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# Role of Serum CEA as Tumor Marker for Predicting Presence of Pelvic and Paraaortic Lymph Node Metastasis in SCC of Uterine Cervix

## Abstract

**Objectives:** Cancer of the uterine cervix is the major cause of death from gynecologic cancer worldwide. Isolated paraaortic lymph node metastasis detected at the initial diagnosis of cervical cancer could be addressed by extended field paraaortic lymph node irradiation. Serum Carcinoembryonic antigen (CEA) could be done for detecting early Para aortic lymph node (PALN) involvement and scrutinizing relapse or recurrence. To assess pelvic and paraaortic lymph node status by computed tomography scan and also correlate with the pretreatment serum Carcinoembryonic antigen levels.

**Materials &Methods**: Twenty one patients of histologically proven squamous cell carcinoma of cervix of any age group were recruited into the study. We assessed the status of pelvic and paraaortic lymph node by computed tomography scans study. Pretreatment serum CEA levels were evaluated in all patients irrespective of the stage from I to IV.

**Results**: We observed that there was an elevation of Carcinoembryonic antigen in those patients having paraaortic lymph node and PALN metastasis.

**Conclusion**: Based on the results, we could opine that serum Carcinoembryonic antigen levels could help to prognosticate the cervical cancer patient, predict the presence of paraaortic and pelvic lymph nodes. To explore the potential of for PALN detection and treatment response assessment.

**Keywords:** Cervical cancer; Squamous cell carcinoma; Carcino Embryonic Antigen; Tumor marker

Research Article

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## Introduction

Cancer of the uterine cervix is the major cause of death from gynecologic cancer worldwide. The reported incidence rates in developing countries are much higher than those in developed countries. Approximately 85% of cervical cancers are of the squamous cell type. Other histological types less frequently found include adenocarcinoma (approximately 10%-15%) and adenosquamous carcinoma (approximately 3%) [1]. It is estimated that 50% of the women in whom cervical cancer is diagnosed each year will have never had cervical cytology testing [2]. Abnormal vaginal bleeding, including postcoital, intermenstrual, and postmenopausal bleeding, is the most common symptom of cervical cancer [3]. Studies of the incidence and distribution of lymph node metastasis in women with stage IB to IIB cervical cancer suggested that PALN involvement is closely tied to the presence of pelvic lymph node metastasis and larger primary tumour size [4].

Analysis of outcome data from 555 women who participated in gynecologic oncology group (GOG) trials (GOG85, GOG120, GOG165) revealed a more positive prognosis for patients who underwent surgical exclusion of paraaortic lymph node involvement versus those who underwent radiographic determination of radiographic determination of paraaortic involvement [5].

One study examined the efficacy of extending the radiation therapy (RT) field to the paraaortic region in patients with paraaortic lymph node involvement and showed therapeutic benefit especially in patients with small volume nodal disease [6]. A randomized controlled trial examining surgical versus radiology staging and treatment of paraaortic lymph node involvement is ongoing [7]. For patients suspicion of positive paraaortic and pelvic lymph node involvement imaging work up for metastatic disease is recommended. Extra peritoneal lymph node dissection should be considered followed by extended field external beam radiation therapy (EBRT), concurrent cisplatin containing chemotherapy and brachytherapy for patients with positive paraaortic lymph nodes [8].

FIGO Staging for carcinoma cervix does not take into consideration the lymph node status of the patient. Para aortic was considered as distant metastasis in carcinoma cervix but at present considered as regional metastases. Lymphadenopathy cannot be judged clinically and it requires radiological investigations like CT scan and PET-CT Scan.

### Tumor markers

A tumor marker is a substance that is produced by the body in response to cancer, or is produced by the cancer itself. Some of these markers are specific to one cancer, while others are seen in several types of cancer. These markers are generally used to evaluate the patient's response to treatment or to monitor for recurrence Tumor markers can be used in conjunction with other tests (scans, biopsies, etc.) to help diagnose a patient who has symptoms suspicious for cancer. Some markers can help physicians to determine prognosis and treatment.

Carcino embryonic antigen (CEA) is a glycoprotein of molecular weight approx. 180 KD found in normal fetal gastrointestinal tissue; it is normally present at very low concentrations in adult plasma but its concentration is increased in the presence of many tumors, particularly colorectal cancers (70%). Increased concentrations have also been described in gastric, bronchial, uterine and ovarian cancers, and in lymphomas.

