The Effect of Overall Treatment Time of Radiotherapy to Local Control of Disease in Head and Neck Cancer

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Abstract

Background : Radiotherapy is commonly used in the management of patients with squamous cell carcinoma of head and neck. Various studies showed the total treatment time effect tumor control.

Purpose : To evaluate the effect of prolonged overall treatment time to the tumor control in squamous cell carcinoma of head and neck.

Methods and materials : Data from 114 patients with histological confirmed squamous cell carcinoma of head and neck (excluded nasopharyngeal cancer) were treated with radiotherapy at Department of Radiation Oncology, Chiang mai University, since 2001 (2544) - 2003 (2546), attention in duration of response and overall survival.

Results : All 114 squamous cell carcinoma of head and neck patients were treated with radiotherapy differentiated into two groups by total treatment time, group A:6-8 weeks and group B: more than 8 weeks. Median overall treatment time was 55.8 days (range 42-88 days). Overall 4-years locoregional progression rate were 47.7% for group A and 60.7% for group B, respectively (p=0.3532). Four year overall survival was 98.7% for group A and 83.3% for group B (p=0.4310).

Conclusion : The prolongation of overall treatment time trends to have poorer outcome in locoregional control and overall survival.

Introduction

Squamous cell carcinoma of head and neck can be successfully treated with radiotherapy. But local tumor control can be adversely affected by prolongation of overall treatment time because head and neck carcinoma is a heterogeneous group of cancer and radiation can induce accelerated proliferation of clonogenic tumor cells.[1] This has been supported indirectly by past experience which various fractionation schedules of primary radiotherapy for squamous cell carcinoma of head and neck.[2-3]

A number of studies have highlighted that tumor cell repopulation can produce losses in local control which, particularly for squamous cell carcinoma of the head and neck region may amount to 1-2% per day of treatment.[4-5] Similar in cervix and non small cell lung cancer (NSCLC) which have indicated respectively 1.6% and 0.8% loss of local control per day of treatment extension.[6,7]

In another prospective randomized study.[8] compared conventionally fractionated radiotherapy (63 Gy in 7 weeks) with accelerated radiotherapy (63 Gy in 5 weeks) in the postoperative setting with the rationale of reduction of the overall treatment time reduces the risk of tumor cell repopulation during treatment and therefore improves the probability of locoregional tumor control. In this study found that postoperative accelerated radiotherapy trend toward better locoregional control rate and the prolongation of the interval time between surgery and radiotherapy reduced in the locoregional control.

I therefore conducted a retrospective study to determine whether the overall treatment time could relate to the local-regional relapse or survival for squamous cell carcinoma of head and neck. This thesis information can use as data support for further management in cases of this situation.

Material and method

Type of study

This is a retrospective study.

Selection of study population

Patients with squamous cell carcinoma of head and neck who received radiotherapy in the Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, Thailand between January 2001 to December 2003.

Inclusion criteria

1. Histological documentation of squamous cell carcinoma of head and neck.
2. Treated with radiotherapy.



Exclusion criteria

1. Prior or concomitant malignancy.
2. Prior received radiotherapy at head and neck area.
3. Metastasis disease.
4. Chemotherapy for treatment head and neck cancer.
5. Nasopharyngeal carcinoma.

Treatment

All patients were divided into 1) operable group who received primary surgery followed by radiotherapy at tumor bed and regional node area. And 2) inoperable group received primary radiotherapy at the tumor and regional node, this included locally advanced stage disease and medical inoperable case.

Radiotherapy

All patients received radiotherapy at head and neck region cover primary tumor or tumor bed and regional lymph node by use three fields technique, composed two laterals of face and neck and one low anterior neck irradiation and immobilization with plastic mask. Total dose 6600-7000 cGy, over 6-7 weeks. Overall treatment time was divided into two groups: (A) 6-8 weeks and (B) more than 8 weeks.

Follow up

The patients were evaluated the primary tumor and regional lymph node response. The most part of the patients followed at one month; then two months; every three months in the first two years; every four month in the third year; every six months in the fourth and fifth year then yearly. The follow up was modified up to patients' condition (performance status, economic problem and distant from their home). This study was stopped collection data on November 2005.

