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Computed tomography for evaluation of cervical carcinoma: Our experience in a tertiary care hospital.

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Abstract
Background:
Cervical cancer is the second most common cancer in India in women accounting for 22.86% of all cancer cases in women and 12% of all cancer cases in both men and women. The incidence of cervical cancer is higher in economically backward countries due to lack of screening programs and education. Globocan 2018 data -New cases registered: 96,922 ;Deaths: 60,078.Median age: 38 years (age 21–67 years).Rural women are at higher risk of developing cervical cancer as compared to their urban counterparts. Cervical cancer is the third largest cause of cancer mortality in India accounting for nearly 10% of all cancer related deaths in the country .Survival rate-The relative five year survival averages to 48.7% .Length of survival depends on the cancer stage at the time of detection. The survival chance of a person becomes better if the cervical cancer is detected and treated at earlier stages. Therefore it is important to avail of cervical cancer screening. Conventional radiological investigations used for International Federation of Obstetrics and Gynecology (FIGO) staging of cervical carcinoma often under diagnose; thereby leading to inappropriate treatment which advocates computed tomography scan as a mandate staging modality prior to initiation of therapy.CT is useful in staging advanced disease and in monitoring patients for recurrence.
Keywords: *carcinoma cervix, FIGO staging, CT scan, cervix tumor staging.*

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I. Introduction:

Cervical cancer an important cause of deaths due to cancer. It is a public health problem in developing countries like India, where India accounts for one-quarters of all cervical cancer cases. It is one of the leading causes of cancer mortality leading to 17% of all cancer deaths among women of 30 to 69 yrs. This prospective study was conducted to determine the role of CT in staging and work up in women diagnosed with cervical carcinoma.

II. Material & Methods

This prospective study was carried out at a tertiary care hospital -Medical College and Hospital, Kolkata, after the study protocol was approved by the Ethics Committee. Diagnosed cases of carcinoma of cervix by histopathology referred for CT scan evaluation were considered. The study was carried out from October 2017 to October 2018 and during this period 78 consecutive patients aged 30 to 80 years who gave written informed consent were included in this study. A total of 94 patients who did not give consent, post surgery and/or did not turn up during the follow up were excluded.

Using revised FIGO staging 2 the patients were evaluated by the gynecological department of our college following referral reviewed by CT, evaluated, recorded and compared. Seventy eight diagnosedcervical carcinoma cases were evaluated with contrast enhanced CT scan of abdomen and pelvis to evaluatetumor size, invasion of other organ systems, pelvic walls,lymphadenopathy and distant metastases. The findings were correlated with clinical findings, barium studies, x-rays, cystoscopy&sigmoidoscopy. All patients were stage II or higher and hence correlation with operative findings was not possible.

Patients underwent contrast enhanced CT of abdomen and pelvis on 16 slice multi-detector CT scanner (Siemens) as per the standard protocol 11 ,120 kV and 160 mAs using Iohexol .Scans covered the thoracic cavity to the symphysis pubis. Delayed scans were performed in cases with suspicion of bladder involvement.

Analysis Definitions:
The CT images were interpreted by three radiologists having experience in gynecological imaging.
Primary tumor-parametrial invasion, ureteral involvement, pelvic wall involvement, involvement of adjacent organs, signs of nodal involvement and metastasis was noted.
Sensitivity/specificities, for other comparisons kappa statistics were derived using SPSS version 17. McNemar test was utilized to determine the difference in clinical staging and CT staging.

FIGO STAGING
Stage 0
The carcinoma is confined to the surface layer (cells lining) of the cervix. Also called carcinoma *in situ* (CIS).
Stage I
The carcinoma has grown deeper into the cervix, but has not spread beyond it (extension to the corpus would be disregarded). Stage one is subdivided as follows:
IA Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion <5 mm and the largest extension <7 mm
IA-1 Measured stromal invasion of <3.0 mm in depth and extension of <7.0 mm
IA-2 Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm
IB Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA
IB-1 Clinically visible lesion <4.0 cm in greatest dimension
IB-2 Clinically visible lesion >4.0 cm in greatest dimension

Stage II
Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
IIA Without parametrial invasion
IIA-1 Clinically visible lesion <4.0 cm in greatest dimension
IIA-2 Clinically visible lesion >4.0 cm in greatest dimension
IIB With obvious parametrial invasion

Stage III
The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydro nephrosis or non-functioning kidney
IIIA Tumor involves lower third of the vagina, with no extension to the pelvic wall
IIIB Extension to the pelvic wall and/or hydro nephrosis or non-functioning kidney

Stage IV
The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV
IVA Spread of the growth to adjacent organs
IVB Spread to distant organs