Studies have focused on Carcinoembryonic antigen (CEA) for over 40 years, suggesting it be a useful tool in the diagnosis of cancer , as it is a cancer cell adhesion marker. Some of the non-neoplastic conditions associated with elevated CEA levels include cigarette smoking, peptic ulcer disease, inflammatory bowel disease, pancreatitis, hypothyroidism, biliary obstruction, and cirrhosis. Levels exceeding 10 ng per ml. are rarely due to benign disease [9].

Elevated levels of CEA (>2.5 ng/ml) were first reported in patients with gynecologic malignancy by Lo Gerfo et al. [10]. Since that time, immunoelectrophoretic and column chromatographic studies have shown that CEA from cervical cancer and from colonic cancer are immunologically similar.

Carcinoembryonic antigen is a reliable tumor marker in patients with adenocarcinoma of the cervix. An excellent correlation has been noted between pre-treatment plasma levels and extent of the disease. High pre-treatment values were associated with bad prognosis. Contrary to squamous cell carcinomas, a low value is equivocal, meaning either that the tumor volume is small or that the tumor releases little or no CEA. The presence of lymph node metastases has more pronounced effect on the CEA values than the size of the primary tumor [11,12].

Para-aortic lymphadenectomy or PET-CT examination is important for planning the treatment of radiotherapy. If isolated paraaortic lymph node metastasis is detected at the initial diagnosis of cervical cancer, the RT field should be extended to paraaortic lymph node lesions. To eliminate paraaortic lymph node micro metastasis and recurrence, more aggressive treatments such as Para-aortic lymphadenectomy, prophylactic paraaortic lymph node irradiation, or additional chemotherapy should be considered in future clinical trials [13]

Disaia et al. [14] studied a group of patients with invasive squamous cell carcinoma of the cervix and found that there was a progressive increase in the percentage of patients with positive CEA values correlating with advancing stage of the disease from 26% in stage I to 88% in stage II. Incidentally 85% of the recurrent cases showed positive CEA values [14].

Pre-treatment levels over 5 ug/l are highly suggestive of metastatic disease as they are associated with metastases in pelvic or Para-aortic lymph nodes in 50% of patients with stage IB disease. Also in advanced stages such as III and IV, 48% of patients had a pre-therapy value exceeding 5 ug [15,16].

## Methodology

Twenty one Carcinoma cervix patients of any age group were examined prospectively who were admitted in the ward. They were clinically staged using FIGO staging classification. The procedure for staging included a detailed history and a physical examination, as well as common laboratory tests and standard chest radiographs, intravenous pyelograms, X- rays, cystoscopies, and sigmoidoscopies. In the evaluation of paraaortic and pelvic lymph node involvement, computed tomography (CT) was performed in all patients. The principle criterion for positive node involvement was based on the axial diameter of the lymph node. Lymph nodes larger than 1 cm in the short-axis dimension were considered abnormal. Then serum CEA levels were estimated by using two-site immunoenzymatic "sandwich" assay (BECKMAN COULTER ACCESS IMMUNOASSAY SYSTEM) in all patients irrespective of the stage from I to IV and nodal status before treatment. All these patients were considered based on the inclusion and exclusion criteria.

The Biopsy proven carcinoma of cervix patients from stage I to stage IV were included in the study. Metastasis to visceral organs and bones, Cigarette smokers, Confirmed or suspected cases of inflammatory bowel disorders such as ulcerative colitis and Chron's disease, pancreatitis, liver disease, pulmonary infections; secondary primary like colorectal, lung, gastric, breast, pancreatic, ovarian and uterine cancer, were excluded from the study.

## Statistical Analysis

Data analysis was performed with statistical package for social sciences (SPSS) version 21.0 statistical package. We have used Mann-Whitney U test for the analysis. The probability value $P< 0.05$ was considered as significant.

## Results and Discussion

The total of 21 patients of carcinoma cervix was taken up for the study .Age of patients ranged between 23-60 years. Stage IB- 1 patient, Stage IIA -1patient, Stage IIB -6patient, Stage IIIB -6patient, Stage IVA -3patient and IVB -4patients were included in the study.

### Pelvic lymph nodes Vs CEA

Most of the patients in the study were aged between 40 -50 yrs. and majority of them were in advanced stages i.e. IIB, IIIB, IVB. Paraaortic lymph node was detected with CT scan in 60 % of patients and 80 % of patients there was pelvic lymph node involvement. CEA value < 3 ng/ml was taken as normal (Tables 1 & 2).

