945 PUBLICATION

Modified partial hyperfractionation in radiotherapy for bulky uterine cervical cancer: Reduction of overall treatment time

M. Chun[1], S.-H. Kang[1], H.-S. Ryu[2], K.-H. Chang[2], Y.-T. Oh[1], H.-J. Joo[3], E.-J. Lee[4]. [1]*Dept. of Radiation Oncology,* [2]*Dept. of Gynecology & Obstetrics,* [3] *Dept. of Anatomic Pathology,* [4]*Dept. of Radiology, Ajou Univ. School of Medicine, Suwon, South Korea*

Purpose: FIGO stage, bulk of disease within each stage, Kamofsky performance status, age, the use of intracavitary radiation, and paracentral dose are accepted as the independent factors of prognosis and outcome in the cure of cervical cancers with radiation therapy. The concurrent boost or accelerated hyperfractionation scheme to reduce the overall treatment time (OT) is not feasible in cervical cancer because of bowel complication unlike the head/neck cancers. In order to improve the local control rate in bulky cervical cancers, we designed non-randomized clinical trial in attempt to find feasibility and toxicity of modified partial hyperfractionation of external beam radiation that could reduce OT by 1 week.

Methods: Thirty-one patients (Group 1) with bulky cervical cancer (≈4 cm with stage II and III, ≈5 cm with stage Ib2) entered BID protocol between September 1994 and December 1996 (18 Gy/10 fx in 2 weeks followed by 18 Gy/12 fx, bid in 6 days, then midline block at 36 Gy with 45 Gy to the whole pelvis and 51–59 Gy to the parametrium). The patients underwent high dose rate brachytherapy with 4 Gy/fx × 7 to point A, biw. During the same period, patients with non-bulky tumor (Group 2, n = 31) received conventional treatment and similar brachytherapy.

Results: All patients were followed minimum 2 years. The OT was 7 weeks or less in 61.3%, 7.1 to 8 weeks in 29% and more than 8 weeks in 9.7% (19.4%, 51.6%, and 29% in Group 2, respectively, p = 0.003). In both groups, the major reason for treatment interruption was frequent holidays over 3 days. During the treatment, patients in Group 1 tolerated treatments well without excessive side effects and unnecessary treatment breaks even in old age group beyond 65 years old. However, the late rectal complication (rectal bleeding) in Group 1 was frequent (4/31 vs 0) but was self limited within 3–6 months except one patient. Local failure rate at 4 years was 16% and 13% in Group 1 and 2, respectively. Overall actuarial survival rates at 4 years in both groups were 87.1%.

Conclusions: Partial Hyperfractionation on 3rd week of radiation permitted the patients to finish their treatment with shorter OT, without excessive acute side effects and with acceptable grade 2 late rectal complications. This treatment scheme could be an effective method in improvement of local control of bulky cervical cancer.

946 PUBLICATION

Change of proliferative activity and cyclin E expression during radiotherapy in locally advanced cervical cancer

S.-H. Kang[1], M. Chun[1], H.-J. Joo[2], M.-S. Cho[1], H.-S. Ryu[3], Y.-T. Oh[1]. [1]*Ajou Univ. School of Medicine, Dept. of Radiation Oncology;* [2]*Ajou Univ. School of Medicine, Dept. of Anatomic pathology;* [3]*Ajou Univ. School of Medicine, Dept. of Gynecology and Obstetrics, Suwon, South Korea*

Purpose: Some studies have described decreased pelvic tumor control and survival rates in locally advanced cervical cancer when the overall treatment time in a course of definitive irradiation is prolonged. Fowler emphasized the importance of rapid proliferation of malignant cells that influence tumor control probability. In this study, we investigated changes in Mib-1, PCNA, and cyclin E indices before and during the radiation treatment to clarify the effects of fractionated radiation on the cell cycle and its underlying mechanism.

Materials and Methods: Five patients with locally advanced cervical cancer were available for the study. All specimens were excised from tumor tissues before and during radiation treatment (day 0, 8, 15, 22 and 29). Slides were prepared for immunostaining with Mib-1, PCNA and cyclin E monoclonal antibodies. One pathologist counted malignant cell numbers (positive or negative with stain) on 400× color photographs.

Results: Mib-1 and PCNA indices were much higher in untreated specimens comparing to cyclin E index. PCNA index was rapidly decreasing with increased radiation dose but Cyclin E index was still high even at 22nd day of treatment. Mib-1 index of 8th day specimen was shown different pattern with patients and since 15th day, there was decreased. There was no recognized tumor cells at 29th day of treatment.

