Two study centres included 100 patients with locally advanced head and neck cancer into this open study. Radiation was delivered with telecobalt machines using standard daily radiation dose of 150–200 cGY in 30–35 fractions over a period of 6 weeks. Two lateral parallel opposing fields were used with the portal area generally being 4 × 6 inches. Patients were randomly allocated to two groups: Patients in the test group were given OE orally three times daily starting 3 days prior to radiotherapy and continuing up to 5 days after completing radiotherapy. Patients in the control arm were not given any drug.

The control group and the test group were comparable with respect to presenting features. In the test group the maximum severity and duration of mucositis, skin reaction, and dysphagia were significantly less as compared to the control group. The duration of these side effects as well as the sum scores of toxicity was also significantly less in the OE group.

In summary the use of OE with conventional fractionated radiotherapy was feasible without significant safety problems. There was a clinically relevant protection against acute side effects of radiotherapy in the OE group. Not only was the severity of acute side effects less but the duration was shorter and the time to onset was also delayed.

635 POSTER

The effect of cervical lymph node biopsy on distant metastases in carcinoma of the nasopharynx

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Purpose: To investigate whether the neck lymph node biopsy increases affects the rates of distant metastasis, neck recurrence, and survival in AJCC T1-3N1-3 nasopharyngeal carcinoma (NPC) patients.

Materials and Methods: We retrospectively analyzed the records of 543 patients with AJCC T1-3N1-3 NPC who had completed the recommended course of treatment (>=64 Gy total dose) and were followed up for more than 5 years. We compared the metastasis, neck recurrence, and survival rates in those with and without pretreatment node biopsy, and between excisional and incisional biopsy.

Results: No significant differences were found in terms of the rates of metastasis, recurrence, or survival in-patients with and without pretreatment biopsy. In addition, the method of biopsy and the time interval between operation and the start of local treatment did not significantly influence the outcome.

Conclusion: Our findings suggest that neck lymph node operation before local-regional irradiation does not increase the rate of distant metastasis in AJCC T1-3N1-3 NPC patients.

636 POSTER

Survival and organ preservation following surgical treatment for hypopharynx carcinoma

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Background: Surgery, usually in combination with postoperative radiotherapy, is believed to provide highest cure rates in patients with hypopharynx carcinoma. However, the percentage of patients suitable for primary surgery, surgical mortality rates, and organ preservation rates for this routinely used therapeutic approach have not been studied in detail. This study seeks to evaluate treatment modalities, mortality following surgery, survival, and organ preservation for a consecutive cohort of unselected hypopharynx cancer patients treated according to a prospective protocol that favors surgery as initial approach to the disease whenever possible and ethically justifiable.

Material and Methods: The charts of 228 consecutive patients with previously untreated hypopharyngeal squamous cell carcinoma seen from 1986 to 1997 were reviewed. No patient was excluded from data analysis. Outcome measures were calculated using the Kaplan-Meier estimator. Surgery was offered as initial treatment if the primary tumor and regional metastases seemed completely resectable, distant metastases were not detected during preoperative work-up, coexisting malignancies did not preclude a curative approach, general health status of the patient was considered sufficient to withstand the operative trauma, patients were willing to undergo surgery, and were judged to be capable of dealing with the consequences of such treatment.

Results: Out of 228 consecutive patients, 136 (59.6%) were found suitable for initial surgical treatment. Of the remaining 92 patients, eighteen (7.9%) had nonresectable lymph node metastases, sixteen (7.0%) had unresectable primaries, thirteen (5.7%) refused surgery, thirteen (5.7%) presented distant metastases during initial diagnostic work-up, eight (3.5%) had coexisting primaries that precluded a curative surgical approach, twelve (5.3%) had severe cardiopulmonary disorders, nine (3.9%) had multiple risks excluding major surgical interventions, and three died prior to the initiation of any kind of therapy. Of those who had surgery, 46 had larynx sparing procedures, 54 total laryngectomy, and 36 total laryngopharyngectomy. Microvascular jejunum loops for pharynx reconstruction were used in 22 patients, and gastric pullup in 14. None of the patients who had surgery died postoperatively. Actuarial five year overall survival was 26.6% for all 228 patients, 35.9% for the 136 patients with surgical treatment, 59.3% for the 46 patients who were treated with larynx-sparing procedures, and 12.9% for those not treated surgically.

Conclusion: Only 59.6% of 228 unselected, consecutive patients were suitable for surgical treatment. For these, no postoperative fatalities were observed. Five year overall survival was significantly better for pa-tients who qualified for surgery (35.9% versus 12.9%), but only 27.5% of them had their larynx preserved after five years.

637 POSTER

Oral cavity squamous cell carcinoma in stage II with a high percentage of DNA content >5C cells, have a significantly short disease free survival

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Purpose: In stage II oral cavity tumours, the classic clinical-pathological variables, have not allowed the identification of worst case prognosis. The outcome after standard treatment is not homogeneous, so it becomes important to identify the tumours that would benefit from a combined and aggressive therapy. The tumour suppressor genes and its products e.g. p16, p27, p53 and pRb, are involved in oral cavity carcinogenesis, representing part of the genetic instability and alterations of DNA content. These variables were used to identify stage II oral cavity squamous carcinomas with high risk of recurrence.

