Is Routine Follow-up Useful After Combined-Modality Therapy for Advanced Head and Neck Cancer?

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**Objective:** To evaluate the usefulness of routine follow-up in a selected group of patients with head and neck cancer.

**Design:** Retrospective cohort study with follow-up of 5 years for all patients.

**Patients:** Three hundred two patients with advanced (stage III or IV) squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx were treated with curative intent with surgery and postoperative radiation therapy between January 1, 1970, and December 31, 1990.

**Main Outcome Measure:** Survival after recurrence of the index tumor or the development of a second head and neck primary tumor.

**Results:** Overall actuarial 5-year survival was 56%. Relapse occurred in 119 patients, and salvage therapy was attempted in 49 patients. Only 2 patients survived to 5 years after relapse.

**Conclusion:** In patients with advanced head and neck squamous cell carcinoma, routine follow-up is more important for evaluation of treatment results and emotional support than of benefit in improving patient survival.


HEAD AND neck squamous cell carcinoma has traditionally been described as a tumor type in which rigorous follow-up is required. This idea has evolved because patients are at risk for developing both recurrence of the original tumor and a new second primary tumor. Many studies have reported rates of second primary tumors after treatment of head and neck cancer; these are usually on the order of 10% to 20%, or around 5% per year.

The successful surgical treatment of recurrent tumors after primary radiation therapy (as single-modality therapy) has been well described. For example, studies of patients with recurrent laryngeal cancer after attempted curative radiotherapy of advanced disease report a surgical salvage rate of 35% to 60%. Data suggesting similar good results for patients with recurrence after having been treated with combined surgery and radiotherapy are lacking in the world literature. It is our impression that these patients do extremely poorly after relapse and rarely have an effective treatment option available.

The aim of this study was to evaluate whether routine follow-up conferred an advantage in long-term survival in a select patient group; in other words, whether curative treatment could be offered to patients with recurrence after combined-modality therapy for advanced head and neck cancer.

**RESULTS**

Three hundred two patients met the selection criteria outlined above. There were 236 men and 66 women. The median age at initial examination was 59 years, with a range of 26 to 83 years.

A breakdown of survival from specific sites is given in the Table. Actuarial 5-year survival for all sites from the date of initial examination was 56% by the Kaplan-Meier method. Fifty-two percent of patients were actuarially disease free at 5 years.

Relapse occurred in 119 patients, which represents 39.4% of the original 302 patients. There were 44 local recurrences, 42 regional recurrences, 50 distant metastases, and only 2 second head and neck primary neoplasms. Fifty per-
PATIENTS AND METHODS

The medical charts of all patients with head and neck squamous cell carcinoma treated at the Queensland Radium Institute, Brisbane, Queensland, between January 1, 1970, and December 31, 1990, were reviewed with the aid of computer-coded data forms. All patients’ cancers were staged according to TNM classification.8 Patients included in the study group were those with histopathologically confirmed stage III and IV squamous cell carcinoma of the oral cavity, oropharynx, larynx, and hypopharynx. Patients must have had no previous malignant neoplasm, and only patients treated with intent to cure were included. All patients were seen at 1 of our Combined Head and Neck Clinics before treatment. Patient treatment was individualized according to tumor type and the patient’s general condition.

Patient entry criteria were strict; only patients who had wide resection of the primary site were included. A neck dissection was performed for all N+ necks (radical or modified radical), for any N0 neck thought to have a high risk of occult disease (modified radical or selective), and for access in some cases. Most patients were treated surgically at the Princess Alexandra Hospital, Brisbane, or the Royal Brisbane Hospital. Free flaps were used in reconstruction of surgical defects in more than 70% of cases. Only patients who received external beam radiotherapy to the primary site and both sides of the neck were included in the study group. This was most commonly given postoperatively (usually 4 to 6 weeks after surgery). All patients were treated by 4- to 6-MV linear accelerators. Treatment volumes usually included through-and-through treatment to the upper part of the neck, with a matched anterior field to the lower part of the neck. Recommended minimum tumor dose was to treat areas where there was tumor before surgery to 60 Gy in 30 fractions during a 6-week period. Clinically negative areas were treated to a dose of 50 Gy in 25 fractions during 5 weeks. The median dose for the patients in the study group was 58 Gy.

During the early part of the period under consideration, neoadjuvant chemotherapy was favored and was used in 85 patients in this study group. This allowed treatment to begin immediately while operations were scheduled, dental extractions to proceed as necessary, and the patients’ general condition optimized. Chemotherapy was abandoned in the late 1980s when randomized studies suggested no clear survival benefit.

The Price-Hill chemotherapy regimen was used early in the study, after which time cisplatin and fluorouracil were used.

Five-year follow-up was available for all patients. The routine follow-up program consisted of recent medical history and head and neck examination at monthly intervals for 3 months, every 2 to 3 months up to 2 years, then every 4 to 6 months up to 5 years (with some variations, depending on the practitioners involved). An annual chest x-ray film was obtained. Additional investigations were performed when indicated.

