define individual variables for radio-sensitivity. Alpha and β values showed a pattern of individual sensitivity that correlates to the clinical toxicity observed in this study.

8532 POSTER

Prognostic impact of comorbidity in elderly patients with head and neck squamous cell carcinoma (HNSCC)

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Background: there is no standard treatment for elderly HNSCC patients and comorbidity is known to be an independent predictor for mortality in head and neck cancer patients. We analyse the influence of comorbidity in survival and toxicity in elderly HNSCC patients.
Materials and Methods: A retrospective review was conducted in all patients with HNSCC over the age of 70 seen in a single cancer hospital from January 2004 till April 2009. Adult Comorbidity Evaluation 27 (ACE27) was used and compared with ECOG to calculated adjusted hazard ratio. All high-grade toxicity events per patient was summarise according to the National Cancer Institute Common Toxicity Criteria across the entire treatment period in a sequence form in those elderly HNSCC patients not intended for best supportive care (BSC)
Results: 77 patients were included. Median age was 76 (range 70−99) with a male/female ratio 4:1. Cancer subsite more commonly are larynx (32.5%) and oral cavity (29.9%). Stage IV was in 59.8%. ECOG 0 was in 23.4%, 1 in 49.4%, 2 in 22.1% and 3 in 5.2%. Comorbidity was severe in 29.9%, moderate in 27.3% and mild in 32.5%. 51.9% was qualify for chemotherapy as induction, concurrent or palliative treatment. BSC was intended for 23.4%. Grade 3−4 toxicity happened in 65% of patients qualify for chemotherapy including two toxic deaths. There were no differences according to age, gender, ECOG or ACE. 7 patients (10.7%) were excluded from analysis survival due to missing data. Compared with patients with mild or moderate comorbidity Kaplan Meier survival curves for patients with severe comorbidity was signifincantly worse in the whole population (median overall survival from diagnosis 36 weeks, 95% CI 25−46, $p < 0.05$, one year survival 28.4%) as well as in patients scheduled to undergo treatment (median overall survival from diagnosis 39 weeks, 95% CI 32−46 $p < 0.05$). In patients qualify for treatment cox regression model shows that adjusted hazard ratio was significantly in ECOG 0 patients (HR = 0.24; $p < 0.005$) and severe comorbidity patients (HR=1.43; $p < 0.05$).
Conclusions: Data from this retrospective review suggested that elderly HNSCC patients ECOG 0 could be worthy for treatment irrespective of ACE, and that elderly HNSCC patients ECOG 1−2 with severe comorbidity should be ruled out from treatments. Elderly HNSCC patients ECOG 2 shouldn't deserve exclusion from treatments solely due to moderate or mild comorbidity

8533 POSTER

The role of postoperative external beam radiotherapy in differentiated thyroid cancer with focal anaplastic change

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Background: Anaplastic thyroid cancer is rare disease and has a very low cure rate with the very best treatments. The major problem with anaplastic thyroid cancer, is that it is usually too aggressive and invasive when it is diagnosed. We examine to determine the role of postoperative external-beam radiotherapy (EBRT) in the patients with differentiated thyroid cancer with focal anaplastic change.
Materials and Methods: Of the 6,345 patients diagnosed as thyroid cancer at our institution between January 1980 and June 2008, 115 had anaplastic thyroid carcinoma. Of these patients, 33 had focal anaplastic change. The median patient age was 53 years (range, 22−75 years). The majority of patients were female (75.8%) and had extrathyroidal tumors (72.7%). Two patients (6.1%) had distant metastasis at diagnosis. Total thyroidectomy was achieved in 25 patients (75.8%). Twenty patients (60.6%) received postoperative EBRT (EBRT group) to a median total dose of 61.2 Gy (range, 54.0−70.0 Gy) and 11 (33.3%) received radioactive iodine (no-EBRT group). The median follow-up duration was 19 months (range, 2−130 months).
Results: The 5-year overall and disease-free survival rates were 96.2% and 57.2%, respectively. The 5-year local failure-free survival rates were significantly different (100% in the EBRT and 52.5% in the no-EBRT $p = 0.024$). There were no significant difference in overall, disease-free, regional failure-free, and distant metastasis-free survival rates between the EBRT group and no-EBRT group. Thyroglobulin, palpable lymph node, anaplastic transformation from previous differentiated thyroid cancer, and multiple foci were significant prognostic factors.
Conclusions: Postoperative EBRT significantly improved local failure-free survival in patients with differentiated thyroid cancer with focal anaplastic change

