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Dr. Maheswaran Satishkumar
Assistant Professor of Surgical
Oncology, Madurai Medical College
and Grh. Tamil Nadu, India

Dr. K Jeyanthi Prasad
Assistant Professor of Obstetrics
and Gynecology, Madurai Medical
College, Tamil Nadu, India

M Ramesh
Professor of Surgical Oncology,
Madurai Medical College
Tamil Nadu, India

Adjuvant hysterectomy after radical radiation in cervical cancers - are we still justified? A prospective analytical study

Dr. Maheswaran Satishkumar, Dr. K Jeyanthi Prasad and M Ramesh

Abstract

Cervical cancer remains the most common female gynecological cancer in India, with squamous cell carcinoma being the commonest histology. Early stage disease is treated with primary surgery or radiation [7], while locally advanced stage and bulky diseases are treated with radical radiation with concurrent chemotherapy [1]. The concept is always single radical modality and never a combined modality, unlike other malignancies in advanced stages. We have conducted a prospective analytical study, where we included patients who were treated with radical radiation, underwent adjuvant hysterectomy (Type 1 with pelvic node sampling) in our tertiary care referral center for oncology, from January 2016 to March 2018. Total of 72 cases were analysed, after meeting the inclusion and exclusion criteria.

Results: Of the 72 patients analysed, 11 patients had residual invasive cancer in cervix, 17 patients had severe dysplasia and 2 patients had pelvic node positivity.

Conclusion: Our study brings a nearly 18 percent discordance between clinical and pathological response after radical radiation in cancer cervix which is significant. It is time for us, to really think about the role for adjuvant hysterectomy in carefully selected cases in order to achieve cure and prevent morbidity and mortality.

Keywords: Squamous cell carcinoma, severe dysplasia, pathological complete response, adjuvant hysterectomy

Introduction

Cervical cancer remains the most common female gynecological cancer in India, with squamous cell carcinoma being the commonest histology. Early stage disease is treated with primary surgery or radiation while locally advanced stage and bulky diseases are treated with radical radiation with concurrent chemotherapy [3]. The concept is always single radical modality and never a combined modality [2], unlike other malignancies in advanced stages. Most patients with cervical cancer present in advanced stages due to ignorance, social stigmata, and lack of awareness or access to early detection facilities, and hence they are offered chemo radiation or sometimes palliative or best supportive care only. There is paucity of literature and strong evidences or recommendations regarding the role of adjuvant hysterectomy in patients with stages IB–IIB disease after radical chemo radiotherapy [4]. Such a procedure is controversial and not routinely performed because of a strong evidence that squamous cell cancer of cervix is always treated with single radical modality and they are radio responsive tumours [5]. However, post treatment follow up of these patients becomes difficult due to development of radiation fibrosis, synechia, adhesive vaginitis or defaulting after completion of radiation due to lack of proper awareness [6]. Such patients might harbor a silent disease inspite of having a clinically good response. In this study, we evaluated the discordance between clinical and pathological complete response, presence of severe dysplasia in cervix (which is a high risk feature for disease recurrence), in our patients with the International Federation of Gynecology and Obstetrics (FIGO) stages IB–IIB cervical cancer who were treated with adjuvant hysterectomy after radical radiation (EBRT plus intra cavitary brachytherapy) and concurrent chemotherapy.

Aims and objectives

To prospectively analyse the discordance between clinical and pathological complete response in patients with carcinoma cervix stage IB1- IIB after radical radiation. Also to study the prevalence of dysplastic changes and other parameters like nodal disease in these patients.

Correspondence

Dr. Maheswaran Satishkumar
Assistant Professor of Surgical
Oncology, Madurai Medical College
and Grh. Tamil Nadu, India

Exclusion Criteria

1. Patients with stages other than FIGO IB to IIB.
2. Non squamous histology
3. Those who did not complete radical RT (defaulters / toxicity factors)
4. Other co-existing malignancies.
5. Progressive disease or static disease after radiation.
6. Clinical or radiological evidence of residual disease after completion of RT.
7. Uncooperative patients.
8. Previous malignancies.

