Cervix: Poster Abstract

Chemoradiation for the management of locally advanced carcinoma uterine cervix: Comparative evaluation of concomitant weekly versus three weekly cisplatin

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Aims and Objectives: To determine and evaluate the difference/s, in terms of tumor control and side effects, between weekly and three weekly cisplatin concomitant with external beam radiotherapyfor locally advanced carcinoma of cervix.
Materials and Methods: The study was conducted in Radiotherapy Department, University of Health Sciences, Rohtak (India), on sixty previously untreated, histopathologically proven patients of locally advanced carcinoma of uterine cervix. The patients were treated with External Beam Radiotherapy (EBRT) 50 Gy/25 fractions over 5 weeks and concomitant cisplatin, followed by intra-cavitary HDR brachytherapy (ICBT) 700 cGy to point A; three times, once in a week. The patients were assigned randomly either of two groups of 30 patients each. In Group I (Study Group) the patients received three weekly cisplatin 75 mg/m^2 for 2 cycles whilein Group II (Control Group) the patients received weekly cisplatin 40 mg/m^2 for 5 cycles. Evaluation of response and toxicity was done weekly during treatment and monthly thereafter up to six months. The data thus obtained was assessed and analysed using LaMorte statistical tool. The study was approved by Ethical Committee of the institute and quality was periodically monitored by senior consultant and guide.
Results: Stage wise disease response in study and control respectively at the end of treatment was as follows: Stage IIA - CR (80% vs 100%), PR (20% vs 0%); Stage IIB - CR (80% vs 76.47%), PR (20% vs 23.53%); Stage IIIA - CR (60% vs 100%), PR (40% vs 0%); Stage IIIB - CR (60% vs 60%), PR (40% vs 20%), NR(0% vs 20%). Stage wise disease status at the end of sixth month follow up was as follows: Stage IIA – NED (80% vs 100%), RD (20% vs 0%); Stage IIB - NED (80% vs 76.67%), RD (20% vs 23.53%); Stage IIIA - NED (60% vs 100%), RD (40% vs 0%); Stage IIIB - NED (60% vs 60%), RD (40% vs 40%). Tumor response was not significantly different in the two groups with respect to age distribution, rural/ urban distribution, histopathological distribution and treatment interruption. Maximum level of hematological toxicity (WHO criteria) observed in study and control group respectively at the end of treatment was as follows: Anaemia; Grade II - 4 (13.33%) in both the groups, leukopenia; Grade II – 1 (3.33%) vs 0 (0%). The worst acute skin reactions observed by the end of treatment in Group I and II respectively were Grade II – 2 (6.67%) vs 0 (0%). The worst acute mucosal reactions were Grade II - 5(16.66%) vs 0 (0%). Upper gastrointestinal toxicity (Grade II & III) was 16.7% versus 13.3% respectively. Lower gastrointestinal toxicity (Grade II & III) was 30.0% versus 36.7%. No significant weight loss was observed in either of the groups. Though, all the patients completed the intended treatment, treatment interruption for more than a week was observed in 10 (33.33%) vs 8 (26.67%) patients respectively, due to acute toxicities.
Conclusion: Three weekly cisplatin, concomitant with radiation seems to be the potential, effective and acceptable alternate as standard of treatment for locally advanced carcinoma cervix; especially for increased work load and limited resource setups.

Cervix: Poster Abstract

Comparison of Keyes punch biopsy instrument with cervical punch biopsy forceps for diagnosing cervical lesions

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Aims: To assess the feasibility and efficacy of Keyes punch biopsy instrument (KP) in diagnosing cervical lesions and compare it with cervical punch biopsy forceps (CP).
Methods: 75 women having adequate colposcopy with abnormal transformation zone were included and paired colposcopic directed biopsies were taken using KP followed by CP from the same target area. The outcome parameters were compared using paired t-test, Wilcoxon signed rank test and McNemar test.
Results: It was feasible in all cases to take cervical biopsy with KP and CP. Volume of gross specimen obtained by KP was less than CP (0.076 ± 0.097 vs 0.101 ± 0.156 cm^3, $p=0.061$), however on microscopic examination, mean length and depth of tissue in KP was greater than CP by 0.06 mm ($p=0.810$) and 0.14 mm ($p=0.634$) respectively. There was an exact agreement with final surgical specimen in 42% of cases in both forceps. Agreement within 1 degree was found in 25% of cases with KP and in 17% of cases with CP. Both the forceps equally missed microinvasive lesions but KP was inferior to CP for invasive cancer.
Conclusion: KP is almost at par with CP for diagnosing preinvasive cervical lesions and is a useful adjunct to the existing armamentarium of biopsy forceps.

