

ROLE OF PALLIATION IN STAGE IV CARCINOMA CERVIX

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ABSTRACT: BACKGROUND: Palliation reduces the severity of disease symptoms, rather than reversing its progression or providing a cure. Metastatic cancer cervix (Ca Cx) is incurable by surgery, radiation or chemotherapy, but these modalities are useful for palliation. Globally about five to six lakh new cases of carcinoma cervix are diagnosed every year. Of these, one lakh cases are diagnosed in India of which 25.0% are from West Bengal only. **OBJECTIVES:** Our objective was to study the role of palliation in Stage IV Carcinoma Cervix. **SETTINGS AND DESIGN:** During the study period of five years from January 2007 to December 2011, consecutive seventy five new cases of stage IV carcinoma cervix diagnosed at Netaji Subhas Chandra Bose Cancer Research Institute, Kolkata, were included in our study. **MATERIALS AND METHODS:** Clinical examination with relevant investigations like kidney function tests (KFT), biopsy, cystoscopy, CT scan etc were done for diagnosis & staging. Treatment was decided based on woman's age, general health and the location & type of the tumour. Treatment options were surgery, radiotherapy (RT), chemotherapy (CT) and simple palliation. In our study, combined CT+RT was done in 18.67% patients most of who presented with Stage IV disease. Radiation was given as brachytherapy following teletherapy. Chemotherapy was used as adjunct to RT or for palliation or as neo-adjuvant chemotherapy (NACT), most commonly using paclitaxel (135mg/square metre), cisplatin (50mg/ square metre) and 5- fluorouracil (600mg/ square metre). At times, chemotherapy could provide pain relief only. Vault smear and metastatic workup was done during follow-up visits every 8-12 weeks after treatment completion. **RESULTS:** Majority of patients belonged to the age group 42-69 years with a median age of 53 years. Bladder involvement was seen in 15(20.0%) cases, bowel involvement in 14(19.0%) and distant metastasis in 46(61.0%) cases. Most cases were of Squamous cell carcinoma (94.0%), clinically presenting with foul smelling vaginal discharge ± bleeding per vaginum (100.0%). In our study, significant amount (30.0%) of disease control for a substantial period (1.5 years) was observed. The overall survival rate in patients of Stage IV carcinoma cervix on various forms of palliative treatment was 18.0%. **CONCLUSION:** Palliation is achieved by surgery, radiation or chemotherapy, though at times, simple palliation is the only feasible option. The poor survival rate was probably due to improper reporting & lack of regular follow up in the given socio-economic background. As cure cannot be achieved in advanced carcinoma cervix, palliation is important in alleviating the distressing symptoms and improving the quality of life.

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KEY WORDS: Palliation, carcinoma cervix, metastatic, radiation, brachytherapy, teletherapy, chemotherapy, neo-adjuvant chemotherapy.

INTRODUCTION: Cervical cancer is a major health problem for women. It is the third most common cancer worldwide. [1,2] Globally about 5-6 lakh new cases of carcinoma cervix (Ca Cx) are diagnosed every year. Of these 1 lakh cases are diagnosed in India. One quarter of this disease burden is shared by West Bengal. Persistent Human Papilloma Virus (HPV) infection is regarded as the most important factor contributing to the development of Ca Cx. [2] Immunization against HPV prevents infection with certain types of HPV (type 6,11,16,18 mainly) & is expected to prevent Ca Cx. [4-8] Type 16 is the most commonly implicated serotype of HPV for this. Other epidemiological risk factors associated with Ca Cx are history of smoking, parity, contraceptive use, early age of onset of coitus, multiple partners, history of sexually transmitted disease & chronic immunosuppression. [9]

During the past two decades, increasing attention has been paid to quality-of-life issues in oncology. [4,10] As the hospice movement has grown in the country, palliative care has developed into an integral part of (rather than the antithesis of) comprehensive cancer care. [4] Most patients who receive the hospice care are referred too late for adequate benefit or never referred at all. Effective palliative care needs an interdisciplinary team approach.

