8012 POSTER

Results of Curative Concomitant Chemoradiotherapy in Patients With FIGO Stage IVB Cervical Cancer Presenting Para-aortic and Left Supraclavicular Lymph Nodal Metastases

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Background: Contrary to the established role of curative extended-field chemoradiotherapy, the role of concurrent chemoradiotherapy(CCRT) still remains undefined in patients with FIGO stage IVB cervical cancer presenting para-aortic and left supraclavicular lymph node (LN) metastases. We performed the retrospective review to determine the efficacy and toxicity of aggressive chemoradiotherapy involving pelvic, para-aortic, and left supraclavicular fossa.
Materials and Methods: 24 women with cervical cancer presenting para-aortic and left supraclavicular LN metastases underwent cisplatin-based CCRT from 2002 to 2010. As a historic control group, we reviewed the clinical outcomes of 71 patients with cervical cancer who received extended-field chemoradiotherapy due to para-aortic LN metastasis without positive supraclavicular LN from 1998 to 2010. The patients in positive supraclavicular LN group received median external dose of 59.4 Gy to the para-aortic and left supraclavicular LNs and 50.4 Gy to the pelvis, followed by 30 Gy in 6 fractions of intracavitary radiotherapy(ICR). The patients in positive para-aortic LN without supraclavicular LN metastasis group received the same median external dose to the para-aortic LN, pelvis and the same median dose of ICR.
Results: Among 24 patients with positive supraclavicular LN, 3 patients did not complete full dose of chemotherapy and 5 did not finish planned radiotherapy because of acute toxicity. The most common acute toxicity was hematologic toxicity. Grade 3−4 hematologic toxicity was observed in 15 (63%) women. 17 (71%) patients suffered from grade 2 acute gastrointestinal toxicity, which was transient and self-limiting. A woman complained of grade 3 late genitourinary toxicity and another encountered grade 3 late soft tissue complication around supraclavicular fossa. 11 (46%) women showed a complete response encompassing the primary mass, and the metastatic pelvic, para-aortic and left supraclavicular LNs. With a median follow-up period of 20 months (35 months for surviving patients), 8 (33%) women had no evidence of disease, while 1 (4%) persistent disease, 6 (25%) distant failure, and 9 (38%) showed both in-field and distant failure. 3-year overall and disease-free survival rates were 41% and 37%, respectively. In comparison, 37 of 71 cases (51%) with para-aortic LN metastasis had no evidence of disease. 15 patients (21%) showed local recurrence, while 9 (13%) experienced distant failure, and 10 (14%) showed both local and distant failure. 3-year overall and disease-free survival rates were 65% and 50%, respectively.
Conclusions: Curative CCRT in the patients with FIGO stage IVB cervical carcinoma presenting para-aortic and left supraclavicular LNs metastases is feasible with acceptable late morbidity and high response rate despite its substantial acute toxicity. More intensive or further chemotherapy may be indicated for these patients, considering most treatment failures were distant metastases.

8013 POSTER

Intraperitoneal Chemotherapy for Stage III Epithelial Ovarian Cancer − Our Experience

