EP-1076

EFFECT OF NEOADJUVANT CHEMOTHERAPY AND HIGH DOSE CONFORMAL RADIOTHERAPY IN T3-4 AND/OR N POSITIVE ANAL CANCER

A.R. Jensen1, M.M. Fode1, J.C. Lindegard2, S. Buntsen3, L. Lundby1
1Aarhus University Hospital, Oncology, Aarhus C, Denmark
2Aarhus University Hospital, Surgery, Aarhus C, Denmark

Purpose/Objective: To evaluate the efficacy of neoadjuvant chemotherapy followed by conformal radiotherapy in patients with locally advanced anal cancer.

Materials and Methods: Between 1997 and 2009, 63 consecutive patients with squamous cell carcinoma in the anal canal, stage T3, T4 and/or regional lymph node metastasis were treated with curative intention in a single institution. The treatment consisted of three courses of induction chemotherapy with CILF (cisplatin, ifosfamide, leucovorin and 5-fluouracil), restaging and definitive 3D conformal external beam radiotherapy consisting of 51.2 Gy/32 fractions to the groins and pelvic and 64.32 Gy in 32 fractions to the primary tumour and pathological nodes. The differential dose levels were obtained by a simultaneous integrated boost technique.

Results: The median follow-up time for all patients was 92 months (29-166). Fifty-two patients (83%) completed 3 schedules of CILF and 53 (83%) had partial or complete response on chemotherapy. Seven (11%) had progressive disease. Only one patient had persistent local disease after EBRT. Local tumor relapse was observed in 16 patients (25%) within a time range of 5 to 24 months after primary treatment and to these patients salvage surgery was offered. The actuarial local control rate was 74% at 10 years. Distant metastasis appeared in 4 patients. No recurrences were observed after two years and recurrence free survival was 68% at 5 and 10 years. Overall survival for all patients was 58% at 5 years and 42% at 10 years. All 20 patients (32%) got a colostomy, 7 (11%) due to local relapse and 8 (13%) due to anal dysfunction.

Conclusions: This analysis suggests that a treatment schedule involving neoadjuvant chemotherapy followed by high dose radiotherapy is effective for local control and anal sphincter preservation in locally advanced squamous cell anal cancer.

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COMBINED MODALITY TREATMENT IN ANAL CANAL CARCINOMA: IMPACT OF FULL DOSE TREATMENT AND CLINICAL STAGE CATEGORY

S. Sole1, C. Solé1, V. Ovalle1, M. Russo1, M. Baeza1
1Instituut de Radiomedicina, Radiotherapy, Santiago, Chile

Purpose/Objective: Since N. Ngio’s report in 1974, combined modality treatment, chemo-radiation (CCRT), has been the standard in anal canal carcinoma. We report the results of this treatment with regard to compliance, toxicity, clinical outcomes and we intent to determine if full dose treatment and clinical stage has an impact in this patient group.

Materials and Methods: Between 1999 and 2009, 42 patients received CCRT with no planned gap (45 Gy at 1.8 Gy/fraction +/- boost 9 Gy at 1.8 Gy/fraction; 5-fluorouracil, 1000 mg/m2, Days 1-4 and 29-32, mitomycin C, 10-15 mg/m2, Days 1 and 29). Median age 62 years (28-83); 11 (26%) males were HIV positive, 16 (38%) females; Stage I = 6 (14%), II = 13 (31%), IIIA = 8 (19%), IIIB =15 (36%). Median overall treatment time (OTT) was 35 (14-53) days, 36 (81%) patients received full dose treatment (FDT), 2 patients had grade 4 toxicity, and 1 treatment related death. Median follow up was 63.8 months with a minimum of 25 months.

Results: For the whole study sample Kaplan-Meier 5-year rate of loco-regional control (LRC) was 78%, colostomy free survival (CFS) 73%, distant metastases free survival (DMFS) 76%, disease free survival (DFS) 65% cancer-specific survival (CSS) 69% and overall survival (OS) 46%. The 42 patients accrued, were analyzed for outcomes by clinical stage into 2 groups (I, II, IIIA vs. IIIB) and compared using log-rank test with significant differences in OS (p=0.002); CSS (p=0.000); DFS (p=0.000); DMFS (p=0.000); CFS (p=0.000); LRC (p=0.000). Patients who received FDT had a significantly better OS (p=0.004) and CSS (p=0.01).

