival probability was 94%. Patients treated initially without selective neck dissection had significantly higher recurrence rates than those with neck dissection, although the survival probability was not adversely affected.

Conclusions. Early (pT1–2, pN0–1) squamous cell carcinoma of the oral cavity is adequately treated by surgery alone, provided the resection margins are tumor free. On the basis of the presented data, we would also advocate routine selective neck dissection. © 2001 John Wiley & Sons, Inc. *Head Neck* **23**: 525–530, 2001.

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The optimum treatment of early oral carcinoma is still disputed. The possibilities available include resection (with or without simultaneous neck dissection), radiotherapy alone, or a combination of surgery and radiotherapy. There are two arguments against the use of radiotherapy in the treatment of these patients. First, there is considerable risk of a second carcinoma developing in the upper aerodigestive tract in the years subsequent to successful therapy, in which radio-

therapy may prove to be imperative.[1–4] Second, there is substantial reduction in the patient's quality of life after radiotherapy of the oral cavity.[5–10]

The data reported in the literature allow the hypothesis that early oral squamous cell carcinoma, stage T1–2, is adequately treated by en bloc resection with tumor-free margins[11–15] without subsequent radiotherapy, provided that a maximum of one lymph node has been invaded by the tumor and no rupture of the capsule has taken place.[14,16,17] The goal of this study conducted by the Head and Neck Surgery Group of the Swiss Society of Otolaryngology was to confirm or disprove this hypothesis.

MATERIAL AND METHODS

Study Design. The study was devised as a prospective multicenter study. The study design required that all cases with histologically verified cT1–2 cN0–1 squamous cell carcinoma treated in the participating centers during the agreed time period should be documented in a standardized manner. Patients who had been treated for another malignancy (with the exception of basal cell carcinoma of the skin) in the preceding 5 years or in whom a second malignancy had been found in the aerodigestive tract before commencement of therapy were excluded from the study. In addition, a thorax x-ray examination was required to rule out the possibility of distant metastases. Palpation of the neck was supplemented by at least one imaging technique (ultrasonography, CT, MRI).

In accordance with local practice, all patients were presented to an interdisciplinary tumor board and informed about the various possibilities of treatment. Each patient was at liberty to choose a form of therapy other than the suggested surgical treatment.

The plan of treatment included the resection of the primary tumor (the choice of access was left to the surgeon) and a neck dissection (at least levels I–III) in cases in which neck metastases were suspected on clinical examination or imaging. If there was no suspicion of neck metastases, the decision whether to perform an elective neck dissection was left to the discretion of the surgeon. In each case the aim was to achieve tumor-free margins by the use of intraoperative frozen sections.

If the histologic examination of the resected specimen revealed that the primary tumor was larger than 4 cm (>T2), the resection was not histologically radical, more than one lymph node had been invaded by the tumor, or the capsule of the lymph node had been ruptured, the patient was removed from the study and referred for additional treatment.

Consequently, all patients with en bloc resection with tumor-free margins of carcinomas, stage pT1–2, pN0–1capsule- or cN0 (if no neck dissection had been performed) remained in the study.

After termination of treatment, the patients were re-examined every 3 months for 2 years, and subsequently every 6 months. In the event of a recurrence or second malignancy, the patient was removed from the study and referred for additional therapy of his or her own choice.

Recurrence of the tumor or the death of the patient marked the end points of the study.

Survival probabilities were calculated in accordance with Kaplan-Meier and compared with the aid of the log-rank test. Fisher's exact test was used to compare the recurrence frequency of different groups.

Study Population. The Departments of Otolaryngology, Head and Neck Surgery of Aarau, Basle, Berne, Geneva, Lucerne and Zurich, all in Switzerland, took part in the study. All patients treated in these six tertiary care centers in the period from May 1995 to April 1997 were recorded. The results were evaluated in May 1999. Hence, the period of observation subsequent to therapy totalled at least 2 years for all patients. However, three patients withdrew from aftercare after fewer than 24 months. The average duration of observation for the surviving patients is 32 months.

Overall, 128 patients with a cT1–2 cN0–1 squamous cell carcinoma of the oral cavity were treated. Eight of these patients had to be excluded because of a metachronous secondary carcinoma (7 carcinomas in the head-neck area, 1 bronchial carcinoma) and 2 because of a synchronous secondary malignancy (1 bronchial carcinoma, 1 malignant lymphoma). Two patients wished to be treated elsewhere, and 11 patients chose a different primary therapy.

Therefore, 105 patients were treated in conformity with the study design. Another 12 of these patients had to be excluded after receipt of the histologic result: 6 cases with N>N1, 1 case with capsule rupture, and 5 cases because of histologically nonradical resection. These patients were referred for additional radiotherapy. Therefore, it

was not possible to implement the planned strategy of therapy in 12 of the 105 patients (11%), leaving 93 patients for the final evaluation.