Inclusion Criteria

All eligible patients with squamous cell carcinoma cervix FIGO stage IB – IIB, who do not have exclusion criteria, listed above.

Materials and Methods

We have conducted a prospective analytical study, where we included patients with squamous cell carcinoma cervix who were treated with radical radiation, underwent adjuvant hysterectomy (Type 1 with pelvic node sampling) in our tertiary care referral center for oncology, from January 2016 to March 2018. Total of 72 cases were analysed, after meeting the inclusion and exclusion criteria. Results were statistically analyzed calculating p value, using chi square test and degree of

freedom values for a 2x2 contingency table.

All patients were clinically and radiologically evaluated for clinical complete response 12 weeks after completion of radiation. Radiological evaluation was done using both CT and MRI. Patients who had adhesive vaginitis, were subjected to examination under anaesthesia, and any grossly obvious/suspicious looking and felt areas were biopsied to rule out residual disease.

Results

Total number of patients who were analyzed, after meeting the inclusion and exclusion criteria was 72. Out of these 72 cases, 3 cases were found to have residual disease after radical radiation and hence underwent radical surgery, which was not included in the study. 69 patients underwent adjuvant type I hysterectomy 12 weeks after completion of radiation. Out of this 69 patients who were analyzed, 13 patients had residual disease (18.8%). Of these 13 patients, 11 patients had residual invasive squamous cell carcinoma in the cervix and 2 patients had pelvic node positivity without residual disease in cervix. 17 patients of these 69 had severe dysplasia in the cervix (24.6%). Among the patients who had severe dysplasia, 9 were in those who had pathological complete response and 8, were present in those who did not have pathological complete response (ie-patients with residual disease).

	P CR positive	P CR negative (disease +)	Total
Adjuvant Type I Hysterectomy	56 (54.62) [0.03]	13 (14.38) [0.13]	69
Radical Surgery	1 (2.38) [0.8]	2 (0.62) [3.02]	3
Total	57	15	72 (Grand Total)

The chi-square statistic value is 3.9872.

The p-value is. 045848.

The result is significant at p <.05.

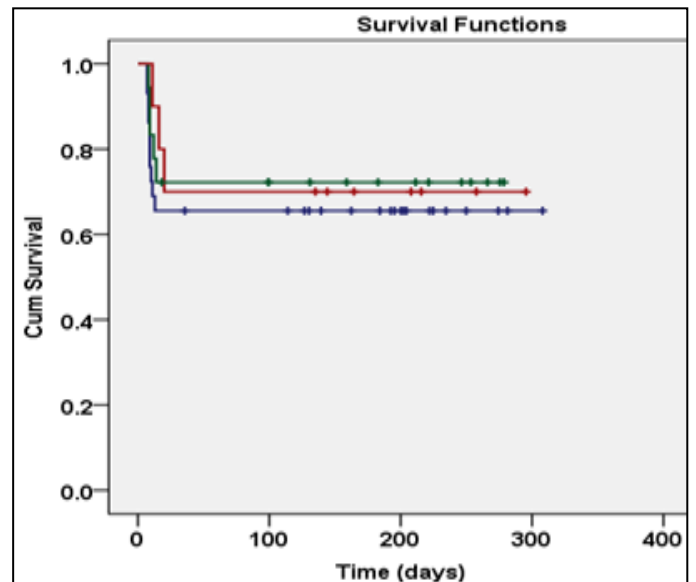
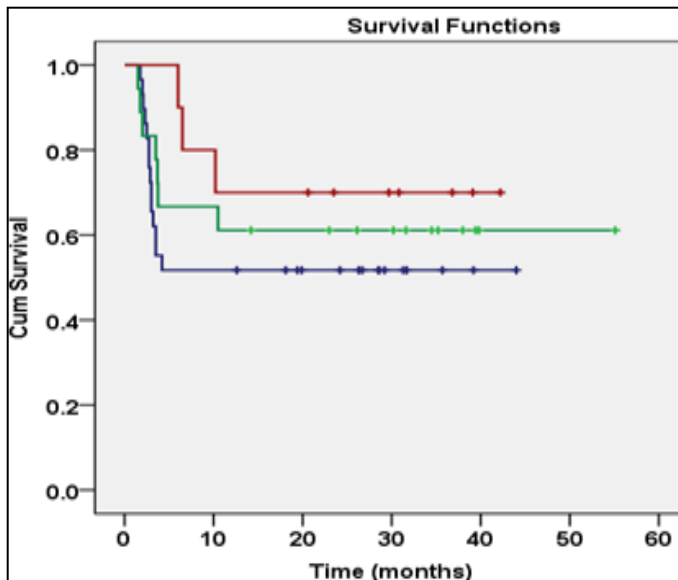
	Severe dysplasia +	Severe dysplasia +	Total
pCR present	9(13.8) [1.67]	47 (42.2) [0.55]	56
pCR absent (disease +)	8 (3.2) [7.18]	5 (9.8) [2.35]	13
Total	17	52	69 (Grand Total)