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Background: Trial GOG 172 has concluded improvement in survival with intraperitoneal (IP) chemotherapy but most of the patients had complications and only 40% could complete all the desired cycles by intraperitoneal route. Major complications were related to the chemoport. We undertook this study to find the means of reducing complications, along with increasing the benefits of IP chemotherapy.
Material and Methods: During January 2007 to December 2010, hundred consecutive patients of stage III epithelial ovarian cancer who had optimal cytoreduction at Manipal comprehensive cancer center underwent chemoport insertion during laparotomy. Initial 20 cases had 9.6F Bard IP chemoport, and later cases had venous port inserted intraperitoneally. Tunneling of the catheter was meticulous, single thrust without great disturbance to subcutaneous tissue. Entry point into the peritoneum was single, 6 cm lateral to the umbilicus and double purse-string suture taken around the catheter to prevent peri-catheter backflow of ascitic fluid or drug. Modified IP chemotherapy regimen (SWOG-9912 trial) was used.
Results: Age of the patient ranged from 34 years to 76 years. In total 600 cycles, 516 cycles (86%) were completed. Seventy patients received all the 6 cycles by IP route. Two patients in the initial 10 had vaginal leak, for whom first 2 cycles were given by IV route and then shifted to IP route. Subsequently all cases had double layer closure of vaginal vault. Catheter block was seen in 5 cases, of which 4 salvaged by heparin injection lock for 2 hours and in subsequent cases IV port access catheter with valve replaced the fenestrated IP catheter. None of the IV catheters had the block. Four cases had backflow of fluid around catheter collecting around the port chamber site. Two patients had severe abdominal pain due to dense adhesions and unequal distribution of drug on radionucleide scan, further cycles were completed by IV route. Cisplatin was replaced with carboplatin in 5 cases with severe toxicity. Longest follow-up is 4 years with median follow up of 1.8 years.70% are disease free on follow up. Local recurrence rate was 18 and systemic in 8 cases. Mortality rate is 4%.
Conclusion: Complications of IP ports are minimal when insertion is done meticulously with a dedicated team. With modified IP dose and drug regimen, side effects are less and most patients can complete all the desired cycles. Long term follow up study is required to assess the PFS and OS.

8014 POSTER

Adenocarcinoma and Squamous Cell Carcinoma of the Cervix: Should They Be Treated Differently?

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Background: The optimal management of adenocarcinoma (AC) of the cervix is still an issue in debate among clinicians, especially whether it should be different from squamous cell carcinoma (SCC).
The purpose of this study is to analyze the differences between AC and SCC in what respects response to treatment, recurrence and survival rates.
Material and Methods: In our retrospective study, we included patients (pts) with AC or SCC of the cervix treated in our institution with concurrent chemoradiotherapy. Data analysis was performed using SPSS version 18.0. Proportions among groups were compared with Pearson Chi-square test. A 5% level of significance was used in the analysis. Overall survival (OS) and disease free survival (DFS) were estimated by Kaplan–Meier analysis. Cox regression models were used to adjust for potential confounders.
Results: All pts were treated with radiotherapy plus concurrent weekly-cisplatin (40 mg/m^2). Results are summarized on table 1.

Table 1. Summary of results

	AC	SCC	*p*-value
Patients (n)	34	229	
Age (median, range)	48 (31−70)	49 (20−75)	
ECOG performance status (median, range)	0 (0−1)	0 (0−1)	
FIGO* stage (n/%)			
IB2	6 (17.6)	19 (8.3)	
IIA2	1 (2.9)	13 (5.7)	
IIB	25 (73.5)	133 (58)	
IIIA	0	5 (2.2)	
IIIB	1(2.9)	52 (22.7)	
IVA	1(2.9)	7 (3.1)	
Lymph nodes metastases	0	12	
Nr of chemotherapy cycles (median, range)	6 (4−6)	6 (1−6)	
External radiotherapy dose (median, range)	50 (42−50) Gy	50 (30−60) Gy	
Brachytherapy dose (median, range)	42 (30–50.4)	40 (30−45)	
Response to treatment (n; %)			
Complete	30(88.2)	165 (72.1)	
Partial	2(5.9)	47 (20.5)	$p = 0.124$
Stable disease	0	13 (5.7)	
Disease progression	2 (5.9)	4 (1.7)	
Recurrence (n/%)	4 (11.8)	33 (14.3)	$p = 0.685$
Median DFS	86.6	85.8	$p = 0.431$
Median OS**	88.3	80.9	$p = 0.158$

n = number of patients.
*According to revised FIGO staging 2009.
**HR = 0.421, 95% CI = 0.10–1.78, p = 0.240, using Cox regression analysis adjusted by tumour stage.