Conclusion: This is a study with a small number of patients. But Mib-1 and PCNA were strongly positive even later part of treatment. We will include more patients to analyse the relationship between tumor response and cell kinetics change.

947 PUBLICATION

Endometrial carcinomas: Prognostic factor in I–II stage

A. Bonetta[1], C. Soatti[1], B. Morrica[1]. [1]*Radioterapia, istituti ospitalieri, Cremona, Italy*

Purpose: To evaluate prognostic factors in patients with stage I–II endometrial carcinoma treated with surgery plus adjuvant radiotherapy (EBRT, EBRT + LDR-BRT, LDR – BRT alone)

Material and Methods: From 1/85 to 12/96, 152 patients were admitted in this study (Ib 37%, Ic 39%, IIa 11%, IIb 13%). RT was performed using box technique on pelvis, Rx 18 Mv, personalised blocks, prescribing 1.8–2 Gy at the minimal isodose around the CTV. Total doses ranged within 46–50.4 Gy. In 71 pts a boost was performed with LDR brachytherapy on the vaginal cuff, doses ranged within 10–20 Gy at 0.5 cm from the applicator surface. Brachytherapy was performed in pts with high risk of local relapses, not only for the well-known prognostic factors, but also for the operative technique or surgical complications. 18 pts received only brachytherapy as adjuvant treatment for critical general conditions.

Results: No grade III–IV WHO toxicities or complications were seen. With a minimal 2 years follow up, we have observed 9 local and 18 distant relapses. Overall 5 years survival is 78% and NED survival 84%. No significative differences were observed among the three groups of postoperative RT (EBRT, EBRT + BRT, BRT alone). Most important prognostic factor in our series is the tumor volume with a difference (small volume 91 pts, NED survival 90% vs 73% in 61 with big volume; p = 0.03). Other factors show only a trend or no significance.

Discussion: In our series adjuvant radiotherapy seems to reduce the incidence local relapses also in high-risk patients. These data invite us to confirm our treatment policy in performing RT, especially delivering local high doses with use of BRT without increase of acute or late toxicities.

948 PUBLICATION

Comparison of different polymerase chain reaction methods for detection of human papillomaviruses

K. Husnjak[1], M. Grce[1], K. Pavelic[1]. [1]*Rudjer Boskovic Institute, Division of Molecular Medicine, Zagreb, Croatia*

Purpose: Many epidemiologic studies and basic research on molecular level strongly support the role of human papillomaviruses as etiologic agents in cervical carcinogenesis. There are more than 70 HPV types of which more than 30 infect genital sites and have different oncogenic potential. Diagnosis of HPV infections is of extreme importance in the prevention of cervical cancer.

Methods: We tested the presence of HPV DNA by polymerase chain reaction (PCR) in cervical scrapes obtained from consenting women with cytomorphologically abnormal cervical smears. In order to evaluate different PCR approaches for screening and detection of HPVs we used and then compared the results obtained with three sets of general primers localised within the L1 region of HPV genome (MY09/MY 11, inosine-containing MY09/MY11 and L1C1/L1C2) on 164 samples. These results have also been compared with results obtained with type-specific primer pairs for HPV types 6, 11, 16, 18, 31 and 33.

Results: HPV DNA was detected in 125/164 (76.22%) cervical scrapes (positive result with at least one set of consensus primers); the concordance of results obtained with three sets of general primers (either positive or negative result) was 53.05%. HPV type was determined in 97/164 (59.15%) samples; in 16/164 (10.37%) samples a multiple HPV infection was found.

Conclusion: Simultaneous use of MY09/MY11 and L1C1/L1C2 primer sets in combination with type specific PCR is a valuable method for HPV screening and typing.

949 PUBLICATION

The association of human papillomavirus, cytomegalovirus and herpes simplex virus infection in human cervical cancer in Taiwan, R.O.C.

C.P. Han[1], S.L. Chen[2], Y.S. Tyan[3], Y.C. Liu[4]. [1]*Armed Force Taichung General Hospital, Obstetrics and Gynecology, Taichung, Taiwan;* [2]*National Defense Medical Center, Microbiology and Immunology, Taipei, Taiwan;* [3]*Armed Force Taichung General Hospital, Obstetrics and Gynecology, Taichung, Taiwan;* [4]*Armed Force Taichung Hospital, Obstetrics and Gynecology, Taichung, Taiwan, China*

Introduction: Human Papillomavirus (HPV) has been suggested to play an important role in cervical carcinogenesis. However, herpes simplex virus