Conclusions: In our experience clinical stage category of disease has a significant impact in all analyzed outcomes, patients who received FDT had an improvement in OS and CSS. Results for more advanced tumours (IIIB) remain poor, and require strategies to improve outcome. Higher doses or better treatment compliance may be required. We discourage planned treatment gaps.

EP-1078

POSTOPERATIVE GASTRIC CANCER CHEMORADIATION: LONG TERM RESULTS WITH CTX DEFINITION BASED ON TUMOR SITE AND P-STAGE

V. Picardi1, R. Tambaro2, G. Macchila1, F. Deodato1, S. Mignogna1, G. Cecere1, P. Facelli1, V. Valentini1, N. Cellerino1, A.G. Moriganti1
1Fondazione di Ricerca e Curia “Giovanni Paolo II” Università Cattolica del S. Cuore, Radiotherapy Unit, Campobasso, Italy
2Fondazione di Ricerca e Curia “Giovanni Paolo II” Università Cattolica del S. Cuore, Palliative Care Unit, Campobasso, Italy
3General Hospital “A. Capecchi”, Surgery Unit, Campobasso, Italy
4Fondazione di Ricerca e Curia “Giovanni Paolo II” Università Cattolica del S. Cuore, Surgery Unit, Campobasso, Italy
5Università Cattolica del S. Cuore, Radiation Oncology Department, Roma, Italy

Purpose/Objective: The 5-year survival of patients with completely resected node-positive gastric cancer ranges from 15% to 25%. Adjuvant chemoradiation represent an effective strategy to increase survival in patients with advanced stage or limited lymphadenectomy. Aim of this analysis was to evaluate feasibility and outcomes in postoperative gastric cancer patients treated by chemoradiation. The chemotherapy schedule was according to Macdonald stage (INT-0116), but a more advanced radiotherapy technique (3D conformal) was used.

Materials and Methods: Patients were simulated and treated in the supine position, using ac-lock for set-up. A 4-field technique was employed to irradiate a target volume including the gastric bed, anastomosis, stump, and regional node areas (perigastric nodes, nodes along the left gastric common hepatic, splenic, and celiac arteries). The lymphatic drainage according to the tumour location was identified using the Japanese Research Society for Gastric Cancer (JRSGC) Lymphnode classification and the Martinez-Monge area classification. Patients received a radiotherapy total dose ranging from 45 Gy to 55 Gy delivered in 25 fractions, five days per week, to the tumor bed and to the regional nodes plus 10 mm margin. Chemotherapy was based on fluorouracil and leucovorin, before, during and after radiotherapy according to the MacDonald schedule. Acute toxicity was recorded according to RTOG criteria. Patients underwent follow-up as scheduled.

Results: 74 patients (M/F: 42/32, median age: 61, range: 34-79; stage I: 5, stage II: 21, stage III: 34, stage IV: 14) were included in this analysis. 69 (93.2%) patients received a radiotherapy total dose of 45 Gy. Four (5.4%) high risk patients received a concomitant boost up to a total dose of 55 Gy. 71 (95.9%) patients completed the treatment at the prescribed dose, 3 (4.1%) patients interrupted the concomitant treatment (1 pt due to clinical sequelae after neutropenia, 2 pts due to surgical complications). Acute toxicity requiring temporary treatment interruption (≥3 RTOG scale) was observed in 6 patients (8.1%). During treatment and first follow-up, in 13 patients (17.6%) was observed a grade 3 acute haematological toxicity and in 5 patients (6.7%) a grade 4 acute toxicity was registered. After a median follow-up of 26 months (range: 1-105 months), 18 (24.3%) patients died (14 for metastatic disease, 1 because of gastrointestinal bleeding, 2 for unknown cause, 1 for neuropathy). Actuarial 3 year local control rate was 86.8%, whereas disease free survival, recurrence free survival and overall survival rates were 56.7%, 61.1% and 69%, respectively.

Conclusions: In comparison with literature data (2D irradiation technique), a 3D postoperative chemoradiation of gastric cancer with CTV definition based on tumor site and p-stage was better tolerated with very encouraging long term outcomes.