Conclusions: There were no statistically significant differences between AC and SCC in what respects to treatment response, patterns of recurrence and survival rates, suggesting that they should be treated equally. Differences between AC and SCC reported in some studies could

be partially attributable to the inclusion of patients with adenoscamous histology in the AC group, which is associated with worse prognosis. A multicentric prospective trial including solely AC histology is needed for better management of this entity.

8015 POSTER

Phase I Clinical Trial of S-1, Cisplatin and Concurrent Radiotherapy for Primary Cervical Cancer

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Background: Cisplatin based chemotherapy plus concurrent radiotherapy is widely used as the standard therapy for women with cervical cancer. S-1 is an oral fluoropyrimidine. A phase II study of S-1 monotherapy for recurrent or metastatic cervical cancer have been shown to be active against cervical cancer. S-1 has been also revealed to act as a radiosensitiser in preclinical models. A phase II study was conducted for locally advanced non-small cell lung cancer, and high response rates and tolerability were shown. In this study, we evaluated the maximum-tolerated dose (MTD) according to escalating dosage of S-1 in combination with a fixed dose of cisplatin and concurrent radiotherapy to patients with cervical cancer.
Materials and Methods: Eligible patients were 20−74 years old, had FIGO stage Ib − IVa cervical cancer, a performance status of 0−2, and no prior therapy. Patients were treated with cisplatin (50 mg/m^2) on day 1 and S-1 (twice daily) on day 1−14 repeated every 4 weeks for two cycles. The S-1 starting dose was 60 mg/m^2/day (level 1), and the dose was escalated to 80 mg/m^2/day (level 2) as the results of adverse events. Radiation therapy was consisted of both external radiation therapy and high-dose-rate intracavitary brachytherapy.
Results: Level 1 and 2 were studied with six patients enrolled, respectively. One patient in level 1 developed grade3 venous thrombosis. In level 2, two patients developed grade 3 hypoalbuminemia (one patient also had grade 3 venous thrombosis), and one patient experienced febrile neutropenia remained for eleven days. The adverse events of those four patients were predetermined dose-limiting toxicities in this study. Level 1 was determined as the MTD and recommend dose (RD). Eleven patients were evaluable for response: eight complete responses and three partial responses were obtained. Ten of eleven patients remained disease-free following treatment.
Conclusions: The use of S-1 with concurrent cisplatin and radiotherapy has acceptable toxicity and could be an active treatment for cervical cancer. This study is the first report of S-1 based chemotherapy and concurrent whole pelvic radiation in the world. We have started phase II study at the RD to evaluate the efficacy of this regimen.

8016 POSTER

Radiotherapy in Cervical Cancer With Positive Para-aortic Lymph Nodes

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Background: The survival outcome of patients with carcinoma of the cervix and positive para-aortic lymph nodes is poor. Retrospective studies of these patients have demonstrated a 5-year survival of about 30%. Treatment failures occur in the pelvis, the para-aortic region, and at distant metastatic sites. The purpose of this study was to evaluate the response to treatments, acute and late toxicity of treatments to cervical cancer patients with positive para-aortic lymph nodes in our department.
Material and Methods: Between 2003 and 2010, we selected patients diagnosed with cervical cancer and para-aortic disease extension treated with extended field radiotherapy (RT) in our department. Response to treatment was evaluated by imaging control and/or cervicovaginal cytology. Toxicities were evaluated accordingly *RTOG Toxicity Criteria*.
Results: Fifty-six patients were eligible, with clinical Stages between IB1 and IVA (FIGO). Median age was 50 years. Thirteen patients had biopsy-proven para-aortic lymph node, remaining patients had clinically imaging positive nodes. Most of the patients (92%) had squamous-cell carcinoma as histologic diagnosis. One (1.7%) patient had surgery before RT, twenty-one (38%) were treated with chemoradiation (cisplatin 40 mg/m^2 i.v. weekly in the first 6 weeks of RT). Twelve (21%) patients had external beam RT with low-dose-rate intracavitary brachytherapy. Ten (18%) patients received radiation treatment with intensity modulated radiotherapy (IMRT). All patients received a median dose of 45 Gy to the pelvis and para-aortic lymph nodes (1.8 Gy/Fr, at 15 or 18MV). We reported acute nausea and vomiting toxicity of at least grade 2 in 35% of patients, and bowel toxicity of at least grade 3 in 30% of patients. Acute toxicity was less reported in patients treated with IMRT, with no grade 3 bowel toxicity. The median duration of follow-up was 13.8 months. Late toxicity of large bowel and rectum of at least grade3 was reported in eight patients, and ureters complication in 4 patients. Nineteen patients (34%) had distant failure (ten patients had supra-clavicular node metastasis) during follow-up, and ten (18%) of patients with local recurrence failure.
Conclusions: Local and distant recurrences remain a problem in patients with para-aortic positive lymph nodes. IMRT provided treatments with less toxicity to surrounding structures. Nevertheless, long term follow-up and studies involving more patients with IMRT are needed to evaluate its respective clinical outcomes.