The chi-square statistic is 11.7469

The p-value is.000609

The result is significant at p <.05.

Kaplan meier survival curves



Conclusion

From our analytical prospective study, we find a 18% discordance between clinical and pathological complete response, in patients with cervical cancer (stage I- II) who underwent radical radiation. Also nearly 25% patients had severe dysplasia in the cervix which is considered to be a potential condition to become malignant in due course. Hence the role for adjuvant hysterectomy should be seriously considered as a part of curative management in carefully selected patients. With the advent of minimally invasive surgeries, adjuvant hysterectomy can be performed safely with minimal morbidity. However, prospective randomized studies are needed to determine the potential role of adjuvant surgery after radical RT in cervical cancer patients, when offered as part of combined treatment.

Discussion

The standard treatment of cervical cancer with radiation generally requires the use of external beam radiation combined with intracavitary brachytherapy. External beam radiation is used to treat the pelvic nodes and parametria, whereas the central disease is primarily treated by the intracavitary brachytherapy ^[1, 3]. Adjuvant hysterectomy after radical chemo radiotherapy has not been shown to be associated with survival benefit ^[5]. However, in carefully selected patients it may be really beneficial, as nearly 18 to 20 percent of cases has residual disease (pathological incomplete response) from our study, even after clinically proved complete response.

Local recurrence is the major cause of treatment failure in bulky cervical cancer. Residual tumour is associated with a higher rate of local recurrence and shorter disease-free survival ^[2]. Adjuvant hysterectomy (Type I) addresses, by removing potential radio- and chemo-resistant foci of disease. In the trial by Keys *et al.*, rates of complete pathological response after concurrent chemo radiation in stage IB2 cervical cancer ranged from 41 to 52%. The 5-year disease-free survival was 62% in those who underwent adjuvant hysterectomy and 53% in the absence of hysterectomy. This benefit was mainly due to the reduced rate of local recurrence after hysterectomy. In our series the pathological specimen showed residual tumours in 13 of 69 patients (18.8%).

The argument against performing adjuvant hysterectomy in previously irradiated patients is because of the potential for a higher risk of complications ^[6]. In our series, patients underwent type I radical hysterectomy with pelvic node sampling (bilateral) after radical radiation therapy and concurrent chemotherapy. Major Surgical morbidity was nearly nil and all patients were safely discharged after the procedure. Few cases of wound infection were present which were treated conservatively. Mortality was nil.

With the current developments in minimally invasive surgery and access to training and better understanding of pelvic anatomy, we hope that adjuvant hysterectomy would be a part of curative modality in selected cases of squamous cell carcinoma cervix which can be safely performed with no added morbidity. However we hope to have further ongoing trials and randomised controlled trials to support this.

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