8534 POSTER

Hyperfractionated radiotherapy with concurrent docetaxel in locally-advanced head and neck cancer

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Purpose/Objective(s): Altered fractionated radiotherapy and/or radiotherapy combined with chemotherapy have been used in locally advanced head and neck cancers to increase local control. Concurrent chemo-radiotherapy is now considered to be a standard treatment option for these cases. This study was designed to evaluate hyperfractionated radiotherapy with concurrent use of low dose docetaxel in locally advanced head and neck cancer.
Materials/Methods: Patients eligible for this study had stage III to IVB squamous cell carcinoma of the head and neck or stage II carcinoma with large tumor volume. Tumor volumes were calculated by a tool in the radiotherapy treatment planning computer. The hyperfractionated radiotherapy was delivered 5 days per week with a 4-MV photon beam at 1.2 Gy per fraction with more than 6 hours apart to a total dose of 72.0 Gy. Docetaxel at 10 mg/m^2 was administered every week during radiotherapy. Toxicities were assessed weekly and graded according to NCI-CTCAE ver.3.0. Treatment response was assessed at 1 month after treatment completion. Statistical analysis of survival was calculated using the Kaplan-Meier method.
Results: From March 2003 to October 2008, 70 patients were treated according to this regimen. Median age was 66 years and sixty-three patients were male. Primary sites were the oropharynx in 25, hypopharynx in 24, larynx in 18, oral cavity in 1 and primary unknown in 2. Eleven of the patients were stage II, 16 were stage III, 33 were stage IVA and 9 were stage IVB. The grade 3−4 hematological toxicities were lymphocytopenia in 29 (42%) and neutropenia in 2. The grade 3 non-hematologic toxicities were mucositis in 42 (60%), treatment related pain in 12 (19%) and dermatitis in 2 (2%). Fifty-five patients (79%) reached complete response (CR) and 13 (19%) reached partial response (PR). The median follow-up period was 18 months (ranging from 2 to 38 months). Seventeen patients developed a relapse or recurrence. Infield recurrence was observed in 11 and metastasis in 6. The two year overall survival rate was 71.7% and three year was 67.9% in entire group, respectively. Significant prognostic factors in two year relapse-free survival rates were primary site (51.5% in hypopharynx, 68.6% in oropharynx and 100% in larynx), clinical stage (100% in stage II-III, 64.8% in stage IVA and 0% in stage IVB) and tumor volume (less than 100 cm^3 in 75% and more than 100 cm^3 in 0%).
Conclusion: Although the follow up period was short, we can conclude that docetaxel combined with hyperfractionated radiotherapy may become a useful approach for the management of stage II to IVA head and neck cancer provided that appropriate measures are taken to reduce mucosal toxicities.

8535 POSTER

Induction chemotherapy within a multimodality treatment of nasal cavity and ethmoid sinus malignant epithelial tumours: report of an homogeneous series of patients

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Background: Ethmoid sinus and nasal cavity cancers are rare diseases, whose prognosis mainly stays upon histology and stage. Optimal treatment can hardly be stated, due to heterogeneity of tumour site, histotype, treatment and within limited series.

We analysed a retrospective series of patients (pts) treated with a multimodal approach including induction chemotherapy (CT).
Material and Methods: Between 2000 and 2008, 29 pts with stage III-IV malignant epithelial tumours of ethmoid and nasal cavity were treated. Adenocarcinoma and salivary gland-type carcinomas were excluded. Treatment consisted of induction CT platinum-based (with docetaxel, 5 fluorouracil or etoposide or vinorelbine) followed by concomitant chemo-radiotherapy (group A, 18 pts) or craniofacial resection (CFR) and postoperative radiotherapy (RT), with or without concomitant cisplatin (group B, 11 pts). Follow up ranged from 7 to 87 months (median 37 months).
Results: See the table.