Methods: forty two patients with stage II oral cavity spinal cell carcinoma (AJCC), admitted and treated consecutively at the Portuguese Oncology Institute of Oporto (IPO) between January 1989 and December 1998, were evaluated for overall and disease free survival relating to the following variables: sex, age, alcohol and tobacco consumption, tumour size and grading, immunoreactivity for p16, p27, p53, pRb, Ki-67 and DNA content by image cytometry.

Results: Mean age of patients was 63.1 ± 10.4 years; 31 males and 11 females; median follow-up was 21 months (1–95 months); the most frequent location was the tongue (47.6%); only 16.6% of patients had no history of alcohol and tobacco consumption; 12 recurrences were observed (28.5%). Immunoreactivity was present for p53 (45.2%), p27 (66.6%), p16 (38.1%), pRb (47.6%), Ki-67 (90.4%). The aneuploidy was prevalent (83.3%); 19% of this cases had a high number (>17%) of tumour cells with DNA content >5c and a significantly short disease free survival rate ($p = 0.01$). The absence of immunoreactivity for p16 and pRb was the most frequent alteration of tumour suppressor genes products. The high rate proliferation cases (Ki-67 > 50%) were significantly related ($p = 0.008$) with absence of immunoreactivity for p27. Of all the variables studied only the aneuploid cases with a high percentage of DNA content >5c cells, showed a negative and significant correlation with disease free survival.

Conclusion: The high percentage of DNA content >5c cells, is a prognostic indicator in stage II oral cavity squamous cell carcinoma.

638 PUBLICATION

Improved results in the treatment of nasopharyngeal carcinoma using combined radiotherapy and chemotherapy versus radiotherapy alone

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One hundred and twenthyfour patients with locally advanced nasopharyngeal carcinoma who were treated in the department of radiation oncology in Agean University Faculty of Medicine between January 1986 and January 1996, were analysed retrospectively in order to evaluate the influence of combining chemotherapy (CT) and radiotherapy (RT) on survival rates:

Forthy one of those patients were treated with only RT (Group A), and 83 of them with RT and cisplatinium based chemotherapatic regimens (Group B). The ages were between 18–82 and 78 of the patients were men and the other 46 patients were women. The number of patients with T1, T2; T3 and T4 tumors were 12 (9.7%), 25 (20.2%), 52 (41.9%) and 35 (28.2%) respectively. The nodal stage distribution was as follows: N0, N1, N2, N3 were 11 (8.8%), 11 (8.8%), 75 (60.6%), and 27 (21.8%). The mean follow up period was 38 months (24–130).

The five years overall survival rate was 40.3% for the whole group. The survival rates were 34.2% and 43.9% for the only RT arm and combination therapy arm, respectively (P: 0.3). Distant metastases rates were 29.2% and 31.3% for Group A and B. Those factors were found to be effective on overall survival statistically; interruption of radiotherapy (p: 0.02), tumoral complete response (P: 0.03), sex (p: 0.04) and age (p: 0.04). Total dose of radiation therapy (p: 0.05) and RT and CT combination therapy (p: 0.02) were the other factors effecting the local progression free survival. The most common acute toxicity was mucositis and the late one was xerostomy, since there was no treatment related deaths. It,s concluded that the patients should be treated with radiation and chemotherapy combination regimens until the development of new treatment modalities where long therm survival advantage is established in randomised trials.

639 PUBLICATION

Amifostine – A radioprotector in locally advanced head and neck cancer

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Purpose: There are some preliminary informations about the beneficial use of amifostine in avoiding side effects in patients with head and neck tumors who underwent radiotherapy.

Patients: Amifostine was given as daily intravenous application (500 mg) 10–15 minutes prior to radiotherapy in 22 patients. The results were compared with another collective of patients which was similar.

Results: According to the WHO-score mucositis became manifest in 12 patients (grade I) and 4 patients (grade II) in the amifostine group versus 10 patients (grade II), 7 patients (grade III) and 1 patient (grade IV) in the control group. Xerostomia has been seen in 16 patients (grade I) and 6 patients (grade II) after administering amifostine. Without the drug 2 patients suffered from xerostomia (grade I), 10 patients (grade II) and 8 patients (grade III), respectively. Administering amifostine had been feasible and non problematic. Only a small rate of toxic side effects like nausea (11%) or emesis (4%) has been document.

Conclusions: We feel that amifostine is an effective radioprotector decreasing acute and late side effects in patients with head and neck tumors.

640 PUBLICATION

Bifractionated radiotherapy (RT) in locally advanced head and neck cancer (LAHNC) – Is it feasible in daily practice?

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Purpose: Recent studies showing local control and/or survival benefit of hyperfractionated RT ± chemotherapy (CT) in LAHNC prompted us to introduce these new strategies into clinical practice. We present the results of bifractionated RT (bRT) ± CT in LAHNC along with its economical and organisational aspects.