The average age of these 93 patients, 56 of whom were men and 37 women, was 59 years (29–89 years). Fifty-three carcinomas involved the tongue, 24 the floor of the mouth, 6 the retromolar trigone, 6 the hard palate or the alveolar process, and 4 the cheek. Clinically, 54 carcinomas were classified as T1, 39 as T2, 82 as N0, and 11 as N1.

Eighty-six of the 93 oral carcinomas were resected transorally and 7 transcervically. In 72 patients a neck dissection was additionally performed (61 homolaterally, 11 bilaterally), with none being conducted in the remaining 21 patients.
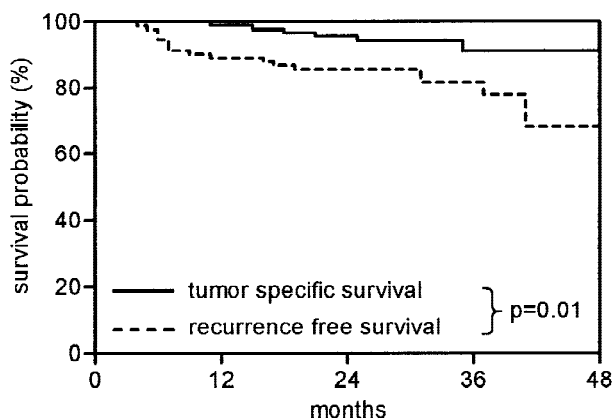
RESULTS

Overall, 17 of the 93 patients treated in conformity with the plan of treatment had a recurrence: 8 local, 2 local and contralateral cervical, and 7 ipsilateral cervical. Three of the 7 ipsilateral neck recurrences were found in the 72 patients with neck dissection, and 4 in the 21 patients without neck dissection (this difference is significant, $p = .04$). On the contralateral side of the neck, no recurrences were found in the 11 patients with bilateral neck dissection, whereas 2 occurred in the 85 patients not treated contralaterally.

In 5 patients the recurrence was treated by reoperation alone, in 7 by reoperation and subsequent radiotherapy, and in 4 patients by radiotherapy alone (no further treatment was performed in 1 patient). Overall, therefore, 11 patients finally underwent radiotherapy. Twelve of the 17 locoregional recurrences were successfully controlled by a second therapy. However, 5 patients died of an uncontrolled locoregional tumor.

In all, therefore, the probability of surviving for 4 years without a recurrence totalled 68%. A comparison of the recurrence-free with the tumor-specific survival probability (Fig. 1) verifies the efficiency of the second therapy for recurrences in this group of patients.

Thirteen of the 93 patients died during the period of observation. Six died of the consequences of the carcinoma (5 of an uncontrolled locoregional tumor, 1 of metastases in the lung despite locoregional tumor control). Seven patients died without evidence of tumor: 5 of a secondary carcinoma (4 bronchial carcinomas, 1 pancreas head carcinoma), 2 of cardiac infarction.

FIGURE 1. Recurrence-free versus tumor-specific survival probability ($n = 93$).

The tumor-specific survival probability after 4 years was therefore 91%.

If the patients excluded because of the histologic result are also incorporated, 13% occult metastases were found. These 13% false-negative assessments compare with 54% false-positive assessments.

DISCUSSION

The optimum therapy of early oral cancer is still disputed; radio-oncologists prefer radiotherapy (percutaneous and/or brachytherapy), whereas surgeons tend to favor surgery (alone or with subsequent radiotherapy). When seeking the optimum therapy, due consideration must be given to the patient's quality of life in addition to locoregional tumor control. Moreover, it must not be overlooked that the prognosis is not only dependent on locoregional tumor control, but that it is influenced to a significant degree by metachronous secondary carcinoma.

The patient's quality of life subsequent to therapy of early oral carcinoma has already been repeatedly examined in the past. Various studies have shown that the impairment of the quality of life after radiotherapy of the oral cavity is greater than after surgical therapy.[5–10] Beeken[5] and Bundgaard[6] have identified dryness of the mouth subsequent to radiotherapy as the major side effect after the treatment of oral carcinoma. Pauloski proved that the oral passage time after RT is significantly longer than after surgical treatment.[9] Finlay[7] successfully demonstrated that totally normal eating is achieved with significantly greater frequency after surgical therapy than after radiotherapy. Overall, the combination of the two therapy modalities proved to be particularly unfavorable.[6]

The problem of metachronous secondary carcinoma after the treatment of squamous cell carcinomas in the area of the aerodigestive tract has been known for a long time now. All in all, it must be assumed that 4% to 6% of patients with successfully treated oral carcinoma will have a secondary carcinoma develop per year,[1,2,4] and approximately half will die of a secondary carcinoma.[3] Because roughly half of these carcinomas occur in the head-neck area, the preceding therapy plays a decisive role.[1] Preceding radiotherapy usually restricts the possibilities of treatment to a much greater extent than previous surgical treatment. No therapy modality that is not absolutely essential for tumor control should ever be used.[18]

