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Original Research Paper

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A PROSPECTIVE STUDY TO ANALYSE THE ROLE OF COMPUTED TOMOGRAPHY SCAN IN URINARY BLADDER CARCINOMA STAGING AND SELECTION OF APPROPRIATE MANAGEMENT MODALITY

Sunny Gupta	PG Resident(2018-2021), Department Of Surgery, Grmc Gwalior, MP, India.
Prashant Shrivastava	Professor And Head Of Department Of Surgery, Grmc Gwalior, MP, India.
Anurag chauhan	Associate Professor Department Of Surgery, Grmc Gwalior, MP, India.
Pankaj Kumar Yadav	Associate Professor Department Of Radiodiagnosis, Grmc Gwalior, MP, India.

ABSTRACT **Background:** Urinary bladder carcinoma is a common malignant tumor of the urinary tract and its management depends on the stage of lesions. The aim of this prospective study was to determine the accuracy of computed tomography (CT) scan in early detection of muscle invasion and local tumor staging of urinary bladder carcinoma. Forty patients with urinary bladder mass lesions were evaluated with Multidetector Computed Tomography (MDCT) (SIEMENS SOMATOM DEFINITION AS 128 slice CT machine) and then patients underwent for conventional cystoscopy and TURBT/TUR biopsy/Radical cystectomy with soft tissue biopsy/specimen sent for histopathological examination. **Results:** On ct, diagnosis of muscle invasive (T2,T3,T4) from non muscle invasive (T1) has sensitivity, specificity, positive predictive value, negative predictive value and accuracy 87.1%, 77.8%, 93.1%, 63.6% and 85.0% respectively. Diagnosis of invasion of perivesical fat, locally invasive bladder tumor(T3,T4) from non locally invasive (T1,T2) has sensitivity, specificity, positive predictive value, negative predictive value and accuracy 85.7%, 100%, 100%, 86.4% and 92.5% respectively.. **Conclusion:**The results of our study and previously published studies suggest a high reliability of MDCT imaging for the diagnosis and proper staging of bladder carcinoma for choosing appropriate management modality.

KEYWORDS : Urinary bladder, Carcinoma, CT, Muscle invasion, Perivesical invasion

INTRODUCTION

Urinary bladder (UB) carcinoma accounts for diagnosed 3% of global cancer and is prevalent in the developed world based on the latest GLOBOCAN data, bladder cancer is the 10th most common and 13th most deadly cancer worldwide.[1] Bladder cancer is four times more common in men than women and more than 90% of bladder cancer diagnoses are made in age older than 55 years[1]. One of the strongest risk factor for bladder cancer is tobacco smoking, accounting for 50-65% of all cases[2]. Gross painless haematuria is the most common presentation.[2] About 90% of bladder cancers present as transitional cell carcinoma and the remaining 10% are squamous cell carcinomas, adenocarcinomas and other subtypes.[3]

At the time of diagnosis, approximately 75% of the UB lesions are limited to the bladder, while 25% are detected in the regional lymph nodes or in distant locations.[4] Bladder cancer survival is directly related to the depth of invasion and the presence and extend of metastatic disease.[5] Five-year survival rates after Cystectomy are reported between 55–80% for tumours restricted to the lamina propria, 40% with invasion of the muscularis propria of UB, 20% with invasion of the perivesical fatty tissue, and 6% in metastatic cases.[5]

Computed Tomography(CT) scan and magnetic resonance imaging (MRI) are the imaging modality for diagnosis and staging of urinary bladder cancer. MRI has many advantages including better detection of tumours, multiplanar imaging, better soft tissue characterization, and superiority in evaluation of pelvic organs invasion.[6] MRI has superiority over CT in local staging, detecting muscle invasion, mainly in superficial and multiple lesions but in perivesical fatty tissue invasion and regional/distant lymph node metastases, these two imaging methods have almost similar accuracy.[7] FDGPET/CT has superiority in the detection of distant organ and lymph node metastasis.[8]

Conventional Cystoscopy and TUR biopsy represents the gold standard for diagnosis but as it is an invasive procedure disadvantages are intense discomfort for the patient, bleeding, the high cost and local complications such as infections and mechanical lesions and they does not provide information about extra-vesical extensions of the tumour whereas CT serves as a noninvasive technique in both staging and visualization of the bladder lesions.