Characteristics	Group A: CT+CT/RT n (%)	Group B: CT+CFR+RT(CT) n (%)
Stage III	4 (22)	3 (27)
Stage IV	14 (78)	8 (73)
T3	5 (28)	3 (28)
T4a	6 (33)	4 (36)
T4b	7 (39)	4 (36)
Squamous cell carcinoma	7 (39)	6 (54)
SNUC	9 (50)	1 (9)
SNEC	1 (5.5)	1 (9)
Small cell carcinoma	1 (5.5)	3 (28)
Neuroendocrine YES	4 (22)	4 (36)
Differentiation NO	14 (78)	7 (64)

SNUC = Sinonasal undifferentiated carcinoma; SNEC= Sinonasal neuroendocrine carcinoma

Only 3 pts showed neck nodal disease at diagnosis (1 N1, 2 N2), all in group A. Radiological response to induction CT showed partial response in all but 4 pts (1 complete remission and 3 stable disease). Globally, 3- and 5-year (yr) overall survival is 68% and 42%. Fifteen pts showed a local recurrence: 11 in group A (9 pts underwent a salvage CFR) and 4 in group B. Only one pt treated with salvage surgery at local site reached ultimate local control. Two pts with isolate node recurrence were treated with surgery. Distant metastasis developed in 4 pts (1 in group A and 3 in group B). Treatment strategy did not impact on DFS. Neurendocrine differentiation in tumours was associated with reduced disease free survival (DFS) ($p = 0.01$). All small cell carcinomas and SNECs recurred in 2 yrs time, while 3 yr DFS of squamous cell carcinoma and SNUC is about 65%.
Conclusions: Survival of advanced stage nasal cavity and ethmoid carcinomas is not satisfactory. Induction CT followed by concurrent CT/RT is able to reach disease control similar to multimodality treatments including CFR, at least in some histotypes. Efforts should be spent to improve treatment of bad prognosis histologies, in particular with neuroendocrine differentiation.

8536 POSTER

Immunohistochemical study to identify prognostic biomolecular markers for nasopharyngeal carcinoma

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Background: We performed immunohistochemical study with pre-treatment biopsy specimens to identify prognostic biomolecular markers for nasopharyngeal carcinoma (NPC).
Material and Methods: From January 1998 through December 2006, 68 patients were histologically diagnosed as non-metastatic NPC and treated with radiotherapy at Seoul National University Hospital. Only 38 patients had the paraffin block for the immunohistochemical study. Thirty-one patients had undifferentiated carcinoma and 7 patients had squamous cell carcinoma. Thirty-two patients (84%) had advanced stage NPC (2002 AJCC Stage III-IV). All patients, except for 6, were treated with induction chemotherapy with two or three cycles of cisplatin based regimen followed by either radiotherapy alone (19 patients) or concurrent chemoradiotherapy with cisplatin (13 patients). Immunohistochemical staining was done for Met, COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, CD138, STAT5, Egr1, CSE1L, STAT3 and LIN28 with the usual methods.
Results: The median follow-up time was 30 months (range, 11−83 months) for all patients and 39 months (range, 19−83 months) for surviving patients. Thirty-five patients were Met positive and 22 patients showed high expression (58%). Twenty-seven patients exhibited CD138 and 17 patients showed high grade (45%). Twenty-two patients showed Egr1 expression (58%). High Met and CD138 expression were statistically significant negative prognostic factors on survival. The expression of Egr1 had a positive prognostic effect on survival. The combined score (CS) of these three prognostic factors, Met (0, low; 1, high) plus CD138 (0, negative; 1, low; 2, high) minus Egr1 (0, negative; 1, positive), was a strong prognostic factor. The median survival curve was distinctly separated according to this combined score (median survival: CS −1 or 0, 76 mo; CS 1, 71 mo; CS 2, 42 mo; CS 3, 24 mo, $P = 0.001$). The patients with Egr1 expression also showed better progression-free survival (PFS) than those without Egr1 expression. No prognostic value was revealed in COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, STAT5, CSE1L, STAT3 and LIN28.
Conclusions: High Met and CD138 expression were evaluated as negative prognostic factors on OS in NPC. The expression of Egr1 was a positive predictive value for PFS as well as OS. The combined score of these markers could be used to stratify biomolecular risk groups.