EP-1079

ROLE OF NEOADJUVANT CHEMORADIATION IN LOCALLY ADVANCED UNRESECTABLE GALL BLADDER CANCERS

R. Engineer1, M. Goel1, S. Mehta1, S.V. Shrikhande2, P. Patil3, S. Chopra1, V. Rangarajan1, N. Purandare1, S.K. Shrivastava1
1Tata Memorial Hospital, Nuclear Medicine, Mumbai, India
2Tata Memorial Hospital, Gastrointestinal Surgery, Mumbai, India
3Tata Memorial Hospital, Gastrointestinal Medicine, Mumbai, India
4Tata Memorial Hospital, Nuclear Medicine, Mumbai, India

Purpose/Objective: Locally advanced gall bladder cancers not amenable for curative surgical resection chemotherapy and radiotherapy (RT) were treated at our centre with concurrent chemoradiotherapy prospectively. We present interim analysis of an ongoing study.

Materials and Methods: Seventeen patients with locally advanced carcinoma gall bladder were treated with concomitant
chemo-irradiation (CCRT) using Helical Tomotherapy (HT) based
Intensity Modulated and Image Guided Radiotherapy with radiation
dose escalation and simultaneous integrated boost to gross disease.
All patients underwent PET CT scan to rule out metastatic disease
prior to starting chemoradiation and 6 weeks post chemoradiation
to evaluate response.
These patients were then planned for concomitant chemoradiation
using Tomotherapy based IMRT to a doses of 57-60 Gy over 25
fractions to the gross tumour as a simultaneous integrated boost
volume and 45-50 Gy to the surrounding tissues and the grossly
uninvolved draining nodes. While planning special care was taken
so that the dose to duodenum was restricted to 50% of the volume
to receive less than 45 Gy. The patients underwent daily MVCT imaging
coupled with PET to rule out metastatic disease prior to RT. All the patients received concurrent chemotherapy with Inj. Gemcitabine (weekly 300mg/m²).

Results: Of the 17 patients 1 patient could not complete RT due to
repeated cholangitis during treatment and 1 developed liver
metastasis during radiotherapy. Rest of the 15 patients could
complete planned treatment. No patient developed acute grade 3 GI
toxicity. Of these 8/17 (47%) underwent R0 resection. Rest either
developed progressive disease or had metastatic disease during
surgical exploration.

Conclusions: Locally advanced gall bladder cancers not amenable
to upfront surgical resection can be down staged by neoadjuvant
chemotherapy to undergo curative surgical resection in almost 50%
of the patients.

EP-1080
FDG-PET SUV AND BIOLOGICAL MARKERS AS PREDICTIVE FACTORS OF
TUMOUR RESPONSE IN ANAL CANCER TREATED WITH RT-CT
M. Krengli1, M.E. Milia1, L. Deantonio1, L. Turri2, G. Loli2, G.
Sacchetti3, R. Boldorini3, E. Maida3, T. Cena3, C. Magnani3
1University Hospital ‘Maggiore della Carità’, Radiotherapy, Novara,
Italy
2University Hospital ‘Maggiore della Carità’, Medical Physics, Novara,
Italy
3University Hospital ‘Maggiore della Carità’, Nuclear Medicine,
Novara, Italy
4University Hospital ‘Maggiore della Carità’, Pathology, Novara, Italy
5University Hospital ‘Maggiore della Carità’, Epidemiology and
Biostatistics, Novara, Italy

Purpose/Objective: PET/CT has an emerging role in management of
anorectal cancer. FDG-PET standard uptake value (SUV) and molecular
biomarkers have been identified as prognostic factors. The present
study analyzed the role of SUV and biological markers as potential
predictors of tumour response in a series of anal canal cancer patients
received radio-chemotherapy (RT-CT).

Materials and Methods: Forty-seven patients (pts), 17 male and 30
female, with a mean age of 67 years (range 40-95), with biopsy
proven anal canal carcinoma and treated with RT-CT were included in
the present analysis. Histology was squamous cell in 35/47 pts (75%),
cloacogenic in 9/47 (19%) and adenocarcinoma in 3/47 (6%). Clinical
stage according to TNM was: 3 T1, 18 T2, 22 T3 and 4 T4. Nineteen
patients had lymph node involvement at presentation: 1 N1, 12 N2
and 6 N3. PET/CT for staging and simulation was performed in 41/47
pts (87%). Maximum (max) and average (avg) SUV was calculated for
each patient. In 20/47 (43%) pts, KRAS, BRAF, EGFR and Ki67
expression and mutations were also analyzed. Forty of 47 pts (85%)
received chemo-RT and 7 pts radiotherapy alone. Chemotherapy
consisted of mitomycin C and 5-fluorouracil (FU) in 19/40 pts (48%)
or cisplatin and 5-FU in 21/40 pts (52%). Response was evaluated by
clinical examination, endoscopy, CT-scan and biopsy 2-4 months after
end of chemo-RT. IMRT was delivered in 8/47 pts and 3D-conformal in
39/47. Dose ranged from 54 to 65 Gy to the tumour target (median 59.4
Gy) and from 39.6 Gy to 45 Gy to the uninvolved lymph nodes (median
59.4 Gy) with 1.8 Gy/fx/daily.