Bladder carcinoma can be roughly divided into three groups, UB tumour without muscle invasion, UB tumour with muscle invasion, and metastatic disease. Intravesical Bacillus Calmette-Guerin (BCG) immunotherapy and / or intravesical chemotherapy following the transurethral resection of bladder tumour (TURBT) is recommended in the UB tumour without muscle invasion.[9] In UB tumour with muscle invasion, Cisplatin-based neoadjuvant chemotherapy followed by radical cystectomy, bilateral pelvic lymph node dissection, and urinary diversion is recommended in patients depending upon the extension of disease.[9] Cisplatin based adjuvant chemotherapy can be considered in high-risk patients.[10] In metastatic disease, cisplatin-based chemotherapy is administrated and in case, patient is not eligible for cisplatin, carboplatin-based protocols or a single drug protocol can be used.[11]

MRI and FDG-PET/CT are more expensive than CT and not widely available and affordable while CT is widely available and is a non invasive procedure in comparison to Cystoscopy and TUR biopsy, thus its role is staging of UB carcinoma and choosing appropriate management modality is evaluated in our study.

METHODS

After obtaining approval from ethical committee the present study was carried out during a period from January 2019- June 2020 after taking well informed and written consent from the patient.The total numbers of OPD patients admitted were 74 in present study, suspected of having carcinoma urinary bladder (UB).

Inclusion Criteria

1. Complaints of haematuria (gross or microscopic) suspected of having carcinoma urinary bladder.

2. Patient with suspected to have urinary bladder mass on ultrasound examination.
3. Patients scanned for some other suspected abdominal/pelvic pathologies and incidentally detected to have urinary bladder mass.

Exclusion Criteria

1. Patients lost to follow-up.
2. Confirmed to have some pathology other than carcinoma urinary bladder.
3. Patients known to be allergic to ionic or non-ionic contrast media or having deranged renal function.
4. Pregnant patients.
5. Patient not giving consent/ patients not willing to participate in the study.

After excluding all those confirmed to have some pathology other than carcinoma urinary bladder, patients known to be allergic to ionic or non-ionic contrast media or having deranged renal function and pregnant patients, total 55 patients enrolled. All the 55 patients of UB carcinoma were explained about the study and informed consent was obtained, out of which 13 patients lost to follow up and 02 patients expired during follow up period of study. After excluding the incompletely filled forms and/or missing data, finally 40 patients comprised of our study population of UB carcinoma.

We did all the relevant preoperative blood, urine investigations and ultrasonography and then patients were evaluated with Multidetector Computed Tomography(CT) (SIEMENS SOMATOM DEFINITION AS 128 slice CT machine) and then patients underwent for conventional Cystoscopy followed by TURBT/TUR biopsy/Radical cystectomy with soft tissue biopsies/specimen send for histopathological examination. Histopathological results were used as the standard reference for our study results.

COMPUTED TOMOGRAPHY TECHNIQUE:

CT examinations were carried out with SIEMENS SOMATOM DEFINITION AS 128 slice CT machine. Oral contrast was given 1.5 hours before the CT examination (1000–1500 cc water/2% iodine opaque). Non-ionic intravenous contrast material was given by automatic injection in a dose of 2 mL/kg at an average rate of 3 mL/sec, after which Multidetector CT examination was performed. In pre-contrast examination, an iliac crest-inferior pubic ramus field was chosen to include the whole bladder, with the bladder full; 120 kVp, 150–200 effective mAs (automatic modulation), soft tissue algorithm, 2.5 mm collimation, 5 mm section thickness and 1.25 mm reconstruction interval were used, and the examination was performed with 1-1.5 normalized pitch and wide FOV (30 cm). After that, non-ionic intravenous contrast material was given and CT examination was performed at 60, 80 and 180 seconds. At delay times of 60 and 180 seconds, the same area was imaged, while at 80 seconds the same parameters were set but the whole abdomen from the diaphragm to the inferior pubic ramus was imaged in order to scan for distant metastasis.

Imaging Analysis:

The examination taken with a delay time of 60 seconds was used to show bladder cancer, and the view taken with a delay time of 180 seconds was used to assess perivesical invasion. The examination with a delay time of 80 seconds was used to show the existence of abdominal or retroperitoneal metastasis. In the 60-second CT images, wall thickening which showed a clear contrast uptake in comparison with adjacent bladder wall or a mass extending to the bladder lumen was accepted as a bladder tumour.

All cases of the study were examined clinically and managed by highly experienced consultant urologist. All CT images sets were analyzed by experienced radiologist who was blind to the results of Cystoscopy and histopathological findings.

