Comparison of CT Scan and Cystoscopy findings of Bladder Involvement in Patients of Carcinoma Cervix in View of Revised FIGO Staging: A Cross-sectional Study

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ABSTRACT

Introduction: Cervical cancer is the 5th most common cancer in humans and the second most common cancer in women worldwide. Bladder invasion is an important prognostic factor and adversely affects the clinical outcome and detecting true bladder invasion is extremely important for prognostication and treatment in patients of cervical cancer. Cystoscopy was the approved method for assessing involvement of the bladder according to International Federation of Gynaecology and Obstetrics (FIGO) staging until the revised FIGO staging 2009 which encourages the use of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scan and does not recommend cystoscopy as mandatory investigation.

Aim: To compare the role of CT scan of pelvis and cystoscopy for bladder involvement in carcinoma cervix.

Materials and Methods: This cross-sectional study was conducted on 100 patients of carcinoma cervix admitted in the Gynaecology wards of Government Medical College, Patiala, Punjab, India, from January 2015 to December 2015. The study involved cystoscopy and CT scan pelvis which were done for pretreatment assessment of all patients who were histopathologically proven to have carcinoma cervix. The sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy of CT scan were calculated.

Results: The majority (33%) of patients belonged to 51-60 years age group with mean age of 50.86±10.75 years. True positives were six cases, where bladder involvement on cystoscopy was histopathologically proven. True negatives were 72 cases where bladder was not involved on CT and cystoscopy. False positive were cases which were involved on CT scan but negative on cystoscopy for bladder involvement which came out to be 22. No false negatives were observed in which bladder was not involved on CT scan but showed involvement on cystoscopy in the present study. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CT scan came out to be 100%, 76.60%, 21.43%, 100% and 78%, respectively.

Conclusion: The positive findings of CT scan for bladder involvement can be used to select patients who need to undergo cystoscopy as CT scan is a moderately accurate modality for assessing bladder involvement in patients of carcinoma cervix. The 100% NPV observed in our study is encouraging to suggest that it can be used as primary modality to avoid invasive procedure like cystoscopy in women with carcinoma cervix specially with CT negative findings for bladder involvement.

INTRODUCTION

Cervical cancer is the 5th most common cancer in humans and the second most common cancer in women worldwide [1]. Cervical cancer is still the most common cancer in Indian females. The age-adjusted incidence rate ranges from 17.2 to 30.1 per 100,000 women [2]. One in five women suffering from cervical cancer belongs to India which has the largest burden of cervical cancer patients in the whole world [3]. Cervical cancer is a clinically staged disease. The clinical staging system developed by FIGO is constructed on the belief that cervical cancer is a local disease until rather late in its course [4,5]. An important issue in treatment planning for cervical cancer is to distinguish early diseases (stage IA, IB and IIA) that can be treated with surgery from advanced disease that must be treated with radiation therapy or radiation combined chemotherapy [6].

The FIGO staging has been universally adopted as standard pretreatment staging and treatment protocol [5]. Inaccuracy in clinical staging is predominantly due to difficulties in evaluating parametrial and pelvic sidewall invasion, bladder or rectal wall invasion and metastatic spread, in evaluating primary endocervical (endophytic) tumours and in estimating primary tumour size. Aside from inaccuracies of clinical staging, evaluation of lymph node metastasis, which is an important prognostic factor and a determinant in treatment planning, is not included in the clinical staging system [7]. Due to these reasons, FIGO clinical staging has shown to result in understaging or overstaging [5]. Despite its error-prone methodology, FIGO staging remains the current worldwide standard of practice. The success of clinical based cervical cancer FIGO staging is mainly built on the fact that it can be used worldwide to stage new patients without necessity of advanced imaging techniques or surgical interventions [8]. But the limitations of FIGO staging need to be addressed for better pretreatment evaluation of patients with cervical cancer. Therefore, a more accurate noninvasive method, like advanced imaging, is urgently needed to improve the tumour staging [9].