8017 POSTER

Distribution Patterns of Metastatic Pelvic Lymph Nodes Assessed by CT/MRI in Patients With Uterine Cervical Cancer

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Background: To investigate distribution patterns of metastatic lymph nodes on pretreatment CT/MRI images of patients with locally advanced cervical cancer.
Materials and Methods: We enrolled 114 patients with uterine cervical cancer who were diagnosed with pelvic node metastases by CT/MRI ($\geqslant$10 mm in shortest diameter). Pretreatment CT/MRI data were collected at 6 institutions. The FIGO stage was IB1 in 2 patients (2%), IB2 in 6 (5%), IIA in 3 (3%), IIB in 49 (43%), IIIB in 50 (44%), and IVA in 4 (4%) patients. The median cervical tumour diameter assessed by T2-weighted MRI was 55 mm (range, 10−87 mm). The anatomical distribution of the nodes was allocated on CT/MRI images by two radiation oncologists and one diagnostic radiologist.
Results: 272 enlarged nodes were assessed as significant and judged as metastatic. The incidence of metastatic nodes according to nodal region was 104/114 (91%) for the obturator (OB), 31/114 (27%) for the external iliac (EI), 16/114 (14%) for the internal iliac (II), 22/114 (19%) for the common iliac (CI), and 6/114 (5%) for the presacral (PS) region. The EI region was subdivided into four categories: lateral, intermediate, medial, and lower. The OB and II regions were subdivided into two categories: upper and lower. The incidence of metastatic nodes was extremely high in both the upper OB region and the medial EI region (111/114). In contrast, the incidence was low in the lateral EI, lower EI, lower OB, lower II and PS regions. All cases with metastatic nodes in the II, CI, PS, lateral EI, and lower OB regions had metastatic nodes in other pelvic nodal regions concomitantly. Lymph node metastases in these regions were significantly related to FIGO stage ($p = 0.017$) and number of metastatic lymph nodes ($p < 0.0001$). Metastases to these regions did not appear in cases with lower FIGO stage disease and a smaller number of metastatic lymph nodes.
Conclusions: We demonstrated distribution patterns of pelvic node metastases on pretreatment CT/MRI images of patients with locally advanced cervical cancer. Individualization of the pelvic node clinical target volume (CTV) based on such findings should be encouraged for external beam radiotherapy in patients with cervical cancer.

8018 POSTER

Prospective Study on Comparision Between 3D CT Based Volumetric Planning With Conventional Planning Using Orthogonal X-rays, in HDR Brachytherapy for Carcinoma Cervix − Jaslok Hospital and Research Centre Experience

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Background: Brachytherapy is an integral part of radiotherapy treatment in cancer cervix. Conventional planning compared with the image guided 3D