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BAX EXPRESSION, APOPTOSIS, Ki67 AND P53 EXPRESSION IN RADIATION TREATED LARYNX CARCINOMA.

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PURPOSE: To assess whether pre-treatment Bax expression, apoptotic index, p53 and ki67 expression are useful in predicting local control and survival in a group of laryngeal cancer patients treated by postoperative radiotherapy.

METHODS: 57 patients with laryngeal carcinoma treated by postoperative radiotherapy (median dose 60 Gy, in 2 Gy daily fractions) were included. Bax, Ki67 and p53 were studied by IHC. Apoptotic cells were scored in hematoxylin-eosin slides.

RESULTS: Bax was related to grade and apoptotic index. Low Ki67 proliferating tumors showed better 5-years local control ($p < 0.01$) and survival ($p < 0.03$). P53 expression was not predictive. Patients with tumors showing low apoptotic indexes had better local control ($p < 0.049$) and survival ($p < 0.056$) than highly apoptotic tumors. Tumor extension and pre-treatment apoptotic index were significant predictive factors for local control and survival in multivariate analysis. The role of BAX in predicting local control will be discussed.

CONCLUSIONS: Ki67 and apoptotic index are useful in predicting clinical outcome of laryngeal cancer patients referred to radiotherapy. The role of BAX will be discussed.

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TITLE: Definitive Radiation therapy for Early Glottic Carcinomas: Analysis of Prognostic Factors

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PURPOSE: Retrospective analysis was performed to assess the influence of disease and treatment related factors on the outcome of patients treated definitively with radiation therapy for early glottic carcinomas.

METHODS: Ninety-nine patients with T1-2N0 glottic carcinomas were treated definitively with radiation therapy from October 1988 to June 1997 at Kobe University Hospital. Prognostic factors on local control analyzed included age, gender, smoking history, hemoglobin, histological differentiation, T stage, anterior commissure involvement, field size, total dose, overall treatment time, use of wedge filter, and combined chemotherapy.

RESULTS: At a median follow up period of 46 months, the five year overall survival and cause-specific survival were 83.8% and 96.1%, respectively. The five year local control rate were 72.0% for all patients, 85.9% for T1a, 63.1% for T1b and 53.2% for T2 patients. By univariate analysis, factors significantly influenced on local control were T stage ($p = 0.03$) and anterior commissure involvement ($p = 0.03$). Use of wedge filter and higher total dose showed positive influence even though they did not reach significant difference. By multivariate analysis, anterior commissure involvement was found to be the only independent factor significantly influenced on local control.

CONCLUSIONS: This retrospective study supports the results of literatures showing the anterior commissure involvement negatively influences the outcome of patients with early glottic carcinomas treated with radiation therapy.

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THE INFLUENCE OF INTERRUPTION IN RADICAL RT OF T₁ AND T₂ VOCAL CORD SQUAMOUS CELL CARCINOMAS

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Purpose: To evaluate the influence of overall treatment time in the local control of patients with the diagnosis of T₁ and T₂ vocal cord carcinomas, after radical radiation therapy.

Methods: We reviewed 112 cases of patients treated between January 1978 and January 1994, treated at the Department of Radiotherapy from the Portuguese Institute of Oncology - Porto. Treatment courses were divided into two groups: patients who did and did not interrupt RT. Survival rates were calculated according to the actuarial life-table method.

Results: From the 112 patients, 28 (25%) interrupted the treatment, for a mean period of 10 days (range 5 to 28), due to several reasons, such as absence, machine malfunction and skin/mucosa side effects, with various grades of severity. Local recurrence occurred in 14 cases (12.5%). The median period of follow-up was 75 months (range 32 to 214). The 2, 5 and 10 year's disease-free survival was 82%, 80.2% and 77%; the overall survival for the same period was 94%, 92.2% and 92.2%, respectively. No local recurrence was observed in the 28 patients that interrupted RT.

Conclusions: Cancer of the larynx represents about 2% of the total cancer risk and is the most common head and neck cancer (skin excluded). At our Institute, it has been our policy to treat essentially all T₁-T₂ with radiation therapy alone, reserving surgery for recurrent or persistent disease. Several publications reported the adverse effects of prolonging treatment time and local control in various neoplasias, head and neck included. Curiously, in our study, the prolonging of overall treatment time had no influence in local control rates.

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CURATIVE RT FOR EARLY STAGE LARYNGEAL CARCINOMA: RESULTS AND TECHNICAL CONSIDERATIONS

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Purpose: To assess the prognostic factors and the technical considerations in patients with early stage squamous-cell laryngeal carcinoma treated with curative RT.

Methods: Seventy consecutive patients with T1-T2 squamous-cell carcinoma of the larynx were treated between 1983 and 1997 with curative RT. The male to female ratio was 6.78 (61/9), and the median age 63 (35-92) years. There were 34 patients with T1a, 11 with T1b, and 25 with T2 tumors. Computer-assisted 3-D conformal treatment planning was done in 29 (41%) patients. The RT technique consisted of 2 lateral photon fields in 50 (72%) patients, 2 lateral photon fields plus 1 anterior electron field in 8 (11%) patients, or 1 anterior electron field in 12 (17%) patients. A median dose of 70 Gy (60-74) was given in median 2 Gy/fr (1.66-2.50) during a median period of 48 days (21-58). Arytenoid protection was assured in 9 patients (13%). The median follow-up period was 58 months (12-153).

Results: In a median period of 15 months (5-58), 17% (n = 12) of the patients relapsed: 8 salvaged with surgery (6/7 for T1; 2/5 for T2), 1 surgical refusal, and 3 disease progression. The 5- and 10- year cause-specific survival was 92% at 5 and 10 years. Local control was 78% at 5 and 10 years. According to the RTOG classification, grade 1 laryngeal edema and cutaneous toxicity was observed in 17 (24%) and 23 (33%) patients, grade 2 in 52 (75%) and 43 (62%) patients, and grade 3 in 1 (1%) and 4 (5%) patients, respectively. Among the numerous factors analyzed (age, stage, grade, RT technique, treatment volume, fractionation, treatment duration) in the uni- (logrank test) and multivariate analyses (Cox model), the male sex ($p = 0.02$), arytenoid protection ($p = 0.02$), and total RT dose < 66 Gy ($p = 0.03$) were found to be the worse independent prognostic factors influencing the local control.

Conclusions: In patients with T1-T2 squamous-cell carcinoma of the larynx treated with curative radiation therapy, a sufficient RT dose is mandatory (66-70 Gy in 6.5-7 weeks), and great caution must be taken with arytenoid protection.