Cervix: Oral Abstract

The impact of tumour regression in locally advanced carcinoma cervix during external beam radiotherapy and the need for adaptive planning

Aim: To study the impact of tumour regression occurring during IMRT for locally advanced carcinoma cervix and study dose distribution to target volume and OARs and hence the need for any replanning.
Materials and Methods: 40 patients undergoing IM-IGRT and weekly chemotherapy were included in the study. After 36 Gy, a second planning CT-scan was done and target volume and OARs were recontoured. First plan (non-adaptive) was compared with second plan (adaptive plan) to evaluate whether it would still offer sufficient target coverage to the CTV and spare the OARs after having delivered 36 Gy. Finally new plan was created based on CT-images to investigate whether creating a new treatment plan would optimize target coverage and critical organ sparing. To measure the response of the primary tumour and pathologic nodes to EBRT, the differences in the volumes of the primary GTV and nodal GTV between the pretreatment and intratreatment CT images was calculated. Second intratreatment IMRT plans was generated, using the delineations of the intratreatment CT images. The first IMRT plan (based on the first CT-scan or non adaptive plan) was compared with second IMRT plan (based on the second CT-scan or adaptive plan).
Results: 35% patients had regression in GTV in the range of 4.1% to 5%, 20% in the range of 1.1%-2%, 15% in the range of 2.1%-3% and 20% in the range of 6%-15%. There was significant mean decrease in GTV of 4.63 cc ($p=0.000$). There was a significant decrease in CTV on repeat CT done after 36 Gy by 23.31 cc ($p=0.000$) and in PTV by 23.31 cc ($p=0.000$). There was a statistically significant increase in CTV D98, CTV D95, CTV D50 and CTV D2 in repeat planning CT done after 36 Gy. There was no significant alteration in OARs doses.
Conclusion: Despite tumour regression and increased target coverage in locally advanced carcinoma cervix after a delivery of 36 Gy there was no sparing of OARs. Primary advantage of adaptive RT seems to be in greater target coverage with non-significant normal tissue sparing.

Ovary: Oral Abstract

A prospective study evaluating preoperative (clinical, imaging) and intraoperative predictors of suboptimal debulking in advanced epithelial ovarian cancer

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Introduction: In advanced epithelial ovarian cancer, there is a survival benefit for patients who achieve optimalcytoreduction. Suboptimallycytoreduced patients are at risk of the increased morbidity of a surgery without associated survival benefit. Predicting which patients can undergo optimal cytoreduction represents a critical decision-making point. Present study analyses the predictors, pre operative (clinical and radiologic) and intraoperative of suboptimal debulking.
Methods: This was a prospective observational study conducted at Amrita Institute of Medical Sciences from March 2013 to May 2015. All the patients with clinically (physical examination, laboratory and imaging results) diagnosed Stage IIIc epithelial ovarian, fallopian tube, or primary peritoneal carcinoma (PPC) who were planed for primary debulking surgery were included. The demographic data and details of tumor markers, radiological investigations including CT scan, intra operative findings and histopathologic details were collected. Statistical analysis was done using SPSS v20.0.

Results: 36 patients fit the inclusion criteria. Gross ascites wasthe clinical parameter found to be associated with suboptimal debulking. CT scan had low sensitivity (35-53%) in diagnosing small bowel mesenteric and porta hepatis disease and high sensitivity in diagnosing diffuse peritoneal thickening, omental disease, diaphragmatic and nodal disease. On univariate analysis diffuse peritoneal thickening and small bowel serosa and mesenteric disease were significantly consistent with sub optimal debulking.
Conclusion: Finding out disease at the sites which are associated with suboptimal debulking (diffuse peritoneal thickening, smallbowel mesenteric and serosal disease) pre operatively or at the beginning of surgery can predict optimal debulking and can help avoid un necessary surgery.

Ovary: Oral Abstract

Evaluation of different methods to assess homologous recombination status and sensitivity to PARP inhibitors in ovarian cancer

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Methods: Matched samples of ascites and tumor tissue were taken from patients undergoing surgery for epithelial ovarian cancer. Tumor samples were formalin fixed and paraffin embedded (FFPE); ascites samples were used to generate primary cultures (PC). HR status was determined in PCs as previously described.[1] IC_{50} for the PARP inhibitor Rucaparib was estimated using SRB assays. DNA was extracted from the FFPE tissue. The following techniques were evaluated in PCs or paired FFPE samples: DR-GFP reporter assay, PARP activity assay, BRCA1 expression on immunohistochemistry, BRCA1 methylation status and BRCA1/2 mutation analysis. A next generation sequencing based assay was used to detect mutations and other genomic alterations in a large panel of cancer-associated genes, including *BRCA1/2*.
Results: Paired samples were collected from 64 patients and characterized for HR function. 47/64 (76%) were high grade serous. 44% (28/64)) were HR defective (HRD) by Rad51 assay and correlated with Rucaparib sensitivity (PPV-92%, NPV-100%). Molecular analysis revealed that all mutations and other genomic alterations detected in ascites derived PCs were also found in matched FFPE tumor tissues. All tumors with serous histology contained *p53* mutations, whilst the remaining tumors without *p53* mutations were non-serous in histology. DR-GFP assay was unreliable in PC due to poor transfection. In a subset of 50 cancers there was reduced BRCA1 expression in the HRD vs. HRC tumours (34.8% vs. 22.7%, ns) whilst in a further subset of 30 cases there was no difference in endogenous or stimulated PARP activity between HRD and HRC tumours. Deleterious *BRCA2* mutations were identified in 7 tumors, 6 of which were HRD. Only 1 deleterious *BRCA1* mutation was detected but methylation of *BRCA1* was identified in 13 of 64 (20%) tumors, 7 of which were HRD. Mutation of *BRCA2* was mutually exclusive to methylation of BRCA1. HRD vs. HRC tumours showed BRCA1 methylation (25% vs. 17%) and BRCA1/2 mutation (21% vs. 0.3%). 14/28 (50%) HR defective tumors do not have *BRCA1/2* mutations or *BRCA1* methylation, suggesting other mechanisms can also result in a HR defective phenotype.28/64 (43%) of samples demonstrated the HR defective phenotype. In all cases HR status correlated with sensitivity to Rucaparib.
Conclusion: As expected, deleterious *BRCA2* mutations conferred a HRD phenotype in cells but methylation of *BRCA1* was not universally associated with HRD. This may be as a result of only partial silencing of the gene by methylation and further work is required to identify thresholds of methylation which may predict HR status. The use of *BRCA1/2* mutation testing alone is unlikely to identify the majority of HR defective ovarian tumors. Assessment of functional status of HRD is the preferred option and further technologies should be developed to simplify the Rad51 assay.