By definition palliation, derived from Latin word *palliare*, is any form of treatment that concentrates on reducing the severity of disease symptoms, rather than striving to halt, delay, or reverse progression of the disease itself or, provide a cure. The goal of palliative care is to prevent and relieve suffering and to support the best possible quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies. [3] Metastatic cancer cervix cannot be cured by surgery, radiation or chemotherapy, but these modalities are useful for palliation. Recurrence is also an indication for palliation.

Our objective was to study the role of palliation in patients of Stage IV Ca Cx.

MATERIALS AND METHODS: During the study period of five years (January 2007 to December 2011), consecutive 75 new cases of stage IV Ca Cx diagnosed at Netaji Subhas Chandra Bose Cancer Research Institute, Kolkata, were included in our study. Staging was done as per FIGO classification for cancer cervix (Table 1).

The study was approved by our Institutional Ethics Committee. Clinical examination with relevant investigations like chest X-ray (CXR), ultrasonography (USG), kidney function tests (KFT), biopsy, cystoscopy, CT scan etc. were done for diagnosis & staging which were tallied with the National Comprehensive Cancer Network (NCCN) 2011 guidelines later. Treatment was decided based on woman's age, general health (as per ECOG scale) and the location & type of the tumour. Treatment options were Surgery, RT, CT and simple palliation in the form of best supportive care possible. Radiation was given as teletherapy (total dose of 60 Gy usually @ 1-1.8 Gy/fraction) followed by brachytherapy. Chemotherapy was used as adjunct to RT or for palliation. At times, neo-adjuvant chemotherapy (NACT) was given in patients with bulky disease, locally advanced cancers etc. Paclitaxel (135 mg/sq.m), cisplatin (50 mg/sq.m) and 5- fluorouracil (600mg/sq.m) were the most commonly used chemotherapeutic agents. Cisplatin was used for concurrent chemotherapy with RT as single agent. However, it was used in combination with the other agents as well without significantly comparable results.

Vault smear and metastatic workup was done during follow-up of these patients every 8-12 weeks after completion of treatment.

RESULTS: Our youngest patient was 21 yrs old and the eldest lady was 79 yrs of age. Majority of patients belonged to the age group 42-69 years with a median age of 53 years (Table 2).

Bladder involvement was seen in 15 (20.0%), bowel involvement in 14 (19.0%) and distant metastasis in 46 (61.0%) cases. Histologically, grade III Ca Cx was the most common presentation (Figure 1). Most cases were of Squamous cell Ca (94.0%) (Figure 2). The most common clinical presentation was foul smelling vaginal discharge ± bleeding per vaginum (100.0%) (Figure 3).

In our study, combined CT+RT was done in 18.67% patients most of who presented with Stage IV disease (Table 3). However, on few occasions, chemotherapy could provide pain relief only. Significant amount (30.0%) of disease control for a substantial period (1 year 6 months) was observed. The survival rate in patients of Stage IV Ca Cx who were given various forms of palliative treatment was found to be 18.0%.

DISCUSSION: Ca Cx continues to be the most common malignancy with a compromised quality of life especially in the developing world. Though incidence of Ca Cx is on the rise, it is expected the introduction of measures like HPV vaccines to go a long way to control the rising trend. HPV vaccine has shown promising results in the short phase of study as per national health surveys.^[11]

The palliative care guidelines are the first NCCN guidelines to include death as an expected outcome and after-death care for the family as an essential part of the continuum of cancer care. All cancer patients should be screened for palliative care needs at their initial visit, at appropriate intervals and as clinically indicated. ^[3] Educational programs should be provided to all healthcare professionals and trainees so that they can develop effective palliative care knowledge, skills and attitudes.