The modern cross-sectional imaging had not been incorporated into FIGO guidelines for routine pretreatment diagnostic modalities of cervical cancer [10,11]. This is mainly due to the belief that staging methods should be universally available and that staging should serve as standardised means of communication between institutions around the world [5]. Among the most important arguments against the use of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) as staging modalities are their high cost and lack of availability, especially in the underdeveloped regions of the world where invasive cervical cancer is most prevalent [7].

The use of CT in initial disease has been restricted for the reason of low sensitivity and specificity for local invasion in the pelvis [12,13]. Due to the criticism associated with FIGO protocol, FIGO staging system underwent a revision in 2009 for carcinoma cervix which encourages the use of CT scan/MRI scan and does not recommend cystoscopy as mandatory investigation and suggest that conventional FIGO clinical staging methods are increasingly being replaced by single comprehensive tests like CT scan or MRI [14]. Bladder invasion is an important prognostic factor and adversely affects the clinical outcome and detecting true bladder invasion is extremely important for prognostication and treatment. Cystoscopy is the approved method for assessing involvement of the bladder according to FIGO until the recent revision [11]. However, it only has a limited role in the evaluation of infiltration or invasion of the bladder wall [15,16]. In recent times, availability of CT scan is progressively increasing in developing countries where cervical cancer is common and its use is definitely on the rise in cervical cancer patients. Developments in imaging could progress the staging of cervical cancer by simplifying the detection of lymph node metastases and micrometastases in distant organs. Such progress could lead to perfections in treatment selection and therefore increase complete survival rates [17]. Therefore, the use of CT scan for evaluating bladder involvement is likely to increase. But CT scan has its limitations in detecting soft tissue infiltration of cervical cancer and local spread of the disease. Hence, the present study was conducted with objectives:

- To compare the findings of CT scan of pelvis and cystoscopy for bladder involvement in carcinoma cervix.

- To demonstrate the accuracy of CT scan for pretreatment diagnosis of bladder involvement in carcinoma cervix.

MATERIALS AND METHODS

This was a cross-sectional study conducted on 100 patients of carcinoma cervix admitted in the Gynaecology Wards of Government Medical College, Patiala, Punjab, India, between January 2015 to December 2015. The study involved cystoscopy procedure and CT scan pelvis which were done for pretreatment assessment of all patients who were histopathologically proven to be carcinoma cervix. After getting approval from Institutional Ethical Committee (BFUHS/2k14/P-Th/1503), an informed consent was taken from each patient. All patients with cervical carcinoma reporting to the Institute in the study period formed the sample population of the study.

Inclusion criteria

- Biopsy confirmed cervical cancer patients.
- Patients who had not undergone prior treatment.
- Patients who were willing to participate in the study.

Exclusion criteria

- Patients who had taken some form of treatment for cervical cancer.
- Patients unwilling to undergo CT scan or cystoscopy procedures.
- Patients who were not willing to participate in the study.

After taking informed consent, detailed history of patient was taken as per proforma. General physical examination was done. Local examination included per speculum, pervaginum and per rectum examination for clinical staging. Computed tomography scan was performed on Siemens somatom emotion and slice third generation spiral CT (6 slice). The details of the procedure were explained to the patient. Patient was kept in supine position on CT table which was then advanced into the gantry. Serial CT slices were obtained at a distance of 8 mm. For permanent record images were saved in the system. Non toxic contrast was used which was given when required by peripheral intravenous (i.v) route. Oral/rectal contrast was done when required.

In this study, irregular cervical margin, parametrial soft tissue stranding, obliteration of periureteral fat planes or an eccentric parametrial mass were considered as signs of parametrial invasion. Involvement of ureter in the form of encasement with or without urinary obstruction and dilatation was noted. Obstructive hydronephrosis on CT was taken as stage IIB disease. The signs of pelvic wall involvement were extension of tumour to within 3 mm of the pelvic side wall, encasement of iliac vessels, enlargement of obturator or pyriformis muscles.