Totally 21 patients participated in the study. Out of these 8 patients were paraaortic lymph nodes positive. All the 8(100%) patients showed their CEA >3ng/ml.

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**Table 1:** Comparison of paraaortic lymph nodes present and paraaortic lymph nodes absent with respect to their CEA levels.

| | Paraaortic Lymph Node Present | | Paraaortic Lymph Node Absent | | P Value |
|---|---|---|---|---|---|
| | Median | Interquartile Range | Median | Interquartile Range | |
| CEA | 5.88 | 7.27 | 1.94 | 1.74 | 0.003 |

**Table 2**: Comparison of pelvic lymph nodes present and pelvic lymph nodes absent with respect to their CEA levels.

| | Pelvic Lymph Node Present | | Pelvic Lymph Node Absent | | P Value |
|---|---|---|---|---|---|
| | Median | Interquartile Range | Median | Interquartile Range | |
| CEA | 4.030 | 7.08 | 1.28 | 0.50 | 0.004 |

15 patients of the total 21 patients had their pelvic lymph nodes positive and 11(73.3%) patients among them had CEA >3ng/ml.

We noted that CEA values were elevated in 73.3% of the patients who had pelvic lymph involvement. CEA values were also elevated more than the normal values in all the patients who had paraaortic lymph nodes involvement detected by CT scan , showing it to be an excellent tumor marker for paraaortic lymph node involvement (i.e. in 100%) (Figures 1 & 2).

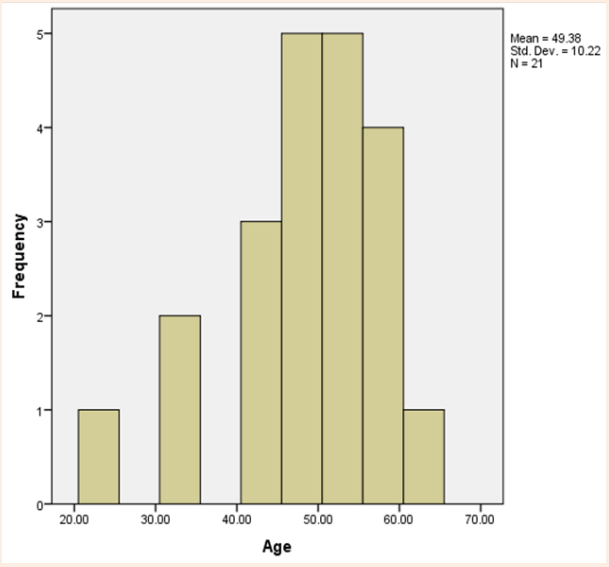


**Figure 1:** Histogram representing the age distribution of 21 participants. The minimum and maximum age of the participants who participated in the study was found to be 23, 65 respectively. The mean ± SD of the age distribution is 49.38 ± 10.21.

## Conclusion

Serum CEA has the potential of prognosticating CA cervix patients especially with the involvement of pelvic and paraaortic nodes. In our Study though small in size we found that it could be a very reliable marker for involvement of pelvic and paraaortic lymph nodes, where sometimes the CT or MRI could be of limited value if size of nodes were less than 1cm. The CEA values, both baseline and post treatment could be serve as a response indicator. This may be an invaluable tool for patient surveillance as detecting early failures may help to salvage the unfortunate patients and give them a chance to prolong their survival.

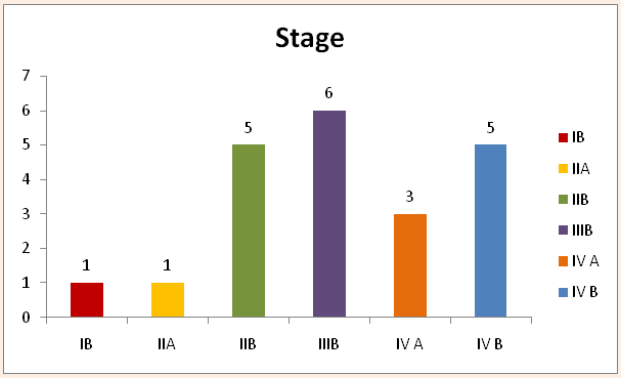


**Figure 2**: Stage distribution drawn for all the 21 participants. Most of the patients were IIB, IIB, and IVB stage.

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## Conflict of Interest

The Author declared no potential conflict of interest with respect to the research authorship, and or publication of the article.

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