Criteria for early consultation with a palliative care specialist are based on patient characteristics, social circumstances and anticipatory bereavement issues.

In the absence of any clear cut indications for palliative care, advanced disease, aggressive disease histology, poor general condition of the patient, presence of distant metastasis, social stigma, toxicity of therapy as compared to the benefit and the treating oncologist's discretion are the main indications for which palliation is used.

Concurrent chemoradiation, using cisplatin-based chemotherapy, is the treatment of choice for stages IB2, II, III and IV A disease based on the results of five randomised clinical trials. ^[3,12,13]

CONCLUSION: Palliation is achieved by surgery, radiation or chemotherapy, however, at times, simple palliation in the form of best supportive care is the only feasible option. ^[14-16] A good clinical history and examination is good enough for a clinical diagnosis of advanced Ca Cx, specially in a setting without adequate facilities like rural Bengal which accounts for a significant proportion of the disease burden. The poor survival rate in our study was probably due to improper reporting and lack of regular follow up in the given socio-economic background. As cure cannot be achieved in advanced Ca Cx, palliation has a great role to play in alleviating the distressing symptoms and improving the quality of life.

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Table 1: International Federation of Gynaecology and Obstetrics (FIGO) staging of carcinoma cervix

Stages	Subdivision	Description
I	I A1	Invasive carcinoma with stromal invasion ≤ 3 mm in depth and ≤ 7 mm in horizontal spread
	I A2	Stromal invasion 3-5 mm in depth with horizontal spread ≤ 7 mm
	I B1	Clinically visible lesion ≤ 4 cm in greatest dimension.
	I B2	Clinically visible lesion ≥ 4 cm in greatest dimension.
II	II A	Tumor without parametrial invasion
	II B	Tumor with parametrial invasion
III	III A	Tumor involves lower third of vagina, no extension to pelvic wall
	III B	Tumor extends to pelvic wall \pm hydronephrosis or non-functioning kidney
IV	IV A	Tumor invades mucosa of bladder or rectum \pm extends beyond pelvis
	IV B	Distant metastases

Table 2: Age distribution (n=75)

Age Distribution (yrs)	Number of women	Percentage (%)
21-30	3	4
31-40	8	11
41-50	16	21
51-60	33	44
61-70	13	17
71-80	2	3

Table 3: Primary treatment given to the patients (n=75)

Treatment	Number of patients	Percentage (%)
Surgery	2	2.7
CT+RT(including NACT)	14	18.67
RT alone	59	78.83

Table 4: ECOG performance status

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

Figure 1: Grade of the tumour as per the histopathological examination (HPE) report