Computed Tomography

Thickening of wall of bladder or rectum with loss of fat plane between them was considered as suspicious for invasion. Presence of fat plane between tumour and adjacent organs (bladder or rectum) was taken as evidence of non involvement of these structures. Intraluminal extension of tumour was considered as a definite sign of the involvement. Any enlargement in size of pelvic and retroperitoneal lymphnodes was noted. Short axis nodal diameter of greater than 10 mm and/or presence of central necrosis on CT were taken as signs of nodal metastasis.

Cystoscopy

Cystoscopy was performed with Karlstone cystoscope under local anesthesia. The details of the procedure were explained to the patient. Patient was required to lie in the lithotomy position. Vulva was cleaned and draped. About 5 cc of 2% xylocaine were injected into urethra to ensure analgesia. In the meantime, intravenous antibiotics were given to ensure antibiotic cover during the procedure. Cystoscope was introduced and findings were recorded. Biopsy was taken from the lesion if present and sent for histopathology. The findings of cystoscopy were divided into four types:

1) Normal study;
2) Bullous oedema;
3) Suspicious: in the form of indentation on posterior bladder wall, elevation without visible mucosal involvement;
4) Frank growth. Cystoscopy guided biopsies were taken from all suspicious and frank cases of bladder involvement. The reference standard for present study was histopathologically proven cases of bladder involvement.

STATISTICAL ANALYSIS

The data was compiled using Microsoft Excel 2007 (Microsoft corporation Redmond, WA) and further analysis was carried out in STATA 13 (Statacorp, College Station, TX, USA). Using the raw data, the measures of diagnostic test accuracy sensitivity, specificity, PPV and NPV were calculated using simple statistical formulas.

RESULTS

The present study was conducted on 100 patients of carcinoma cervix admitted in the Gynaecology Wards in the age group of 28-72 years. The socio-demographic characteristics and clinical features have been shown in [Table/Fig-1]. The majority (33%) of patients belonged to 51-60 years age group with mean age of 50.86±10.75 years. The most common presenting complaint in the present study was menstrual disturbances in premenopausal age group (68.6%) and discharge per vaginum in postmenopausal age group (83.7%). The majority of women in the study belonged to lower socio-economic status with 29% belonging to class V and 34% belonged to class IV socio-economic status according to modified Kuppuswamy Scale [18]. All patients had histopathologically proven cervical carcinoma (n=100). Squamous cell carcinoma was the most common histopathology in 92% of patients. Remaining 8% women had adenocarcinoma. Most women in the present study presented in stage II of FIGO staging (59%) followed by stage III (26%), stage I (9%) and stage IV (6%).

Variables	Frequency (n)	Percentage (%)
Age (in years)		
≤30	3	3%
31-40	19	19%
41-50	27	27%
51-60	33	33%
>60	18	18%
Menopausal status		
Premenopausal and perimenopausal	51	51%
Postmenopausal	49	49%
Parity		
Nullipara	1	1%
1-4 children	14	14%
>4 children	85	85%
Socio-economic status		
I Upper class	2	2%
II Upper middle class	8	8%
III Lower middle class	27	27%
IV Upper lower class	34	34%
V Lower class	29	29%
Clinical features		
Premenopausal (n=51)		
Menstrual disturbances	35	68.6%
Discharge pervaginum	27	52.9%
Postmenopausal (n=49)		
Discharge pervaginum	41	83.7%
Postmenopausal bleeding	37	75.5%
Pain lower abdomen	19	38.8%

[Table/Fig-1]: Demographic profile and clinical features of patients of carcinoma cervix.
(clinical features are more than 1 for some patients)

Cystoscopy and abdominopelvic CT scan was done in all patients (n=100). The observations of cystoscopy findings were divided into four types:

- Normal findings were observed in 85 (85%) patients;
- Bullous oedema was seen in 3 (3%) patients;
- Suspicious findings (bossing of the posterior bladder wall or indentation without apparent mucosal involvement) was seen in 6 (6%) patients;
- Frank bladder involvement (growth in the lumen of bladder) was seen in 6 (6%) patients.