Response to treatment evaluated by clinical examination and appropriate investigation on the date of follow up.

Data collection and management

All data on cases of squamouss cell carcinoma of head and neck were obtained from ENT records and radiation oncology medical records from January 2001 to December 2003.

Statistical analysis

Locoregional control, disease free survival and overall survival were calculated from the day of start radiotherapy by Microsoft excel program. Overall treatment time calculated day by day from the date of start radiotherapy to the last day of radiotherapy.

The univariate analysis LRC and overall survival were estimated with Kaplan-Meier method. To test the statistic significant of difference between curves uses logrank test.

Results

General information

From January 2001 to December 2003, 114 patients were included in this study. The median age was 66.7 years. The most common site of primary tumor was the oropharynx (63.16%) followed by hypopharynx (33.33%) and larynx (1.75%) respectively. Stage IV was found predominantly in this study (67.5%) (table 1). Thirty nine patients (34.2%) had received surgery and post-operative radiotherapy and seventy five patients (65.8%) had received primary radiotherapy alone. Mean radiation dose was 6282.56 cGy in postoperative group and 6854.52 cGy in radiotherapy alone groups. Mean overall treatment time was 55.8 days (range 42-88 days) (table 3). Mean follow up time was 726.62 days (table 2).

Table 1 Patient characteristics

Characteristic	Total (%) (N=114)	
Site of cancer		
Hypopharynx	38	(33.3)
Oropharynx	72	(63.2)
Neck node unknown	1	(0.9)
Oral cavity	1	(0.9)
Larynx	2	(1.7)
Stage		
I	3	(2.6)
II	10	(8.8)
III	24	(21.1)
IV	76	(67.5)

Table 2 Treatment characteristics

	Postoperative radiotherapy	Radiotherapy
Number of patients (%)	39 (34.2)	75(65.8)
Mean radiation dose (cGy)	6282.56 (5000-7170)	6854.00 (5000-7400)

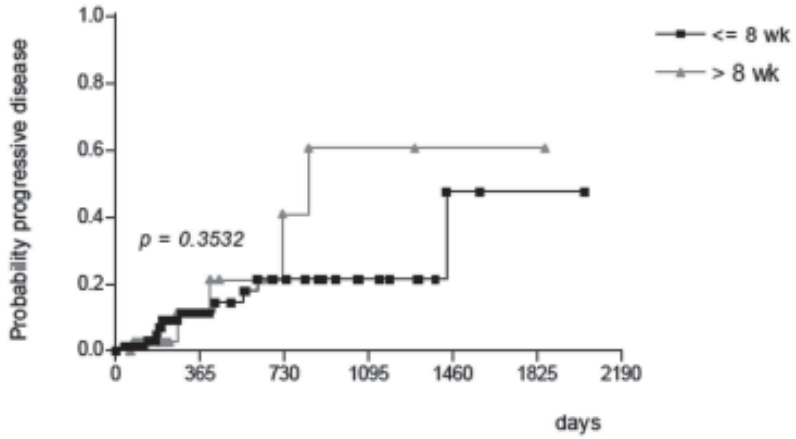
Table 3 Overall treatment time

Duration of treatment	Number of patients (%)	
Group A (6-8 weeks)	72	(63.2)
Group B (>8 weeks)	42	(36.8)

Outcome

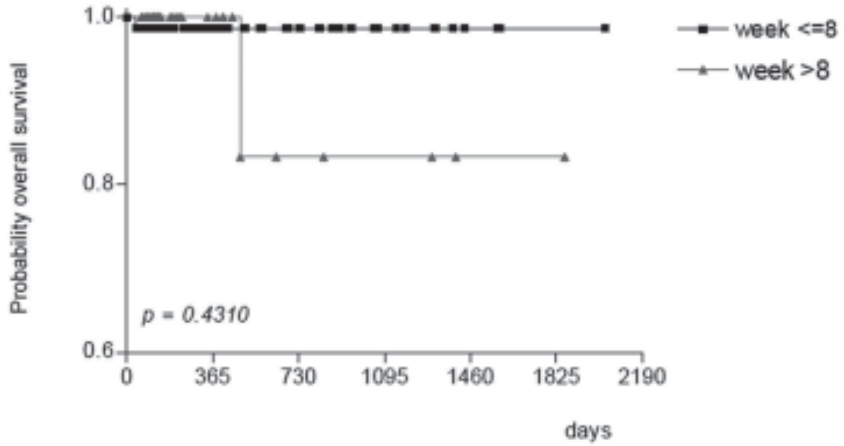
The corresponding at 48 months probability of progressive disease were about 47.7% in group A and 60.7% in group B (p=0.3532). The probability curves of progressive disease are shown in figure 1.

