

Cervix: Oral Abstract

Comparison of the outcomes between locally advanced cervical squamous cell carcinoma and adenocarcinoma patients treated with definitive chemoradiation

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Objective: To present comparison of survival outcomes between locally advanced adenocarcinoma and squamous cell carcinoma patients treated with definitive chemoradiation.

Methods: It is a retrospective analysis and direct comparison between adenocarcinoma and squamous cell carcinoma cervix treated from January 2011 to December 2015. Of 73 patients analyzed 61 had squamous carcinoma histology and remaining 12 had adenocarcinoma. Inclusion criteria were patients with locally advanced stage (IIA) who have completed definitive chemoradiation and were available for response evaluation at 3 months of completion of treatment. Endpoints for the study were disease response evaluation at 3 months, progression rate, median progression free survival, median recurrence free survival, median loco-regional control, median distant metastasis free survival, median overall survival.

Results: There was no significant difference between the two histology groups with respect to rate of achieving complete response (78.6 vs 75%, $p = 0.718$) and rate of disease progression (36% vs 50%, $p = 0.517$). There was no significant difference between median PFS (57.75 vs 17.74 months; $p = 0.964$), median RFS (NR vs 66.03 months; $p = 0.876$), median loco-regional control (not reached for both; $p = 0.315$), median DMFS (NR vs 66.03 months; $p = 0.438$) and median OS (NR vs 66.13 months; $p = 0.884$).

Conclusions: Locally advanced squamous cell carcinoma and adenocarcinoma treated with definitive chemoradiation have similar outcomes. Small sample size is the limitation of this study.

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Role of complementary cytology, colposcopy and histopathology in detecting premalignant and malignant lesions of cervix

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Objective: Cervical cancer is the second most common gynecologic malignancy worldwide. India alone accounts for one fifth of total number of cases worldwide. The aim of our study was to calculate sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate of complementary cytology and colposcopy with histopathology as gold standard for detection of premalignant and malignant cervical lesions.

Methods: A cross sectional study was conducted at Vardhman Mahavir Medical College and Safdarjung hospital, Delhi, India. 100 non pregnant females with complaint of post coital or irregular vaginal bleeding and those who had unhealthy cervix on visual inspection were included in study.

Results: Colposcopy exhibited a high degree of accuracy in diagnosis of high grade lesions. Overall sensitivity of cytology was 50% whereas that of colposcopy was 83.3%. Cytology had specificity of 93.4% whereas colposcopy had specificity of 89.4%. 100% of high grade and invasive cancers on colposcopy were associated with similar findings on histology. The degree of agreement between cytology and colposcopy with histology was significant ($p < 0.001$).

Conclusion: Colposcopy is sensitive method as compared to cytology, especially in the higher grade lesions and combination of both methods appears to be of higher diagnostic importance.

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

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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.

Methods and Materials: 40 patients undergoing IM-IGRT and weekly chemotherapy were included in the study. After 36Gy, 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 36Gy. 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 4.63cc ($p=0.000$). There was a significant decrease in CTV on repeat CT done after 36Gy by 23.31cc ($p=0.000$) and in PTV by 23.31cc ($p=0.000$). There was a statistically significant increase in CTV D98, CTV D95, CTV D50 and CTV D2 in repeat planning CT done after 36Gy. 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 36Gy there was no sparing of OARs. Primary advantage of adaptive RT seems to be in greater target coverage with non-significant normal tissue sparing.

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Clinical comparison of toxicity pattern of two linear quadratic model-based fractionation schemes of high-dose-rate intracavitary brachytherapy for cervical cancer

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Introduction: Carcinoma cervix is the fourth (GLOBACON 2012) most common cancer among women worldwide, and the main cancer affecting women in Sub-Saharan Africa, Central America and south-central Asia. In India, approx. 1,23,000 (GLOBACON 2012) new cases of carcinoma cervix are diagnosed each year. Brachytherapy is an integral part of treatment of cancer cervix. In the context of a developing country like us where maximum utilization of the resource is of prime importance to provide treatment to the large patient cohort, shortening the treatment duration

and number of fractions always increases efficiency. In order to maximize the logistic benefits of HDR-BT while improving patient compliance and resource sparing, various fractionation regimens are used. Fractionation and dose adjustments of the total dose are radiobiologically important factors in lowering the incidence of complications without compromising the treatment results.

Aim: To compare patient outcomes and complications using two linear-quadratic model-based fractionation schemes of high-dose-rate intracavitary brachytherapy (HDR-IC) used to treat cervical cancer.

Materials and Methods: A prospective randomized study on 318 patients, with histologically proven advanced carcinoma cervix (stages IIB-IIIIB) was enrolled in the study. All patients received External Beam Radio Therapy (EBRT) 50 Gy in 25 fractions with concurrent chemotherapy (cisplatin 35 mg/m²) followed by IntraCavitary brachytherapy using high dose rate equipment. Patients were randomised after completion of EBRT into two arms: (1) Arm 1: HDR ICRT 6.5 Gy per fraction for 3 fractions, a week apart. (2) Arm 2: HDR ICRT, 9 Gy per fraction for 2 fractions, 1 week apart. On completion of treatment, patients were assessed monthly for 3 months followed by 3 monthly thereafter. Treatment response was assessed according to WHO criteria after one month of completion of radiotherapy. The RTOG criteria were used for radiation induced toxicities. We analyzed late toxicities in terms of Rectal, Bladder, Small Bowel toxicity and Vaginal Stenosis.

Results: Acute reactions in both the groups were comparable. None of the patient developed Grade 4 toxicity in our study and no toxicity related mortality was encountered. A slightly high frequency of late toxicity was observed in 9Gy Arm patients but was not statistically significant.

