p = 0.008), while death with high tumoural VEGFR1 mRNA (HR for death 1.71, 95% CI 1.02–2.87, p = 0.041) and VEGFR3 mRNA (HR for death 1.76, 95% CI 1.09–2.83, p = 0.02). In multivariate analysis, node-negative status, supraglottic primary and low tumoural VEGFR1 mRNA were favourable predictors of relapse-free survival, while node-negative status and low tumoural VEGFR1 were prognostic for prolonged survival (Table 1).
Conclusions: VEGFR1 mRNA expression in patients with operable laryngeal cancer provides adverse prognostic information and may justify targeted therapeutic interventions.

8505 ORAL

DNA Methylation in Tumour and Normal Mucosal Tissue of Head and Neck Squamous Cell Carcinoma (HNSCC) Patients − New Diagnostic Approaches and Treatment

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Background: Cigarette smoke and alcohol consumption are considered to cause HNSCC. Despite advances in therapy, survival of HNSCC patients has not improved significantly during the last 20 years and recurrent disease is frequently observed. Interestingly, DNA methylation of cell cycle control genes, p16 and Ras association domain family 1A (RASSF1A) or death associated protein kinase (DAPK) gene was suggested to contribute to oncogenesis, metastasis and treatment failure.
Material and Methods: The possibility of detecting pre-malignant cells or malignant cells at diagnosis time in HNSCC patients was investigated. Fifty-nine biopsies obtained from 41 HNSCC patients were used. Forty-one were tumour biopsies and 18 of these biopsies were normal mucosal tissue, located at least five cm from the tumour margin. DNA methylation of p16, DAPK or RASSF1A was examined by multiplex methylation specific PCR (MSP). The ethical committee approved this study.
Results: Thirty-nine of 41 (95%) tumour biopsies showed DNA methylation of p16 gene. DAPK and RASSF1A methylation were detected in 7 (17%) and 8 (20%) of the tumour biopsies. In spite of normal mucosal phenotypes observed by the ENT specialist and confirmed by the pathologist, DNA methylation of p16, DAPK and RASSF1A were detected in these biopsies. Of the 18 distant normal mucosal tissue, 15(83%) showed methylation of p16 gene. Methylation of DAPK and RASSF1A gene in these normal mucosal biopsies were 2 (11%) and 4 (22%), respectively.
Conclusion: More than 80% of HNSCC patients carried pre-malignant cells or malignant cells in the normal mucosal tissues as indicated by DNA methylation. These cells were undetected by conventional macroscopic and microscopic examination. Thus, the low cost and simple molecular analysis such as multiplex methylation specific PCR in combination with histopathologically assessment will provide a better prognostic base for evaluation and treatment of HNSCC patients. Since DNA methylation was reversible by pharmacological means, the role of anti-methylation drugs in HNSCC need further investigation.

8506 ORAL

Sentinel Lymph Node Biopsy in Oral Cancer Patients − Single Centre Experience of 130 Cases

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Introduction: Oral cancer is one of the most common cancers in Indian subcontinent. Lymph node status is the most important prognostic factor and it has therapeutic implications. The only way to reliably assess lymph node status has been neck dissection but it is associated with significant morbidity. The other method of staging the neck like USG, CT scan and PET scan has low accuracy and high false negative rate. The Sentinel Lymph Node Biopsy (SLNB) is found to be most reliable alternative to neck dissection with >90% accuracy. We are presenting our experience of 130 cases of SLNB in oral cancer patients.
Methods: It is a retrospective analysis of prospective database from 1st February 2008 to 15 April 2011. In this period, patients of oral Squamous cell carcinoma clinically staged T1−4N0−1M0 (N1 − only soft non suspicious LN) underwent sentinel lymph node biopsy. All sites of oral cancer were included. The SLNB was performed either by blue dye or by combined technique. First phase was consist of validation and second was therapeutic phase. In validation phase, all patients underwent neck dissection after SLNB. The results of SLNB compared with final histopathology of remaining neck nodes. In therapeutic phase, no neck dissection was performed in SLNB −ve patients whereas SLNB +ve patients underwent MND I. The intra-operative assessment of SLN was done by Intraoperative touch cytology and its results were compared with histopathology.
Results: Total 130 patients were included in study. Mean age was 50 years and male: female ratio was 97:23. Sixty-two patients were in validation study and 68 underwent therapeutic SLNB. The identification rate was 100% in therapeutic phase. The mean SLN/patient was 2.95. The sensitivity, specificity, NPV and accuracy of SLNB in validation phase were 81.8%, 100%, 90.4% and 93.3% respectively. The sensitivity, specificity, NPV, PPV and accuracy of touch cytology in therapeutic phase were 88.88%, 98%, 96.07%, 94.11, 95.58% respectively. With a median follow up of 10 months in therapeutic phase, only 2 patents had neck nodal relapse and it was associated with local relapse.
Conclusion: Lymph node status is an important prognostic factor in oral cancer. The present evidence suggests SLNB has the best balance between accuracy and morbidity to stage the neck. It should be the preferred method of staging the neck in oral cancer to avoid the morbidity of neck dissection and high failure rate in observation group.

8507 ORAL

Accelerated Clinical Pathways Have Caused a Significant Reduction in Time for Diagnosis and Treatment of Head and Neck Cancer in Denmark in 2010 Compared to 2002

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Background: Significant tumour progression has been observed during the waiting time for treatment of head and neck cancer. A meta-analysis of clinical observations in head and neck cancer has shown that the risk of local recurrence and death increases with increasing waiting time for treatment. A Danish study (Primdahl *et al.* Acta Oncol 2006) showed that compared to 1992, the waiting time before start of radiotherapy was significantly longer in 2002 (median 70 days versus 50 days). In 2008, the Danish national policy of fast track accelerated clinical pathways was introduced. Patients with suspicion of cancer are given the highest priority in the health care system. Local infrastructure has been improved by telephone hotline, reserved slots in ENT departments and radiology, fast pathology reporting, and multidisciplinary tumour boards and clinics twice weekly. The aim of the current study was to evaluate the potential influence of fast track by comparing waiting times in 2010 to the observations from 2002.
Patients and Methods: Charts of all consecutive new patients with squamous cell carcinoma of the oral cavity, pharynx, and larynx at the five Danish head and neck oncology centres from Jan-Apr 2010 were reviewed and compared to similar data from 2002. Number of patients was 253 (2010) vs. 221 (2002). Stage distribution 2010 vs. 2002 was stage I: 22% vs. 20%, stage II: 15% vs. 23%, stage III: 11% vs. 23%, and stage IV: 52% vs. 35%. Primary treatment was radiotherapy (73% vs. 81%), surgery (11% vs. 6%), combined treatment (4% vs. 1%), or palliative/none (12% vs. 12%).
Results: Total time from first health care contact (GP, ENT or hospital) to start of definitive treatment was median 41 calendar days in 2010 compared to 69 days in 2002 (p < 0.001). Median time used for diagnosis was 13 days compared to 17 days in 2002 (p < 0.001) and median time from diagnosis to treatment start was 24 days in 2010 versus 47 days in 2002 (p < 0.001). Significantly more diagnostic imaging was done in 2010 compared to 2002 (CT 59% vs. 21%; MR 43% vs. 16%; US 38 vs. 19%; PET 21% vs. 6%).
Conclusion: The study showed a significant reduction in time for diagnosis and treatment of head and neck cancer in Denmark in 2010 compared to 2002. More imaging was used and higher stages seen in 2010. Reducing waiting time by fast track clinical pathways is possible, but requires a substantial dedicated concerted effort of the involved health sectors.