The patient's quality of life subsequent to therapy and the problem of metachronous secondary carcinoma, therefore, make radiotherapy of early oral carcinomas (alone or additionally) inadvisable, unless it is vital for locoregional tumor control. The question whether adequate locoregional tumor control is achieved after surgical treatment alone has not yet been resolved. This question can probably only be answered definitively by a randomized study (radiotherapy alone versus surgery alone versus surgery + radiotherapy). However, we did not consider such a study to be ethically justifiable in view of the points given earlier.

The relevant literature allows the hypothesis that locoregional control of $\geq$85% can be achieved with surgical therapy alone of a T1–2 N0–1 oral carcinoma.[12,16] An essential prerequisite for this is that an en bloc resection with tumor-free margins is achieved.[6,12–15,19,20] A further requirement is that a maximum of one cervical lymph node has been invaded by the tumor, and that the lymph node capsule has not been ruptured.[4,13,14,16,17] It was the goal of this study to confirm or disprove this hypothesis.

It was possible to implement the plan of treatment forming the basis of this study in 89% of the patients and can therefore be termed as feasible. In 6% the extent of cervical metastatic spread had been underestimated, and in 5% resection of the carcinoma had not been histologically radical, a rate that can be described as acceptable on the basis of the literature.[21]

The tumor-specific survival probability of 91% after 4 years observed by us confirms the hypothesis that early oral carcinoma is adequately treated by resection alone, and that there is no need for radiotherapy. However, it must not be overlooked that 16% of the patients had to be referred for a second therapy because of recurrence. Unlike studies described in the literature,[14,15,22] the salvage rate of 71% was very good, so that no drawback resulted for the patient from the wait-and-see approach.

Overall, only 23 of the 105 patients treated within the framework of the study received radiotherapy: 12 because of nonradical resection or to the underestimated extent of metastatic spread in the neck and 11 because of recurrence. These 23% patients who underwent radiotherapy contrast with the 77% who were spared an impairment of the quality of their lives by radiotherapy.

The importance of neck resection in the surgical treatment alone of these carcinomas is still being debated.[23] Overall, ipsilateral neck metastases occurred in 19 of the 105 (18%) patients who underwent surgery within the framework of the study. In 6 patients they were diagnosed primarily, in 9 patients occult neck metastases were found during the neck dissection, and neck metastases occurred secondarily in 4 patients without neck dissection. Our rate of 18% neck metastases is slightly less than that described in the literature. In particular, the rate of 9% occult metastases lies substantially below the values of 21% to 28% described by various authors.[11,18,22] However, it must be noted that imaging techniques were used to search for lymph node metastases in all patients. The high rate of false-positive neck node assessments can be explained by the liberal interpretation of these imaging techniques. In view of the considerable probability of occult metastases, Hicks,[12] Kligermann,[22] and Cunningham[11] consider the performance of an elective neck dissection to be essential. Conversely, Davidson,[24] Vandenbrouck,[25] and Ho[26] found no difference in survival between patients with and without elective neck dissection and hence favor a wait-and-see approach. Our own data show a significantly higher rate of cervical recurrence with no neck dissection but no relevant worsening of the survival probability and would therefore justify a wait-and-see approach. Nevertheless, in view of the minimal morbidity, we would plead for routine supraomohyoid neck dissection (removal of levels I–III), thereby improving the staging[27] and sparing the patient the trauma of recurrence and a second therapy. Under no circumstances would we dispense with neck dissection in patients for whom reliable aftercare cannot be guaranteed.

CONCLUSIONS

Squamous cell carcinoma of the oral cavity is adequately treated by surgical therapy alone provided:

- It is no larger than 4 cm (pT1–2)
- En bloc resection with tumor-free margins has been performed (R0)
- There is a maximum of one lymph node involved (pT0-1), with no rupturing of its capsule
- Reliable aftercare guarantees the early diagnosis of possible recurrence

This ensures that

- Local tumor control is achieved in more than 90% of patients
- 77% of patients are spared radiotherapy of the oral cavity with the resultant impairment of their quality of life and reduced possibilities of therapy in the event of a secondary carcinoma

However,

- Just under one fifth of patients must expect a recurrence and, hence, a second therapy
- If a routine elective neck dissection is not performed, higher recurrence rates must be expected (the influence of these secondary neck metastases on survival probability has not been clarified)

What remains to be clarified is

- The question whether and to what extent subsequent therapy (RT) improves the prognosis in nonradical resection
- The question of elective neck dissection

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