Figure 1 probability curves of progression of disease



The four year overall survival was 98.7% in group A and 83.3% in group B (p=0.4310). The probability of overall survival curves are shown in figure 2.

Figure 2 probability curves of overall survival



Discussion

There were many studies that showed prolonged overall treatment time effect to tumor control.

A retrospective analysis conducted in Japan, 52% local control achieved in oral tongue cancer patients irradiated more than 35 days compared with 100% local control in less than 35 days. This result indicated prolonged overall treatment time associated with loss of local control.[9]

Decreasing of overall treatment time of radiotherapy is has been tried as a mean of reducing the time available for accelerated repopulation of clonogenic tumor cells.[10] Data from DAHANCA study showing that a moderate reduction in the overall treatment time from 6.5 to 5.5 weeks of radiotherapy increases the 5-years locoregional control from 60 to 70% and accompanied with acceptable increase in acute side effects. But without any significant increase in late side effects, commonly used in management of patients with squamous cell carcinoma of the head and neck. The treatment outcome is differenced to total dose and overall treatment time of radiation.

Study by Wang et al.[11] and Inoue et al.[12] and Quynh-Th XL. supported the result that there was trend to improved tumor control in T1 glottis cancer patients who completed their radiotherapy within 43 days. Wang et al.[11], Overgaard et al.[2] reported a higher failure rate in T2-3 laryngeal cancer patients treated with longer overall time.

Review of 496 cases of T2-3 laryngeal cancer treated with definite definitive radiotherapy at the Christie Hospital, Slevin et al.[5] showed that a time factor of 0.5-0.6 Gy/day was required to overcome the adverse effect of accelerated tumor repopulation when the overall was longer than 3 weeks. And for optimal tumor control, higher total dose was necessary when overall time was prolonged. In Quynh-Thu's study,[1] no one failed when the overall time was <50 days and the total dose was >65 Gy. In contrast, 54% of the patients failed when the overall time was >50 days and the total dose was <65 Gy. And in high total dose group (>65 Gy) was more local relapses when the overall time was prolonged. Quynh-Thu recommened the overall treatment time of radiotherapy for T2 glottis cancer should be less than 50 days.

In an important article published in 1993, Cox et al. analyzed the Radiation Therapy Oncology Group (RTOG) database of patients treated with radiotherapy alone for stage III NSCLC; they found that prolonged treatment time was significantly associated with worse local-regional control and survival, 0% 5-year survival in delay treatment, 15% who did not have delay treatment.[13]



Data from Fowler JF's review determining the magnitude of time factor relating local control to overall treatment time. In all but only two of data sets, a significant loss of local control was observed with prolongation of radiotherapy. The median local control rate was decrease 14% in only 1 week, 26% in 2 weeks. It is clear that modest prolongation of radiation is associated with lower chance of local control.[9]

This study shows the effect of the overall treatment time to tumor control of squamous cell carcinoma of head and neck at the Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University.

This retrospective study dose not confirms the adverse effects of treatment prolongation to tumor control.

However, the results of this study trend to have poor outcome in prolongation of overall treatment time, both probability of disease progression and overall survival. Data from this study is non statistically significant difference because of small sample size and disproportion number between group A (6-8 weeks, 72 patients) and group B (more than 8 weeks, 42 patients) and short time of follow up due to the general poor health in this group of patients (median time of follow up = 246 days). Longer follow up time is needed to confirm the final outcome of this study.

Conclusion

The prolongation of overall treatment time trends to have poorer outcome in locoregional control and overall survival

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