

Retrospective Analysis on the Need for Surgery for Residual Disease after Chemoradiation in Carcinoma Cervix

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Received on: 09 January 2023; Accepted on: 30 January 2023; Published on: 16 September 2023

ABSTRACT

Introduction: Concurrent chemoradiation is the treatment of choice for patients from stage IB3–IVA disease. We analyzed patients with carcinoma cervix who underwent definitive chemoradiation, and had residual disease either clinically or radiologically during the period from July 2021 to August 2022. In the past 1 year, we treated 11 patients with definitive chemoradiation residue. We did radical surgery for those patients.

Results: Out of the 11 patients who had residual disease after definitive chemoradiation, 4 patients had clinical residual disease and 7 patients on imaging. Postoperative histopathological examination (HPE) showed 4 out of 10 patients were without any disease and all those patients were diagnosed by imaging. Out of 11 patients, 1 had an intraoperative ureteric injury, 2 patients had postoperative ureteric/vesicovaginal fistula, 1 patient had intraoperative bleeding, 1 patient had intraoperative bowel injury and there was 1 death. Three patients had minor complications.

Conclusion: Even though our numbers are less, we found out that there is a possibility of misinterpretation of postradiation changes as a residual disease by magnetic resonance imaging (MRI) and while operating for these patients, we should anticipate more complications and chances of no residual disease. We suggest a strong clinical correlation along with histopathological confirmation before surgical intervention, which may avoid unwanted radical surgery for such patients. At the same time, we cannot neglect the possibility of a real risk of residual disease (6/10 had residual disease) progressing further leading to a missed opportunity for a cure.

Keywords: Cervical cancer, Cervical malignancy, Cervix, Chemoradiation, Magnetic resonance imaging.

Journal of South Asian Federation of Obstetrics and Gynaecology (2023); 10.5005/jp-journals-10006-2232

INTRODUCTION

Among women, out of all malignancies, carcinoma cervix holds the fourth position.¹ It is the fourth most common cause of death among women with respect to cancer. Around 85% of carcinoma cervix occurs in developing or underdeveloped countries.² It accounts for about 6.6% of all female malignancies.³ According to the data given by the International Federation of Gynecology and Obstetrics (FIGO) staging system in 2018, locally advanced carcinoma cervix (LACC) is defined as cancer with stages from IIB to IVA.⁴ The most common histological type is keratinizing/non-keratinizing variants of squamous cell carcinoma.⁵

The standard of care for LACC is definitive chemoradiation which consists of platin-based chemotherapy regimen along with radiation therapy (intensity-modulated radiotherapy), followed by intracavitary brachytherapy.⁶ In 2018, FIGO included lymph nodes in their staging system either by MRI or histopathological examination.⁷ Concurrent chemoradiation in LACC improves the local control of the disease. Also, it can significantly reduce the risk of recurrence in the pelvis.^{8–12}

According to FIGO's 26th annual report, patients with LACC had an overall survival (OS) of about 22% in stage IVA disease. It is 40% for stage III disease and 66% for patients with stage IIB disease.¹³ However, any adjuvant surgery in the form of hysterectomy after concurrent chemoradiation does not have any role in preventing the loco-regional disease in LACC. The adjuvant surgery does not have any impact on the overall survival of those patients. So, adjuvant surgery after completion of concurrent chemoradiation should be strictly avoided because of the high morbidity rate.^{14,15}

Magnetic resonance imaging (MRI) is routinely used in pretreatment evaluation for T-staging and also is used for response assessment after concurrent chemoradiation in LACC.¹⁶

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How to cite this article: Shanmugam S, Balakrishnan S. Retrospective Analysis on the Need for Surgery for Residual Disease after Chemoradiation in Carcinoma Cervix. *J South Asian Feder Obst Gynae* 2023;15(4):382–384.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patients and the patient's parents for publication of the article.

The radiation-induced changes after chemoradiation may be misinterpreted by MRI for tumor residue. When MRI is performed in a span of 3 months of chemoradiation, there might be a high chance of misinterpretation.¹⁷

MATERIALS AND METHODS

In our study, we analyzed patients who were diagnosed with carcinoma cervix and underwent definitive chemoradiation, and had residual disease either clinically or radiologically. The period of study was from July 2021 to August 2022. In the past 1 year, we treated 114 patients with LACC with definitive chemoradiation, and we found 11 patients had a residual tumor after definitive chemoradiation.

For all patients for whom we suspect carcinoma cervix, we routinely do an MRI of the abdomen and pelvis followed by a

Table 1: Results of analysis

Total number of patients	11
Number of patients with clinical residual disease	4
Number of patients with MRI wise residue disease	7
Postoperative HPE with no residual disease	4

HPE, histopathological examination

Table 2: Complications which we encountered

Ureteric/vesicovaginal fistula	2
Intraoperative bowel injury	1
Intraoperative bleeding	1
Intraoperative ureter injury	1
Death	1

biopsy of the lesion. After confirmation of diagnosis, such patients underwent examination under anesthesia and cystoscopy for exact mapping of disease, and PET-CT scan was done if the patient is having significant nodes in the MRI imaging.

After local and metastatic evaluation for the disease, we subject the patients with loco-regionally advanced disease to definitive chemoradiation. After concurrent chemoradiation, 12 weeks later, we do an MRI of the abdomen and pelvis to assess the treatment response and to rule out any local residual disease.

RESULTS

Out of those 114 patients, 11 patients had residual tumor after the definitive chemoradiation.