Patients who had suspicious and frank bladder involvement (n=12) underwent cystoscopy guided biopsy. All patients with frank bladder involvement (6, 6%) came out to be positive for bladder involvement on histopathology. These 6% patients were considered true positives in the study. All the patients with suspicious findings on cystoscopy (n=6) had negative histopathology and were considered true negatives (no bladder involvement on bladder biopsy).

Out of 28 women who showed bladder involvement on CT, only six women were positive on cystoscopy with biopsy (true positive for CT scan), indicating a low PPV (21.4%) for CT for involvement of bladder. The remaining 22 women were negative on cystoscopically (false positive for CT). Rest of 72 women with negative CT findings for bladder, were also cystoscopically negative (true negatives for CT), indicating a very high NPV (100%) for CT involvement of bladder. There was no false negative case found in our study who was cystoscopically positive with negative CT findings of bladder involvement [Table/Fig-2].

Findings of CT	Cystoscopy		
	Involved (n=6)	Not involved (n=94)	Total
Involved (n=28)	6	22	28
Not involved (n=72)	0	72	72
Total	6	94	100

[Table/Fig-2]: Findings of Computed Tomography (CT) and cystoscopy in urinary bladder involvement (n=100).

The sensitivity, specificity, PPV, NPV and accuracy of CT scan came out to be 100, 76.6%, 21.4%, 100% and 78%, respectively in the present study as shown in [Table/Fig-3].

Diagnostic performance parameters	CT scan
True positive	6%
True negative	72%
False positive	22%
False negative	0%
Sensitivity (%)	100%
Specificity (%)	76.6%
Positive Predictive Value (PPV) (%)	21.4%
Negative Predictive Value (NPV) (%)	100%
Accuracy (%)	78%

[Table/Fig-3]: Diagnostic performance of Computed Tomography (CT) scan for bladder involvement (n=100).

DISCUSSION

In the present study, bladder involvement on cystoscopy was seen in 6% cases which was comparable to Sharma DN et al., (2005) (5.59%) Sundborg MJ et al., (1998) (6.1%), Liang CC et al., (2000) (8%), and Prasad TV et al., (2014) (4%) as summarised in [Table/Fig-4] [2,19-23].

Author and year of study	Sample size	Bladder involvement on cystosopy	Bladder involvement on CT scan
Prasad TV et al., [23] (2014)	50	2 (4%)	13 (26%)
Jeong BK et al., [22] (2012)	590	25 (4.23%)	29 (4.91%)
Sharma DN et al., [2] (2001)	305	17 (5.59%)	42 (13.81%)
Chung H et al., [21] (2001)	296	8 (2.7%)	8 (2.7%)
Sundborg MJ et al., [19] (1998)	49	3 (6.1%)	5 (10.2%)
Liang CC et al., [20] (2000)	100	8 (8%)	10 (10%)
Present study (2021)	100	6 (6%)	28 (28%)

[Table/Fig-4]: Various studies comparing cystoscopy and CT findings of bladder involvement [2,19-23].

As shown in [Table/Fig-5], the results of the present study were comparable to Prasad TV et al., where sensitivity and NPV of CT scan was found out to be 100% and 100%, respectively [23]. Sharma DN et al., conducted a study on 305 patients with same results in terms of sensitivity and NPV [2]. The accuracy of CT scan was comparable to Prasad TV et al., i.e., 78%. The PPV in current study was 21.4% which is comparable to Prasad TV et al., [23].