Ovary: Oral Abstract

Evaluation of supragastric lesser sac using a laparoscope during cytoreductive surgery in epithelial ovarian carcinoma: A site for occult metastasis

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Background: The supragastric lesser sac (SGLS) is a site of metastasis from epithelial ovarian cancer (EOC). Since this region is difficult to access and represents a confluence of critical structures, it may be a barrier to complete cytoreductive surgery (CRS).
Methods: The SGLS was explored in consecutive patients undergoing CRS with EOC. After a xipho-pubic laparotomy incision, the SGLS was examined; visualisation and treatment was aided by using a laparoscope. Resectable disease was cleared using the following methods alone or in combination: direct tumor excision, argon beam coagulation, plasma jet or electrocautery.
Results: 30 patients were evaluated between November 2013 and August 2014 in NGOC, Gateshead. SGLSM was present in 21/30 (70%) of EOCs, 19/25 (76%) high grade serous disease, 21/26 (81%) stage ≥3 disease, 18/20 (90%) with PCI score ≥15, 12/15 (80%) with ascites ≥500 ml, 13/18 (72%) at primary surgery and 8/10 (80%) at interval surgery. Sites included: lesser omentum (11), caudate lobe (10), groove of ligamentum venosum (6), floor (20), upper recess (7), subpyloric space (6), FOW (13), coeliac axis (5), porta hepatis (6), anterior surface of pancreas (2) retro-pancreatic (2). Size of metastases: <2.5mm = 3, <1 cm = 8, ≥1 cm = 7. Pre-operative CT scan identified 4/22 (18%) cases. In 18/21 patients SGLSM was completely resected or ablated; there were no complications. End Result: Optimal 27/30 (90%) including no visible disease = 18, <2.5 mm = 5; 17/21 (81%) cases would have been ≥2.5 mm residual disease if SGLS was not evaluated/treated. In a further cohort of 30 patients evaluated at Tata Medical Center, Kolkata, SGLSM was present in 18 (60%) of patients. CC1 resection was obtained in >90% cases.
Conclusion: EOC frequently metastasizes to the SGLS and is often resectable. Lack of meticulous examination may result in incomplete resection; evaluation should be performed at least in stage ≥3 disease when the surgical intent is total clearance of disease.

Ovary: Oral Abstract

Implementing quality indicators for cytoreductive surgery in ovarian cancer: Experience from a tertiary referral center in Eastern India

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Background: Debate continues whether primary surgery or neo-adjuvant chemotherapy (NACT) or primary debulking surgery (PDS) should be offered in advanced epithelial ovarian cancer as frontline therapy. Since 2015, there has been a paradigm shift at Tata Medical center, whereas increasing number of patients are being offered PDS and a quality improvement programme was initiated. Recently, ESGO in October 2015 has published a document indicating 10 quality indicators for cytoreductive surgery in advanced ovarian cancer surgery.
Aim: We compared our performance against all 10 quality indicators.
Results: Primary cytoreduction rate has increased from 20% in 2012 to >70% at the end of 2015. Optimal cytoreduction rates were obtained in 90% cases and recently complete (CCO/CC1) cytoreduction rates are being achieved in >80% cases. All 10 quality indicators were achieved successfully including prospective documentation of morbidity and surgical findings in all cases. Morbidity figures are showing a downwards trend after the initial learning curve.
Conclusions: Implementation of a quality improvement programme is the key to overcome the barriers of implementing a cytoreductive program in advanced ovarian cancer. However, standards similar to developed countries can be achieved through a dedicated team effort.

Ovary: Oral Abstract

Clinico-pathological correlation of homologous recombination status in epithelial ovarian cancer: Surgeon's perspective

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