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Outcome of surgery and post-operative radiotherapy of major salivary gland carcinoma: a single institute experience

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Background: We intended to determine clinic-pathologic features, management & recurrence pattern of major salivary gland carcinoma treated with surgery & post-operative radiotherapy (PORT).
Material and Methods: We retrospectively reviewed 106 cases of major salivary gland tumor seen at our centre (1998−2008). 65 cases were selected for analysis (exclusions: benign, palliative, non-carcinomas). Statistical analysis was performed using SPSS 15.0. Recurrence free survival (RFS) was obtained using Kaplan-Meier method.
Results: Median age was 35 years with male: female ratio of 1.3:1. Tumour location was parotid (56, 86.2%) or submandibular gland (9, 13.8%). Histology was: 28 mucoepidermoid (43%), 10 adenocarcinoma (15.4%), 7 adenoid cystic (10.8%), 4 squamous cell carcinoma (6.2%), 3 salivary duct carcinoma (4.6%) and 13 other (20%). 39 cases (60%) were primary while 26 (40%) were recurrent. Optimal surgery was performed in 59 pts (90.8%). 43 pts (66.2%) underwent neck dissection, of which 14 (32.5%) had nodal metastasis. Surgical margins were: negative 41 (63.1%), positive 11(16.9%), close 4(6.2%) & unknown 9 (13.8%). Tumor size was: <2 cm = 7, 2−4 cm = 17, >4 cm =14 & unknown = 27. Other pathologic findings were: perineural invasion 9 (13.8%), soft tissue infiltration 20 (30.8%), bony involvement 1 (1.5%), skin infiltration 8 (12.3%) and facial nerve involvement 10 (12.3%). Overall, 61 (93.8%) pts complied with the prescribed radiotherapy. Median dose of PORT was 60 Gy. Common radiotherapy techniques used were electron-photon combination (38, 62.3%) and photon wedge pair (18, 29.5%). RT plan was conventional in 36 (59%) and CT-based in 25 (41%). Median interval between surgery & PORT was 48 days (range: 20−210). Median duration of PORT was 45 days and overall treatment time was 93 days. The median follow-up was 13.1 months (range 2−70). Mean RFS was 42.68 months. 12 pts (18.5%) recurred with a median time to recurrence of 16.9 months. Sites of recurrence were local (2), nodal (4) and distal (5). One patient had both local & distal recurrence. The site of metastasis was lung, liver, brain & bone. Salvage therapy was given to 5 pts. At last follow-up 43 (70.5%) were disease free, 10 (16.4%) were alive with disease & no data was available for the rest.
Conclusion: Surgery and PORT is an effective combination for major salivary gland carcinoma with over 90% compliance and <20% recurrence. Newer therapy including chemotherapy & targeted therapy should be explored.

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Clinical experience with Cetuximab and Paclitaxel combination in metastatic/recurrent squamous cell cancer carcinoma of the head and neck (SCCHN) - retrospective analysis of a single institution

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Background: Results of a recent phase III randomized study with cetuximab and platin-5FU chemotherapy support its use in recurrent/metastatic SCCHN. However, many patients (pts) are not able to be treated with platin combinations. Paclitaxel (P) and Cetuximab (C) have shown an encouraging activity in a similar patients subset. We review the data of the patients treated with this schedule in our centre.
Material and Methods: From our database, we conducted a retrospective study of 20 patients with recurrent SCCHN who did not meet criteria for platin therapy and were treated with weekly P (80 mg/m^2) and C (initially 400 mg/m^2 followed by 250 mg/m^2) until progression or intolerable toxicity. We have collected data regarding previous treatments, response rate (RR), progression free survival (PFS), overall survival (OS) and toxicity.
Results: From January 2007 to November 2008, 20 patients were included (18 male, 2 female) with a median age of 63 (50−81). Oral cavity (35%) and oropharynx (25%) were the most frequent locations. Most of the pts (13/20) had been treated with previous chemotherapy combinations (range 1−3 lines). All pts were evaluable for response and toxicity. Overall RR was 45% (1CR, 8 PR) and 35% of the pts (7/10) had SD. Response in radiated areas were 35% (6/17). With a median follow up of 10 months the median PFS and OS were 6.5 and 7 months respectively. Main related toxicities (Gr 2/3) were acne-like rash (30%), asthenia (15%), anemia (10%) and mucositis (10%).
Conclusions: Our analysis supports the results of efficacy and safety of weekly paclitaxel-cetuximab combination in metastatic/recurrent SCCHN. Treatment is very well tolerated and could be considerated as an alternative to platin-based chemotherapy in unfit patients for this therapy.