In present study, the incidence of bladder involvement came out to be 6% which is comparable to Sharma DN et al., Sundborg MJ et al., Liang CC et al., and Chung et al., [Table/Fig-5] [2,19-21]. This means that 94% patients underwent cystoscopy unnecessarily. CT scan was able to detect bladder involvement in all of the cases found involved on cystoscopy as well. The NPV of CT scan in present study was found out to be 100%. That implies that no patient of true bladder involvement was left undetected on CT scan. Although the reliability of CT scan to accurately detect bladder involvement is still questionable with present study showing the accuracy to be 78%, CT scan may still prove useful in selecting the cases which should undergo

Author and year of study	No. of patients	Sensitivity	Specificity	Positive predictive values	Negative predictive values	Accuracy
Sundborg MJ et al., [19] (1998)	42	100%	96%	60%	100%	96%
Liang CC et al., [20] (2000)	100	100%	98%	80%	100%	98%
Massad LS et al., [24] (2000)	97	0	95%	0	91%	-
Chung H et al., [21] (2001)	296	100%	98%	57%	100%	98%
Sharma DN et al., [2] (2005)	305	100%	92%	40%	100%	92%
Jeong BK et al., [22] (2012)	411	68.2%	96.4%	51.7%	100%	98%
Prasad TV et al., [23] (2014)	53	100%	77%	15.38%	100%	78%
Present study (2021)	100	100%	76.6%	21.4%	100%	78%

[Table/Fig-5]: Various studies showing performance of Computed Tomography (CT) for bladder invasion in cervical cancer patient [2,19-24].

cystoscopy. Based on the results of our study, we conclude that the patients with bladder involvement on CT should undergo cystoscopy [2,19-24].

One of the drawbacks of cystoscopy is that it can only tell about bladder involvement when mucosa is infiltrated [25]. The role of imaging modalities like CT/MRI lies in detecting patients who have bladder involvement not yet progressed to mucosa in order to assess the mode of treatment best suited for them. Although the imaging modality of choice for pretreatment evaluation in cervical cancer remains MRI [26], the lack of availability of MRI at our institution was a drawback in the present study.

Nodal involvement is one of the important prognostic factors however it is not incorporated in the FIGO staging system [11]. The added advantage of investigation modality like CT is the detection of lymph node status in evaluation of the patient alongwith distant metastasis. This information helps in better planning of chemoradiotherapy given to patients with advanced cervical cancer. The involvement of ureters and kidneys is an important prognostic factor in long term survival of the patient which can also be detected by CT scan.

The disadvantage of CT scan in evaluation was the inability of CT scan to detect primary tumour, as malignant growth appears isodense to cervical stroma on contrast enhanced CT scan [15]. CT scan is unable to detect parametrial and pelvic wall involvement accurately which correlates poorly with clinical findings. In the present study the accuracy and PPV of CT scan was low i.e., 78% and 21.43%, respectively. Hence, the bladder involvement on CT scan needs additional confirmation once it has been diagnosed. The CT scan machine used in our institution was a Siemens somatom emotion and slice third generation spiral CT (6 slice). The resolution of this machine was poor which may explain the low accuracy and specificity found in the study. A better configuration of the machine might have been more valuable in detecting true bladder involvement.

Limitation(s)

The use of a low resolution CT scan used in the present study was one of the major limitations. A higher resolution CT scan may help to improve the accuracy of assessing bladder involvement in patients of carcinoma cervix. As this study was conducted in a small population, similar studies involving a larger sample size as a multicentric study needs to be conducted to generalise the findings of the study.

CONCLUSION(S)

The findings of CT scan for bladder involvement can be used to select patients who need to undergo cystoscopy. In this study, moderate accuracy, low PPV for CT in identifying involvement of bladder, indicates that women with positive bladder findings on CT scan must undergo cystoscopy, whereas its high NPV for identifying bladder involvement indicates that cystoscopy, being an invasive procedure, can be avoided in women with negative findings on CT scan.

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