Conclusion: In our setup, HDR brachytherapy at 9 Gy per fraction in two fractions is safe, effective and resource saving method with good local control, survival, and manageable normal tissue toxicity.

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Identification of T- and B-cell epitopes in HPV-16 E7 gene isolated from cervical cancer patients

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Introduction: In India, cervical cancer is the most common cancer among females. Persistence infection with high risk human papillomaviruses (HR-HPV) is an etiological agent for cervical cancer development, especially HPV-16 is found to be exclusively high in cervical cancer cases in Indian population. The continuous expression and transforming ability of HPV E7 helps in progression of cervical cancer and other HPV related disease, which make E7 as a suitable targets for the development of therapeutic vaccines. **Objectives:** Identification of T- & B-cell epitopes HPV-16 E7 gene isolated from in cervical cancer patients.

Materials and Methods: A total of 80 cervical cancer tissue biopsies were collected and processed for DNA extraction, HPV diagnosis and genotyping. E7 gene of HPV-16 positive samples were amplified and sequenced. Epitopes in E7 gene sequence were predicted by online freely available tools.

Results: In the present study we got 72 samples (90%) were positive for HPV and out of which 68 samples (94.4%) were positive for the HPV-16. HPV-16 positive samples were sequenced and translated. IEDB server was used for epitope analysis; 12 potent epitopes for the MHC-I alleles were identified in isolated E7 gene of HPV-16. The most potent epitopes were MHGDTPTLHEYM for HLA-C*07:01; LLMGTLGIVCPI for HLA-A*02:01 and MHGDTPTLHEYML for HLA-C*07:01; having percentile rank 0.2 for all three and antigenicity score of 0.20011, 0.15358 and 0.10735, respectively.

Conclusion: This is an effective strategy to design immuno-therapeutics and therapeutic vaccine against HPV using E7 as target. These findings will be helpful in the development of effective vaccine for particular geographical region.

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Role of interstitial brachytherapy using template (mupit) in locally advanced carcinoma cervix

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Introduction: Locally advanced carcinoma cervix includes stages IIB, IIIA, IIIB and IVA. Interstitial brachytherapy has the potential to deliver adequate dose to lateral parametrium and to vagina. Hence, it is preferable in cases with distorted anatomy, extensive (lower) vaginal wall involvement, bulky residual disease post EBRT and parametrium involvement upto lateral pelvic wall.

Aim and Objective: To determine clinical outcome and complications (acute and chronic) in locally advanced carcinoma cervix, treated with interstitial brachytherapy using template (MUPIT - Martinez universal perineal interstitial template).

Materials and Methods: This study is a retrospective analysis of 37 cases of locally advanced carcinoma cervix (stage IIB-2, IIIB-30, IVA-5), treated with EBRT (dose-median 45Gy/25#) ± concurrent chemotherapy (CCT) - Inj. Cisplatin/Inj Carboplatin, followed by interstitial brachytherapy using MUPIT from December 2009 to June 2015. Initial treatment with EBRT ± CCT was followed by interstitial brachytherapy. Under spinal anaesthesia and epidural analgesia, MUPIT application was done. Straight and divergent needles (median 26, range 19-29) were inserted to cover parametrium adequately. Needle position was verified with planning CT scan and Brachytherapy planning was done. Dose was normalized to 5 mm box surface from outermost needle with optimization of dose to OAR (Bladder, Rectum and Sigmoid colon). Prescription dose -25Gy in 5#. Treatment was delivered by Microselectron HDR using Ir192 source. Treatment fractions were delivered twice daily with min 6 Hrs. gap in-between fractions.

Results: The median duration of follow-up was 25 months. Local control was achieved in 28 patients with residual disease in 7 patients and local recurrence in 2 patients. 10 patients had acute lower GI toxicity {Grade 1 (n=6), Grade 2 (n=4)}, 2 patients had acute Grade 1 bladder toxicity. 1 patient had grade 3 and 1 patient had grade 4 chronic bladder toxicity. Chronic rectal toxicity was seen in 10 patients {Grade 2 (n=4), Grade 3 (n=4), Grade 4 (n=2)}.

Conclusion: Local control was achieved in 28/37 patients (75.6%) and overall survival rate of 81.1% at median follow up of 25 months in patients with locally advanced carcinoma cervix and unfavorable prognostic factors.

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Pattern of distant metastases in treated cases of carcinoma cervix : An analysis

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Aims: To analyze pattern of distant failure, site of metastases, number of metastases and duration in patient with carcinoma of cervix treated with concomitant chemoradiation.

Materials and Methods: From May 2011 to December 2015, 73 patients of carcinoma cervix who treated with radical treatment (concomitant chemoradiation followed by 3 session of HDR brachytherapy) with distant metastases presented at Department of Radiotherapy-II, Pt BDS PGIMS, Rohtak were evaluated retrospectively.

Results: Most of the female with metastases were in age group of 50-59 years (82%), 12% were in age group >60 and 6% were in < 50 year age group. Initial stage of presentation was 40% (29/73), 48% (35/73) and 12% (9/73) in stage II, III and IVA respectively. Out of which 93% had squamous cell carcinoma histology and 7% were having adenocarcinoma at time of presentation. Among them 49/73 (67%) had solitary metastases, 19/73 (26%) had two metastatic sites and 5/73 (7%) had multiple metastatic sites. Commonest site of distant metastases was paraaortic lymphnodes in 40% of cases, followed by liver, lungs, brains, cervical lymph nodes and one case of cutaneous metastases was also seen. Paraaortic lymphnodes, liver and lung metastases