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Assessment of oxidative stress in tumors cells and histologically normal mucosa from head and neck squamous cell carcinoma patients

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Background: One of the cancers with strongest link to oxidative damage and oxidative stress is head and neck squamous cell carcinoma (HNSCC) since tobacco and alcohol are clearly defined as etiologic factors for these malignancies. Oxidative damage is the main mechanism mediating the clinical treatment effect of radiotherapy, the increased resistance to oxidative stress by many malignant cells is associated to treatment failure. Indeed, the response to radiation treatment varies from patient to patient. The purpose of this study was to compare the tissue levels of glutathione in HNSCC tumoral tissue (Tum) and corresponding adjacent histollogically cancer free mucosa (Muc) biopsies and to determine the potential variability in terms of radiosensibility.
Material and Methods: 27 newly diagnosed HNSCC patients were prospectively included in the study. All the patients were smokers. 27 tumoral specimens and an equal number of specimens from normal mucosa were examined. The ratio oxyded reduced glutathione is realised with the capillary electrophoresis kit Ceofix GSH/GSSG kit of Analis (Namur, Belgium). Two hundred microl of total blood, healthy and tumoral tissues were harvested on patient directly grind with 600 microl metaphosphoric acid 5% and centrifuged (within 3 hours). 100 microl of the supernatant was mixed with 400 microl of the kit diluent containing Naphthalene sulfonic acid as internal standard. Analysis is performed on a P/ACE 5000 series with a 37 cm and 75 micro m i.d. capillary maintained at 25°C. The separation was realized at 8 kV with a borate buffer pH8.2 containing SDS. The glutathione peaks were detected at 200 nm and integrated. The area of the oxyded glutathione peak is divided by the reduced one. Clinicopathological parameters were also analyzed as potential factors explicating the potential variability of oxidative stress status in HNSCC tumoral tissue.
Results: The ratio oxidized glutathione (GSSG)/reduced glutathione (GSH) determinated in tumoral tissue was higher in 12/27 of the cases comparing the ratio in adjacent normal tissue.
Conclusion: Pre therapeutic HNSCC tumoral tissue presented different GSH levels regarding adjacent cancer free mucosa. This difference is not related with clinicoanatomopathological parameters. GSH determination could have the potential to predict individual radiosensitivity of tumors of the head and neck area.

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Gene hypermethylation in tumor tissue of oral squamous cell carcinoma patients: experience from Serbia

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Background: Oral squamous cell carcinoma (OSCC) is most frequently presenting as an aggressive and locally advanced disease with overall survival rate less than 40%. The mechanisms underlying the process of carcinogenesis and tumor aggressiveness act through an accumulation of genetic and epigenetic alterations that disrupt normal function of tumor suppressors and oncogenes. Epigenetic changes alter expression of genes without changes in DNA sequence. The most common epigenetic modification occurring in human tumors is DNA methylation and histone deacetylation. The aim of this study was to investigate the influence of gene hypemethylation on clinical course of disease of OSCC patients. Genes studied are known to be involved in various cellular processes such as cell cycle control (p16), apoptosis (Death associated protein kinase – DAPK), Wnt signaling (adenomatous polyposis coli – APC), cell-cycle adhesion (E-cadherin – E-cad) and DNA repair (O^6-Methylguanine-DNA-methyltranspherase – MGMT, Werner syndrome – WRN).
Materials and Methods: 77 OSCC patients with stage II (n = 18) and stage III (n = 59) patients were included. All underwent surgery as primary treatment and subsequently were treated with radiotherapy. DNAs for gene