TNM Staging
Primary Tumor (T)
- Tx: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ
- T1: Cervical carcinoma confined to the uterus
  - T1a: Invasive carcinoma diagnosed only by microscopy
  - T1b: Clinically visible lesion confined to the cervix
- T2: Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina
  - T2A: Tumor without parametrial invasion
  - T2B: Tumor with parametrial invasion
- T3: Tumor extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis
  - T3a: Tumor involves lower third of vagina, no extension to pelvic wall
  - T3b: Tumor extends to pelvic wall and/or causes hydronephrosis
- T4: Tumor invades bladder or rectum, and/or extends beyond true pelvis

Regional Lymph nodes (N)
Nx: Regional lymph nodes cannot be assessed.
No: No regional lymph nodes metastatsis

N1: Regional lymph node metastases

Distant Metastasis (M)

M0: No distant mets

M1: Distant mets (including peritoneal spread, involvement of supraclavicular, mediastinal or para-aortic lymph nodes, lung, liver or bone).

III. Results

Primary tumor was demonstrated on CT in 54 (69%) of 78 patients. Parametrial, vaginal and pelvic wall invasion are better evaluated with physical examination, where CT underestimates. The urinary bladder and rectal invasion were overestimated often by CT when compared with cystoscopy & sigmoidoscopy. CT had 100 percent negative predictive value to exclude bladder and rectal involvement. CT detection of lymph node enlargement and lung metastases were useful in management.

Difference between FIGO and CT staging was significant ($P < 0.001$). Absolute agreement between the modalities in staging was analyzed and was found to be 34.6%, with kappa value of 0.0833; suggesting poor agreement between the two staging modalities.

Though the tumor was clinically assessable by per vaginal examination in all the 78 patients, it could only be demonstrated on CT in 54 (69%) of the patients. Size of tumor varied from 2-8 cm clinically and between 2.5–10 cm on CT scan which was insignificant.(Table 1)

Of the 78 patients, 48 (61.5%) showed vaginal involvement on clinical examination

Sensitivity 25%, Specificity 80%, PPV 66.7%, NPV 40% accuracy of CT when compared with clinical examination was 46.2%.(Table 2)

The percentage of agreement between CT and clinical examination in evaluation of parametrial invasion was 41%. CT underestimated parametrial invasion. (Table 3)

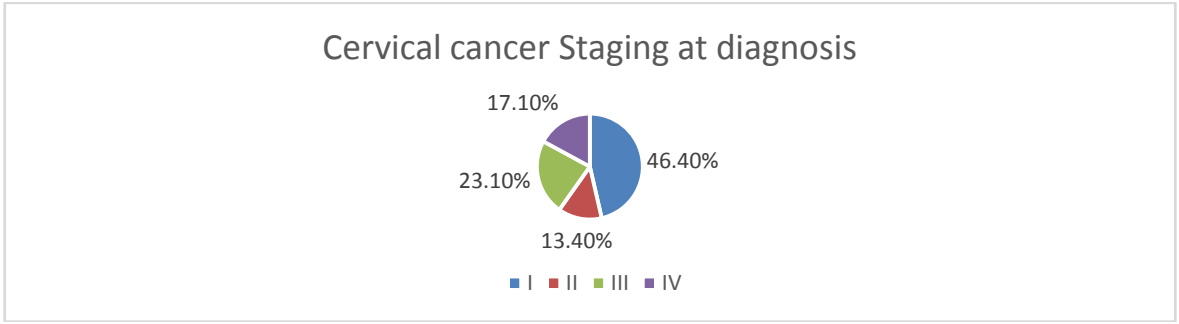
Of the 78 patients 20 (25.64%) had clinical features of unilateral pelvic wall involvement, 24 patients (30.76%) had bilateral involvement. CT showed pelvic wall invasion in 11 patients (14.10%). CT underestimates the pelvic wall invasion when compared with clinical examination.The percentage of agreement between CT and clinical examination in evaluation of pelvic wall invasion was 48.7%. CT underestimated pelvic wall invasion.(Table 4)

IVU was performed in 75 patients .3 patients (4%)showed involvement of urinary bladder whereas CT showed involvement in 19 patients (25.3%). Accuracy 78.7% Sensitivity 100 % Specificity 77.8% PPV 15.8% NPV 100%.(Table 5)

CT showed definite involvement of rectum in 21patients (26.92%) of 78. Sensitivity 100% Specificity 76% PPV 14.3% NPV 100%. Accuracy of CT in assessment of invasion of rectum by cervical cancer was 76.9% .(Table 6)

IV. Discussion

Worldwide, uterine cervical carcinoma is the second most common gynecologic malignancy.Invasive cervical cancer remains a burden to the society which claims deaths tolls of 60,078 in developing countries as the recent Globocan 2018 reports in India.