Relapse was considered to be local recurrence, recurrence in either side of the neck, distant metastasis, or the development of a second head and neck primary neoplasm. For second primary malignant neoplasms, the criteria proposed by Warren and Gates9 were used: (1) the lesion must be clearly malignant as determined by histological examination; (2) each neoplasm must be graphically separate and distinct; and (3) the possibility that the second neoplasm represents a metastasis should be excluded.

The purpose of follow-up is 4-fold: (1) for the detection (and therefore treatment) of locoregional recurrence, distant metastasis, or second primary tumors; (2) for clinical audit, to allow evaluation of treatment results; (3) for emotional support; and (4) for the detection of complications resulting from treatment.

Routine follow-up, as opposed to symptom-based follow-up, should be considered useful if the asymptomatic lesions it detects are more curable than symptomatic lesions. This assumes that timely detection of recurrent disease will more often allow curative secondary treatment, an assumption that has yet to be proved for head and neck squamous cell carcinoma. Studies of other cancer types have suggested that routine follow-up is of limited benefit in improving overall survival.11-13

A study of routine follow-up in 661 patients with all stages of carcinoma of the head and neck showed a recurrence “cure rate” of only 1 in 113 consultations.13 The authors concluded that routine follow-up should be limited to patients with treatment options remaining, such as laryngeal tumors treated with radiotherapy. Patients

cent of all relapses were detected within 1 year, and 89% were detected within 3 years.

Salvage was attempted in 49 of these 119 patients with relapse. This involved different combinations of surgery, radiotherapy, and chemotherapy. Only 2 patients survived 5 years after relapse (Figure 2 and Figure 3). One patient had a recurrence in the contralateral undissected side of the neck 6 months after combined-modality treatment of a T3 N0 oral cavity squamous cell carcinoma. He was treated with a radical neck dissection and was free of disease at 5 years. The other patient had a recurrence at the primary site 8 months after combined-modality treatment of a T4 N0 oral cavity squamous cell carcinoma. He was treated with wide excision of the recurrent tumor and remained free of disease at 5 years. Both of these patients were symptomatic with their recurrence at the time of follow-up consultation. Median survival for patients with relapse was longer in the group undergoing attempted salvage: 6 months for the treated group compared with 4 months for those left untreated. This difference was significant (P<.001) but almost certainly results from a selection bias, whereby patients with less advanced disease are more likely to be considered candidates for curative treatment.

COMMENT

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with recurrence after combined-modality therapy for the index tumor did poorly.

Another study of routine follow-up in 428 patients with head and neck carcinoma concluded that routine follow-up is indispensable. However, in the subgroup of patients with advanced squamous cell carcinoma treated with combined therapy, no data were published to support this conclusion.

In this study group, routine follow-up detected only 2 patients with recurrent disease in whom curative secondary treatment was successful. Both of these patients were symptomatic with their recurrence, raising the possibility that symptom-based follow-up would have detected the recurrent disease at a similar stage.

Fifty percent of relapses were detected within 12 months (including the 2 “cures”), and 85% were detected within 3 years. This agrees with other published data and suggests that follow-up after 3 years may not be useful.

In this series, only 2 second malignant neoplasms in the head and neck were seen. This in part may reflect the difficulty in differentiating recurrence from second primary tumor in areas previously treated with extensive surgery and radiotherapy. However, it does concur with a previous study, whose authors raised the possibility that symptom-based follow-up would have detected the recurrent disease at a similar stage.

The cost of the follow-up used is impossible to accurately calculate, but any estimate must include the following:

- the cost of each visit to the medical practitioner
- the cost of travel to the medical practitioner
- the cost of routine investigations (eg, chest x-rays)
- the cost of further investigations ordered as a result of follow-up, eg, computed tomographic scans, contrast swallows, examinations under anesthesia or endoscopies
- the cost of treatment (including complications) if recurrent disease was found
- the cost borne by the community resulting from loss of productivity of the patient

Routine follow-up in these 302 patients was performed at considerable financial expense, not to mention morbidity of treatment for recurrent disease.

For the purposes of this study, relapse was considered to be locoregional recurrence, distant metastasis, or the development of a second head and neck primary neoplasm. While it could be said that the development of a pulmonary second primary neoplasm should be included as part of the relapse figures (else why the routine chest x-ray examination at follow-up?), reports indicate that this patient group has an almost uniformly poor prognosis.

This study attempts to clarify the survival benefits of follow-up in patients with advanced head and neck squamous cell carcinoma treated with combined surgery and radiotherapy. The results cannot be extrapolated to all head and neck cancer follow-up; patients initially treated with single-modality therapy have more treatment options available for recurrence and should be closely observed during the ensuing years.

### CONCLUSIONS

Despite numerous advances in head and neck surgery during the last 3 decades, the likelihood of a surgical cure is probably most dependent on tumor biology. The best chance of cure of a primary tumor resides in its initial treatment. In patients with advanced head and neck can-
cancer treated with combined-modality therapy, this study suggests that routine follow-up is more important for evaluation of treatment results and for patient reassurance than of benefit in improving patient survival.

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