analysis were isolated from tumor tissue. After DNA bisulphite modification, methylation of the examined genes was performed by methylation-specific PCR of CpG islands. Results: 65/77 patients had at least one gene hypermethylated. The observed percentage of promoter hypermethylation were: 58% for p16, 34% for MGMT, 36% for DAPK, 23% for WRN, 43% for E-cadherin and 18% for APC gene. E-cadherin hypermethilation showed increase with raising tumor size (T3/T4 vs T1/T2, Fisher exact test, $p < 0.01$). The presence of E-cadherin promoter hyperemethylation was associated with a decrease in overall survival (cancer related survival) (log-rank test, $p = 0.039$). Stratified analysis by the lymph node involvement showed that hypermethylated E-cad is associated with poor prognosis only in N+ patients (log-rank test, $p = 0.024$).
Conclusion: Obtained results indicate that multiple genes are aberrantly methylated in OSCC patients. E-cad promoter methylation analysis may be valuable for the evaluation of tumor aggressiveness and prognosis of oral sqamous cell carcinoma.

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Outcome of T3 laryngeal cancer treated by primary surgery or primary (chemo) radiation

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Background: Laryngeal cancer is the second most common site of head and neck cancer after pharynx cancer. Organ sparing approaches like primary radiotherapy or concomitant chemoradiation permit larynx preservation in patients with locoregional advanced laryngeal cancer but do not provide a survival advantage over laryngectomy.
Methods: Files of patients diagnosed with T3 Nx M0 laryngeal cancer at the Ghent University Hospital between January 1998 and January 2005 were selected. A retrospective analysis was performed studying patient characteristics, treatment modality and outcome.
Results: 71 patients with laryngeal cancer were withheld for this analysis (87% men, 13% women). Mean age at diagnosis was 63.1 years for men, 57.9 years for women. 42 patients were treated with primary surgery followed by adjuvant radiotherapy (except for 2 patients). After a mean FU of 4.59 years in this group, 19 patients (45%) were alive. Locoregional control rate was 88%. 29 patients were treated with primary (chemo) radiation. After a mean FU of 3.42 years in this group, 10 patients (35%) were alive. Locoregional control rate was 76%. In this study, 15 patients were diagnosed with T3N0M0 glottis cancer. 5 patients received primary surgery, none of them showed a local recurrence (mean FU of 5.4 years). 10 patients received primary (chemo)radiation. After a mean FU 4.2 years, 2 patients showed a local recurrence and received a salvage laryngectomy after which one patient remained disease free.
Conclusions: This retrospective analysis of 71 patients diagnosed with laryngeal cancer shows acceptable outcomes with regard to survival and locoregional control rate fot both primary surgery and primary (chemo)radiation.

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Functional and psychological evaluation after exclusive chemo-radiation therapy in oral and oropharyngeal cancer

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Background: The treatment of head and neck tumours often negatively affects speech, swallowing, body image and quality of Life (QoL). Aim of this study was the evaluation of the impact of exclusive chemo-radiation therapy (CH-RT) on QoL and psychological functioning.
Materials and Methods: Twenty-eight patients, affected by a carcinoma of the oral cavity and oropharynx received exclusive CH-RT. Late effects of CH-RT and psycho-oncological assessment included: Radiation Therapy Oncology Group (RTOG), European Organisation for Research and Treatment of Cancer (EORTC) late radiation morbidity scoring system, DISCHE morbidity recording scheme, Hospital Anxiety and Depression Scale (HADS), Montgomery Asberg Depression Rating Scale (MADRS), Mini Mental Adjustment to Cancer (MINI MAC) and EORTC QoL Head and Neck 35.
Results: After a median follow-up of 42 months (range 12−60 months) moderate-severe late toxicity was as follows: taste impairment (89.20%), salivary function (82.12%), subcutaneous tissue (7.08%). Concerning dysphagia 39% of patients complained some discomfort, 28% had a more severe toxicity whereas 7% could not have an oral feeding; patients with severe dysphagia showed higher levels of anxiety ($p < 0.05$): dysphagia influences the QoL, fatigue and physical-social functioning. Rates of depression and anxiety were generally low: 78.6% of our sample did not show clinical relevant anxious symptoms and 82.1% of patients did not reach the threshold of an overt depression. Just a fair concordance in rate of depression between self- and hetero-evaluated scale was observed, with higher rates relieved by MADRS compare to HADS depression subscale using 8 or 10 cut-off (Cohen's k test = 0.401)
Conclusions: Our data suggest low rates of anxiety and depression, in patients treated with CH-RT, with a different evaluation between self-evaluative and hetero-evaluative scales.