8537 POSTER

Hemophagocytosis-related keratinization in squamous cell carcinoma and carcinoma in-situ of the oral mucosa

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Background: Round-shaped dyskeratosis (RSK), a kind of keratin pearl, is one of the histological features of carcinoma in-situ (CIS) of the oral mucosa. Our hypothesis for the histopathogenesis of this peculiar structure is that RSK foci are generated by keratinization of basal cells which are exposed to oxidative stress by hemoglobin derived from erythrocytes which are extravasated due to the collapse of blood vascular channels in the stroma.
Material and Methods: To stage the RSK formation process in oral CIS, a total of 50 surgical specimens of oral CIS and squamous cell carcinoma (SCC) containing RSK or keratin pearl foci were investigated by immunohistochemistry for various cytokeratin (CK) subtypes and vascular endothelium- and erythrocyte-related antigens. ZK-1, a human oral SCC-derived cell system, was exposed to erythrocytes or hemoglobin and examined for its CK phenotypes and heme oxygenase-1 (HO-1) expression levels by immunofluorescence and RT-PCR. In addition, the dynamics of protease activated receptor-2 (PAR-2), a candidate for regulating hemophagocytosis, were determined to confirm the molecular mechanisms underlying this phenomenon.
Results: RSK specifically immunopositive for CK10 and CK17, and CK10/CK17/HO-1 expressions were also confirmed in the basal cells facing collapsed blood vessels, around which erythrocytes were disseminated. ZK-1cells showed erythro-/hemo-phagocytosis when incubated with erythrocytes or hemoglobin, and phagocytotic ZK-1 cells showed enhanced immunofluorescence intensities for CK10, CK17, and HO-1. At the same time, mRNA expression levels were elevated for the three molecules. Those expression levels were also enhanced when ZK1 cells were stimulated with PAR-2 agonist peptides.
Conclusions: RSK and some of the keratin pearls in oral CIS and SCC, characterized by their particular expressions of CK17 and CK10, are obviously induced by hemophagocytosis-related oxidative stress. PAR-2 may be involved in the hemophagocytosis by CIS or SCC cells, which seems to be induced by hemolysis due to rupture of intraepithelial blood vessels, which are also characteristic of oral CIS. Based on the results, we propose a new concept of abnormal keratinization caused by hemophagocytosis. This 'hemophagocytosis-related dyskeratosis' starts from the basal end of the epithelial layer, which is in a reverse direction to that of normal keratinization.

8538 POSTER

Xerostomia and dysphagia related quality of life in patients treated with interstitial brachytherapy boost for head neck cancer

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Background: To study patients' perspective of xerostomia and dysphagia after treatment for head and neck cancer with external beam radiation (EBRT) and interstitial brachytherapy (BRT)
Methods: Patients with head and neck cancer previously treated with BRT either alone or in combination with EBRT who were controlled and attended the follow up clinic were considered suitable for the study. Xerostomia questionnaire (XQ) and dysphagia questionnaire (DQ) were served to consecutive eligible patients from Jan 2008 to Jan 2009 at a single head neck unit. XQ (Meirovitz 2006) consisting of 8 questions with scores from 0−10 and higher score indicating more xerostomia was selected. Each item score was added and the sum score transformed linearly to a final score ranging between 0−100. DQ (Murry 1998) was used in which each item was scored on 3 point scale and the final score for each patient was the mean score of the 10 items with higher score suggesting better outcome.