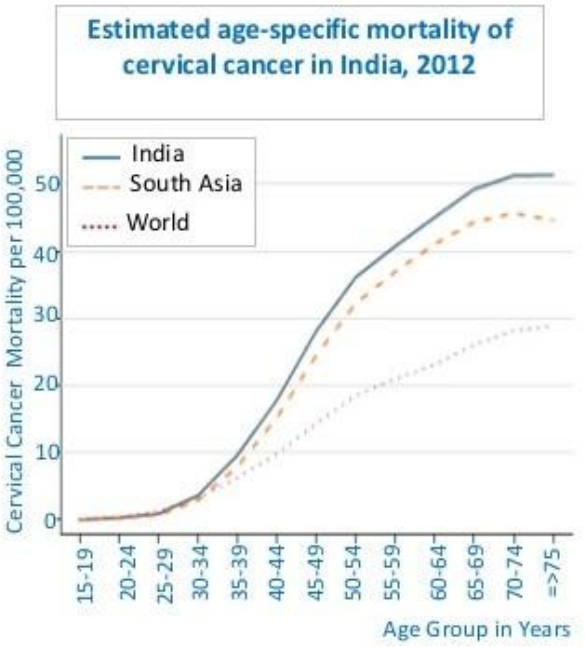


Squamous cell carcinoma (SCC) accounts for 85% of all cervical cancers mostly associated with human papilloma virus (HPV), especially subtypes 16. Non squamous origin includingadenocarcinoma (HPV 18), adenosquamous, undifferentiated which have a poorer prognosis comprise of about 15%.Other predisposing factors for cervical carcinoma include low socioeconomic status, early sexual life, multiple partners, immunosuppression and smoking[8].

Prognosis of invasive cervical carcinoma is strongly associated with the stage of the disease at the time of diagnosis hence screening and an early diagnosis holds the key as the 5 year survival rate is high (approx. 90%)without lymph node involvement and metastases. It drops significantly otherwise.

Early cervical cancer diagnosis remains a clinical challenge and screening is based on results derived from the Pap smear test. Imaging alone is not adequate for the diagnosis of cervical cancer since it cannot discriminate between invasive cancer and precursor lesions or other non-neoplastic pathological processes, like cervicitis; therefore, biopsy of suspicious lesions on colposcopy, is currently the gold standard method for cervical cancer diagnosis.

- Globally 528,000 cases of cervical cancers (CaCx). It kills 266,000 women each year
- **In India, every year 122,844 cases and 67,477 deaths**
- **334** cases per day and **185** deaths everyday
- HPV 16 and/or 18 is responsible for 83%
- It ranks as **2ND** most common cancer in women aged 15 to 44 years in India



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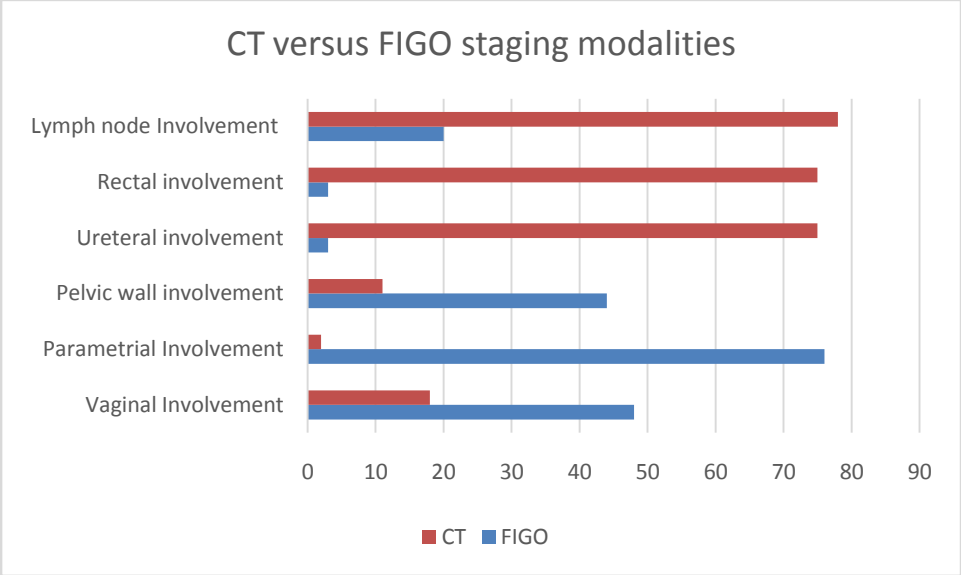
Cervical cancer imaging refers to the evaluation of patients with macroscopically visible tumors [International Federation of Gynecology and Obstetrics (FIGO) ≥IB]. Available imaging modalities fail to demonstrate microscopically present tumors (FIGO ≤ IA). MRI may detect lesions smaller than 1cm[6] and the investigation of choice[1].Positron emission tomography/ computed tomography (PET/CT) may detect small FDG-avid tumors 7 mm or less[7]. PET/MRI, a newer hybrid imaging method seems promising. However as discussed above cervical cancer is more prevalent in low socioeconomic status, CT is the more preferred modality and readily available.