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Induction chemotherapy with cysplatin and epirubicin followed by radiotherapy and concurrent cysplatin in locally advanced nasopharyngeal carcinoma observed in a non-endemic population

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Background: Chemoradiotherapy (CRT) represents the main therapy choice in the treatment of locoregionally advanced nasopharyngeal carcinoma (NPC). Aim of this study was the clinical evaluation of neoadjuvant chemotherapy (NACT) followed by CRT in a non endemic population affected by advanced NPC.
Materials and Methods: Patients with locoregionally advanced NPC were treated with three cycles of induction chemotherapy (CHT) with cysplatin (100 mg/m^2) plus epirubicin (90 mg/m^2), followed by cysplatin (100 mg/m^2) and concomitant radiotherapy (70 Gy).
Results: In 40 patients treated with such protocol, after the completion of induction CHT and CRT we observed the objective response rates of 90% and 100% respectively. Treatment tolerability and toxicity were easily controllable. With a median follow-up time of 54.5 months 3 and 5 years disease free survival was 75% and 65.4% and 3 and 5 years overall survival was 84% and 77.5%. Three and five years loco-regional control was 82.4% and 70.3% and five years distant metastases free survival was 75%.
Conclusions: NACT with cysplatin and epirubicin followed by concomitant CRT represents a feasible, efficient treatment for patients with advanced NPC. This regimen ensures an excellent locoregional disease control and overall survival with a low incidence of distant metastases.

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Induction chemotherapy with carboplatin and taxol followed by radiotherapy and concurrent weekly carboplatin + taxol in locally advanced nasopharyngeal carcinoma

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Background: in nasopharyngeal carcinoma (NPC), the role of chemo-therapy (CHT), remains controversial for the initial management of the disease. Recent trials and meta-analysis highlight that now, concomitant chemo-radiationtherapy (CRT) appears to be the standard treatment for locally advanced (T2b and more) and/or node positive patients. No phase II trials have investigated a two-drug combination during conventional, non splitted, RT after a complete course of induction CT. Aim of this study is the evaluation of the clinical outcome of neoadjuvant CHT with carboplatin + taxol followed by RT with weekly carboplatin + taxol combination in locally advanced NPC observed in a non endemic population.
Materials and Methods: patients with locoregionally advanced NPC were treated with three cycles of induction chemotherapy (CHT) with paclitaxel (175 mg/m^2) plus carboplatin (AUC 6), followed by paclitaxel (60 mg/m^2) plus carboplatin (AUC 1) and concomitant RT (70 Gy).
Results: in 30 patients treated with such protocol, after the completion of induction CHT and CRT we observed the objective response rates of 90% and 100%, respectively. Treatment tolerability and toxicity were easily controllable. With a median follow-up time of 54 months, 3- and 5-year disease-free survival was 80% and 73% and 3- and 5-year overall survival was 92% and 83%. Three- and 5-years locoregional control was 94% and 80%, and 5-year distant metastases free survival was 85%.
Conclusions: NACT with paclitaxel and carboplatin followed by paclitaxel plus carboplatin and concomitant CRT represents a feasible, efficient treatment for patients with advanced NPC. This regimen ensures an excellent locoregional disease control and overall survival with a low incidence of distant metastases.