Results: We observed 22/47 (47%) complete response (CR), 23
(49%) partial response (PR) and 2/47 (4%) no response. SUVmax and
SUVavg significantly correlated with T-stage (p=0.02 and p=0.01) and
with clinical response (p=0.0023 and p=0.0291). Histology significantly
influenced SUVmax. No significant correlation was found between SUV,
grading and increased risk of N+. Higher SUVmax of the primary
tumour was associated with a significant worse disease-free survival
by LogRank Test (p=0.01). All pts were wild-type BRAF and 3
mutations of KRAS were observed. Two pts had high polymy of
EGFR. We did not find a correlation between EGFR amplification,
KRAS mutations and treatment response.

Conclusions: SUVmax and SUVavg were associated with response
to CRT. Our results are in accord with those of the literature and confirm
the negative predictive value of SUVmax and SUVavg and their association with a poor DFS. No correlation was found between
biological markers and response.

EP-1081
LOCOREGIONAL CONTROL AFTER RADIOCHEMOTHERAPY FOR ANAL
CANCER: A SINGLE CENTRE RETROSPECTIVE ANALYSIS
F. Zehentmayr1, W.C. Wolf2, M.E. Kreis1, C. Belka4
1Ludwig-Maximilian-University, Academic Department of Radiation
Oncology, Munich, Germany
2Ludwig-Maximilian-University, Academic Department of Surgery,
Munich, Germany

Purpose/Objective: To evaluate long term loco-regional control- and
survival rates after radical radiochemotherapy for anal cancer in non-
selected patients treated outside of controlled trials a retrospective
analysis was performed.

Materials and Methods: Between 07/2002 and 12/2010 109
consecutive patients with anal cancer were identified from the
institutional data base. Chart review, data from the Munich Cancer
Registry (MCR) and telephone follow up were undertaken to collect
data.

Results: 109 (69 female / 40 male) patients who received radical radiochemotherapy for anal cancer in a curative intention were identified. The median age at diagnosis was 63y (range 28-93). The disease stages (UICC 7th ed., 2010) were distributed as follows: 2/109 (1.8%) UICC 0, 19/109 (17.4%) UICC I, 47/109 (43.1%) UICC II, 23/109 (21.1%), 11/109 (10.0%) UICC III and 4/109 (3.7%) UICC IV. The 5-year disease-free survival rate was 75% (95% CI 69-81). No correlation was found between
biological markers and response.

EP-1082
ROLE OF PRETREATMENT CEA LEVEL IN PATIENTS WITH RECTAL
CANCER RECEIVING PREOPERATIVE CHEMORADIOThERAPY
S. Yeo1, D. Kim2
1Soonchunhyang University College of Medicine, Department of
Radiation Oncology, Cheonan, Korea Republic
2National Cancer Center, Center for Colorectal Cancer, Gunay, Korea
Republic

Purpose/Objective: The pretreatment serum carcinoembryonic
antigen (CEA) level is an independent prognostic factor in colorectal
cancer. However, few studies have evaluated its prognostic
significance after preoperative chemoradiotherapy (CRT), which has
become widely adopted in patients with rectal cancer. Here, the
significance of the CEA as a prognostic or predictive factor was
investigated.

Materials and Methods: In total, 609 patients with locally advanced
cStage II-III) mid to distal rectal cancer who underwent preoperative
CRT and radical surgery between 2001 and 2008 were analyzed
retrospectively. A prognostic factor analysis was performed using the
log-rank test and Cox proportional hazards regression. Predictive
factors for pathologic CRT response were determined using
dmultivariate logistic regression.

Results: Elevated CEA levels (> 5 ng/mL) were observed in 201 (33.0%)
patients at diagnosis. Following preoperative CRT, a downstaging
to ypStage 0-II was observed. The median follow-up period was 60 months and the 5-year disease-free and overall survival rates