Ozsarlak et al reported the overall accuracy of staging for clinical examination, CT, and MRI to be 47, 53, and 86 per cent respectively when compared with surgical findings[2]. Approximately half of the tumors are isodense to cervical stroma and hence not detected on contrast-enhanced CT[2]. Chances of missing a primary tumor are quite high if the tumor size is small as discussed earlier. Ureteric involvement and hydro nephrosis was detected in 3 out of 75 patients by IVU, Whereas CT demonstrated ureteric involvement and hydro nephrosis in 19 of them. Earlier studies have suggested CT to be superior or equal in demonstrating ureteric involvement and hydro nephrosis[5].

As per the FIGO guidelines all patients with cervical cancer should undergo cystoscopy and biopsy to detect involvement of bladder mucosa. In our study, CT showed definite involvement of urinary bladder in 19 patients .The high sensitivity and NPV of CT in determining urinary bladder & rectal invasion make CT an effective preliminary screening modality. Nodal involvement is one of the important prognostic factors; however, it is not incorporated in the FIGO staging system, In our study, CT was valuable in detecting involvement of pelvic nodes and retroperitoneal nodes respectively. None of the 19 suspected patients demonstrated lung involvement, however CT was helpful in detecting lesions in two of them. Treatment was as per clinical FIGO stage and physical status of the patients. CT findings considered for the objective assessment of tumor, burden, planning of radiotherapy and prognosis individually.



Interpretation & Conclusion:

Whilst ureteric, renal involvement, nodal or distant metastases are better demonstrated on CT thus aiding the FIGO staging. Clinical correlation can never be undermined especially in regards to parametrial, vaginal and pelvic wall invasion. Clinical staging of cervical cancer cannot be replaced completely currently by cross-sectional imaging for various reasons including lack of availability of resources in low-income countries, however, cross sectional imaging studies like CT which are affordable and readily available in developing countries like India along with FIGO staging provide additional information for the evaluation of patients with cervical cancer and thus improving the algorithm for treatment and proved to be a boon for the clinicians.

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TABLE1: Correlation of FIGO Clinical Staging and CT scan Staging

FIGO Stage	CT Down Stage	CT Same Stage	CT Over Staging	TOTAL	
2	18	9	3	30	
3	27	9	6	42	
4	0	6	0	6	
Total	45	24	9	78	
Agreement	18	9	28	34	34.6%
By chance	17.31	12.92	0.69	30.9231	
Cohen's Kappa =	0.0833				

Table 2: Comparison of CT and Clinical assessment of vaginal involvement

CT	Vaginal involvement Clinical Examination	
	Involved	Not involved
Involved	12	6

Not Involved	36	24
Total	48	30

Calculated Diagnostic Accuracy Parameters:

Sample size* = *78

Sensitivity = 25%

Specificity = 80%

PPV = 66.70%

NPV = 40.0%

Accuracy = 46.2%

Table 3 : Comparison of CT and clinical assessment of parametrial involvement

CT	Clinical Assessment		
	No Involvement	U/L involvement	B/L involvement
No Involvement	2	5	17
U/L involvement	0	2	22
B/L involvement	0	2	28

The measure of agreement (Kappa)between clinical evaluation and CT scan in assessing parametrial involvement is 0.058

Table 4 Comparison of CT and clinical assessment of lateral pelvic wall

CT	Clinical Assessment			
	No Involvement	U/L Involvement	B/L Involvement	
No Involvement	32	17	18	
U/L involvement	0	3	3	
B/L involvement	2	0	3	

The measure of agreement (Kappa)between clinical evaluation and CT scan in assessing pelvic wall involvement is 0.125

Table 5 Comparison of CT and clinical assessment of urinary bladder involvement (n=75)

CT	IVU		
	Involved	Not Involved	Total
Involved	3	16	19
Not Involved	0	56	56
Total	3	72	75

Calculated Diagnostic Accuracy Parameters :

Sample size= 75

Sensitivity = 100.0%

Specificity = 77.8%

PPV = 15.8%

NPV = 100%

Accuracy = 78.7%

Table 6 Comparison of CT and clinical assessment of rectal involvement (n=78)

CT	Sigmoidoscopy		
	Involved	Not Involved	Total
Involved	3	18	21
Not Involved	0	57	57
Total	3	75	78

Calculated Diagnostic Accuracy Parameters:

Sensitivity = 100%

Specificity = 76.0%

PPV = 14.3%

NPV = 100%

Accuracy = 76.9%