Methods: Out of 70 patients (pts), 34 were treated with induction CT (iCT) followed by bRT, 28 with bRT alone, 6 with iCT followed by concomitant bRT + CT (cbRT + CT) and 2 with cbRT + CT. bRT dose was 74.4 Gy given with 1.2 Gy bid for 5 d/week. iCT included up to 4 cycles of cisplatin (DDP) and fluorouracil (FU) or DDP, FU and navelbine (VNL). cCT included weekly DDP. A prophylactic supportive care protocol with fluconazole, pilocarpin etc. has been introduced. Economical (cost of RT) and organisational (staff and machine workload, patient's care) aspects of therapy have been evaluated.

Results: All but 7 pts completed therapy; the mean bRT time was 46.5 days, mean follow-up 10 months. Response was achieved in 37 pts (84%) out of 44 evaluable pts; 31 CR and 6 PR. Acute toxicity included: mucositis (62 pts), skin toxicity (58 pts), weight loss (46 pts), myelotoxicity (22 pts), nausea, vomiting (15 pts) and others. In 31 pts (44%) G3 or G4 mucositis and in 13 pts (18%) G3 leukopenia were observed. Late xerostomy was observed in the majority of pts and mandible necrosis in 1 pt. The cost of our bRT scheme is 20% more expensive than the conventional RT (70 Gy/35 fr), however as far as the machine workload is concerned, bRT should be considered as a RT of 2 separate pts. Then one has to add the costs of medical and nurse staff workload as well as the costs of supportive care increased due to higher acute toxicity (detailed assessment of workload and time of RT set-up will be presented).

Conclusion: Interesting results of bRT ± CT have been observed, however, its high acute toxicity and increased staff and machine workload require particular organisation of the work of a RT department. Thus these new treatment strategies should be employed within clinical studies in the specialised centres.

641 PUBLICATION

Concomitant radiochemotherapy with 5-fluorouracil and mitomycin c in locally advanced head and neck carcinoma

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Purpose: Giving chemotherapy and radiotherapy simultaneously (concomitant therapy) is one approach to improve results in advanced head and neck cancer.

Materials and Methods: 35 patients with advanced squamous carcinoma of the head and neck were treated from March 1995 to June 1998 with a continuous intravenous infusion of 5-fluorouracil, 600 mg/m^2 per 24 h for days 1 to 5 (120 h) and mitomycin-C 10 mg/m^2 intravenously on day 5 during the first week of radiotherapy and on day 36. Thirty-two patients had stage IV disease; two stage III; and one stage II. Ages ranged from 42 to 69 years (median 56.7 years). The tumours involved were as follows: oral cavity (11); oropharynx (14), hypopharynx/larynx (10). Radiotherapy was delivered to a total dose of 70 Gy with conventional fractionation (2 Gy/fraction, 5 times a week).

Results: Chemotherapy was well tolerated and all patients received the intended dose. Mild nausea occurred in five patients. With a mean follow-up of 11.8 months (8–46), 8 patients (23%) are alive (7, 8, 9, 18, 18, 31, 38, 41 months after treatment). A complete response was seen in 28 (80%). When a recurrence appeared, it was in the first year after treatment. One and 2-year survival rates were 46 and 20% for overall and disease-free survival, respectively. Grade 3 or 4 mucositis occurred in 17%. Grade 1–2 thrombopenia occurred in 3 patients (8%), grade > 2 leukopenia in 4 patients (11%), grade "2 anaemia in 2 patients (6%). We observed a treatment interruption of one week for 3 patients because of mucositis. Febrile neutropenia or aplasia were not observed.

Conclusion: The concomitant use of 5-fluorouracil, mitomycin C and radiotherapy in locally advanced head and neck carcinoma is well tolerated in this group of patients. This protocol showed good locoregional response with a very low toxicity profile.

642 PUBLICATION

Resection and reconstruction with the use of pectoralis major flap, in patients receiving radio/chemotherapy

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Purpose: Radiotherapy (RTH) and chemotherapy (CHTH) may impair the survival of island flaps used for reconstruction after extensive resection of head and neck cancer. We assessed the value of pectoralis major (PM) island flap used for reconstruction in patients receiving additional RTH or CHTH.

Methods: The PM flap was used in 51 patients (42 M 9 F, aged 26–78 years, mean 55). In 9 cases (17.6%) surgery was followed by RTH, in 26 (51%) – surgery was performed after neoadjuvant CHTH. Additionally, there were 16 (31.3%) cases of salvage surgery after previous radical RTH. The primary site of cancer was: oropharynx, floor of mouth, tongue – 43 cases, lower lip – 4, submandibular – 3 and parotid – 1. In three cases, flap pedicle could not be tunnelled under the skin, and was covered by a skin graft.

Results: Partial necrosis of skin island was observed in 2 cases, none of them required subsequent surgery other, than necrectomy. A fistula developed in further 2 patients, one of them requiring surgical closure. Thus, serious complications ocurred in 4/51 (7.8%) cases.

Conclusion: PM flap is extremely reliable for reconstruction after wide cancer resection in head and neck region, in patients receiving additional RTH or CHTH.