For the patients for whom we found residual disease either by clinical examination or by radiological method, we did radical surgery in the form of

- Radical hysterectomy – 7 patients
- Anterior pelvic exenteration – 2 patients
- Laterally extending endopelvic resection (LEER) – 1 patient, depending upon pelvic side wall and bladder involvement.

One patient went inoperable due to dense adhesions (Table 1).

Postoperative histopathological examination (HPE) showed 4 out of 10 patients without any disease and all those patients were diagnosed by MRI.

None of the patients had positive nodes in the final histopathological examination.

COMPLICATIONS

Out of 11 patients we encountered, 5 patients had major complications. Three patients had minor complications such as surgical site infection and prolonged paralytic ileus. We encountered one death among these 11 patients. The cause of death of that one patient was a cardiovascular event (Table 2).

Out of those six major events, four events occurred in patients with whom we diagnosed residual disease using MRI. All four patients landed up with no residual disease in the final histopathological examination. The patient who became inoperable had intraoperative bowel injury and was also diagnosed by MRI as 8 mm residual disease. The cause of death of that one patient is due to a cardiovascular event.

DISCUSSION

In carcinoma cervix, patients who had residual disease confined to the cervix without any evidence of metastasis were usually treated

by salvage surgery, such as radical hysterectomy or anterior/posterior pelvic exenteration based on bladder and rectum involvement, respectively. The postoperative complication rates are high in patients who underwent surgery after chemoradiation for residual disease, probably due to the damage caused by radiation therapy on tissues.¹⁸ The morbidity related to salvage surgery can reduce the quality of life as well as the life expectancy of those patients. It may also have an impact on the overall survival of these patients.^{19–22} At the same time, we cannot neglect the real risk of death in patients who are going to have residual disease.

For all our patients with central recurrence, we did a radical hysterectomy. If the disease extends into the bladder/over the bladder serosa, we did anterior pelvic exenteration. For one patient, the disease was extending up to the side wall. So, we performed LEER for that patient.

Kim et al. reported the course of disease in patients with stage IB1–IVA who had tumor residue after definitive chemoradiation for LACC using MRI in the third month. During the third month follow-up, among those patients, they found that around 60% of patients had a residual tumor but without any evidence of progression. So, they concluded that if tumor residue is less than 2 cm, close observation can be done for those patients with proper follow-up.²³

The response assessment timing after chemoradiation is quite controversial. Moreover, the tumor regression after chemoradiation may vary depending on the diversity of the tumor and the way it responds to radiotherapy.

There is no clear-cut evidence to propose the method of choice of imaging after chemoradiation for the purpose of treatment response. Sequential MRI or positron emission tomography (PET-CT) may add a burden to health-care system, especially in developing and underdeveloped countries. These serial imaging and clinical examination also affect the mental health of these patients.²⁴

In our cases, we had 40% of patients with no residual disease on the final histopathological examination report. Since all these patients were diagnosed with residual disease with MRI and these patients had no disease on clinical examination, the salvage radical surgery based on radiological findings alone is highly questionable. Moreover, we encountered more complications rate with patients after definitive chemoradiation compared with upfront surgical candidates.

In one of the patients, we diagnosed residual disease with MRI (8 mm residual disease), which turned out as inoperable due to dense adhesions, and the patient had a bowel injury which was diagnosed intraoperatively and repaired along with a covering ileostomy. These surgery-related morbidity can affect the lifestyle of the patient, and may cause psychological, economical burdens to the patient, and their families.

In order to avoid the unwanted surgical morbidity and to diagnose patients with the true residual disease, we have devised a protocol in our institution (Fig. 1).

We planned surgery for all the patients with residual disease on clinical examination. In patients without any clinical disease with radiological findings suggestive of residual disease, we planned for examination under anesthesia and biopsy from any suspicious lesion. If the biopsy turns out to be positive for malignancy, we proceeded with salvage surgery for those patients. If negative, the patient was kept under close observation with serial imaging.

In serial imaging, if there is a progression in the size of the old lesion or any appearance of a new lesion, we planned for salvage

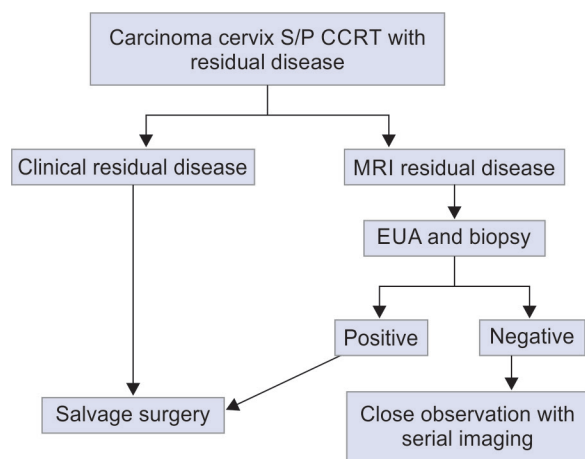


Fig.1: Carcinoma cervix S/P cort with residual disease

surgery in this set of patients. In patients with static or regressing lesions, we planned for close observation.

The results of our protocol are awaited and we hope that it will help to intervene in cases with real risk of residual disease while avoiding unnecessary surgery and resultant morbidity for patients who did not have real residual disease.

CONCLUSION

Even though we had less number of cases, we found out that there is a possibility of misinterpretation of postradiation changes as a residual disease by MRI. While performing operations for these patients, we should anticipate complications and there are chances of no residual disease in the final histopathological examination. We suggest a strong clinical correlation and histopathological confirmation along with imaging. It may avoid unwanted radical surgeries without missing the golden opportunity for cure for those who have residual disease.

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