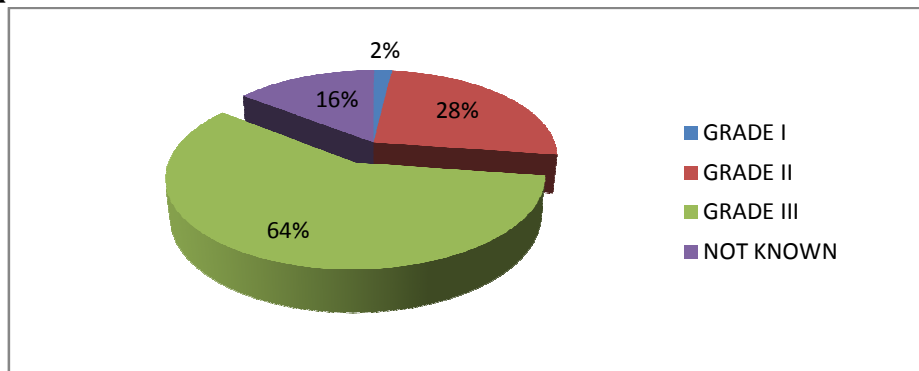


Figure 2: Histopathological distribution of patients

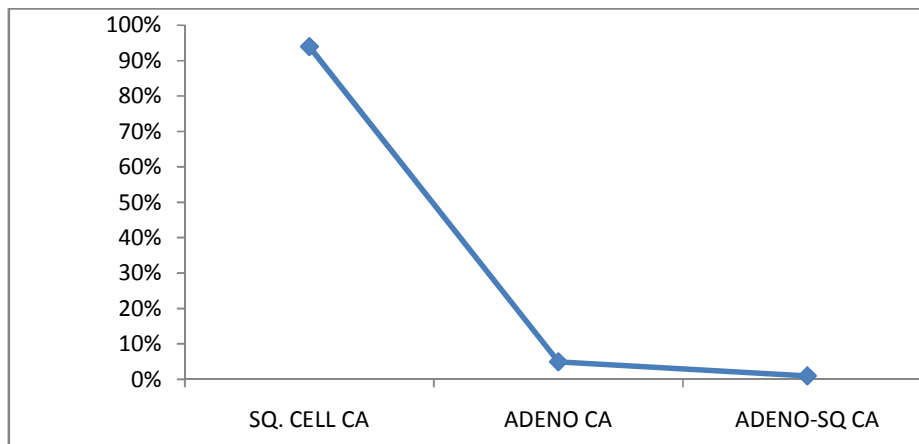


Figure 3: Symptomatology of the patients

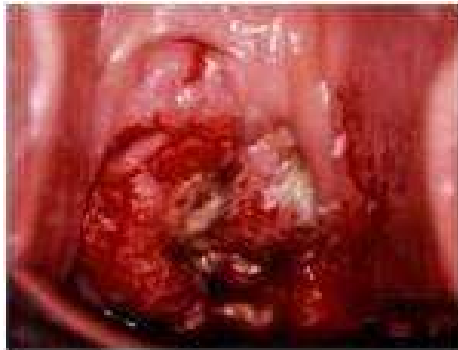
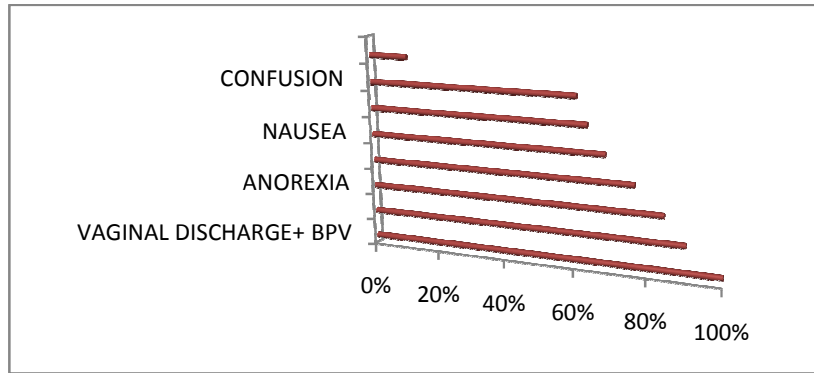
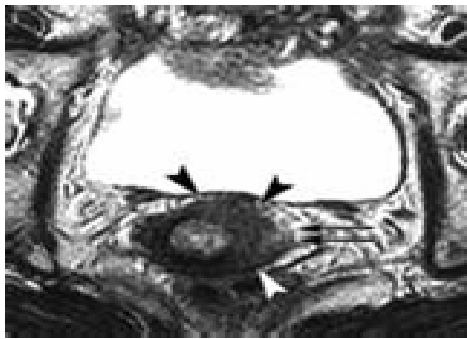


Image 1: Speculum view of advanced Ca Cx in one of our patients



Image 3: Hysterosalpingography (HSG) showing a vesicovaginal fistula



Images 2 (a) and (b): Urinary bladder infiltration as per MRI images in a diagnosed case of Ca Cx.



Image 4: Recto-Vaginal Fistula (RVF)



Image 5: Cystoscopic view of Vesico-Vaginal Fistula (VVF)