Statistical Analysis

The statistical analysis of this study was done by using suitable statistical methods. The programs MS EXCEL and Epi Info™ For Windows Download Version 7.2 were used.

Descriptive statistics of continuous variables are given as mean, standard deviation, median, minimum, and maximum values. Categorical variables are presented as frequencies and percentages and qualitative data, compared between groups by Pearson's chi square test.

The significance of the results was assessed in the form of P value that was differentiated into the following: non-significant when P value > 0.05, significant when P value ≤ 0.05, and highly significant when P value ≤ 0.01.

The study was conducted in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki.

RESULTS

Out of 40 patients, 36 (90%) were males and 4 (10%) were females. The male to female ratio was 9:1. Age of study population of carcinoma UB ranged from 21 to 74 years with mean (55) years ± standard deviation (13.6) years. Majority were in age group 41-80 years (80% of study population) showing increase prevalence of the Carcinoma UB at elderly age. Most common symptom affecting the study population was gross haematuria (92.5%). Majority of participants were tobacco users / smokers (92.5%). Most common co-morbidity observed was HTN (30%) followed by diabetes (25%).

Table 1.1- CT 'T' staging of study population having Carcinoma UB

CT 'T' STAGE	No. of patients (out of 40)	Percentage
T1	11	27.5%
T2	11	27.5%
T3	11	27.5%
T4	7	17.5%
TOTAL	40	100%

Table 1.2- CT (T) STAGE distribution of urinary bladder masses on the basis of muscle invasion

CT 'T' STAGE	No. of Patients (out of 40)	Percentage
NON MUSCLE INVASIVE (NMIBT)	11	27.5%
MUSCLE INVASIVE(MIBT)	29	72.5%
TOTAL	40	100%

Table 1.3- CT (T) STAGE distribution of urinary bladder masses on the basis of local invasion.

CT 'T' STAGE	No. of Patients(out of 40)	Percentage
Organ confined tumour or non locally invasive tumour(t1,t2)	22	55%
Locally invasive tumour(t3,t4)	18	45%
Total	40	100%

From above table, out of 40 patients, T staging of the urinary bladder tumours according to CT findings revealed 11 (27.5%) patients with T1, 11 (27.5%) patients T2, 11 (27.5%) T3, and 7 (17.5%) T4, considering T1 as non-muscle invasive bladder tumour (NMIBT) while T2, T3 and T4 as variable degrees of muscle invasive bladder tumour(MIBT) and T1 and T2 as organ confined or non locally invasive tumour and T3 and T4 as locally invasive tumours.

Table 2.1- Histopathology (pT) STAGE distribution of urinary

bladder masses

HISTOPATHOLOGY (pT Stage)	No. of Patients	Percentage
pT1	9	22.5%
pT2	10	25%
pT3	13	32.5%
pT4	8	20%
TOTAL	40	100%

Table 2.2- Histopathological pT STAGE distribution of urinary bladder masses on the basis of muscle invasion

HISTOPATHOLOGY (pT Stage)	No. of Patients (out of 40)	Percentage
Non Muscle Invasive (NMIBT)	9	22.5%
Muscle Invasive (MIBT)	31	77.5%
TOTAL	40	100%

Table2.3- Histopathological pT STAGE distribution of urinary bladder masses on the basis of local invasion.

HISTOPATHOLOGY (pT Stage)	No. of Patients (out of 40)	Percentage
Organ Confined Tumour Or Non Locally Invasive Tumour(T1,T2)	19	47.5%
Locally Invasive Tumour(T3,T4)	21	52.5%
TOTAL	40	100%

From above table, out of 40 patients, pathological pT staging of the urinary bladder tumours according to histopathology findings revealed 9 (22.5%) patients with pT1, 10 (25%) patients T2, 13 (32.5%) pT3, and 8 (20%) pT4, considering pT1 as non-muscle invasive bladder tumour(NMIBT) while pT2, pT3 and pT4 as variable degrees of muscle invasive bladder tumour (MIBT).

Table 3: Upstaging and Downstaging of study population having Carcinoma UB

Downstaging –

CT T stage	Histopathological pT stage	NUMBER (out of 40)	%
T2	T1	2	5%
Total		2	5%

Upstaging-

CT T stage	Histopathological pT stage	NUMBER (out of 40)	%
T1	T2	4	10%
T2	T3	3	7.5%
T3	T4	1	2.5%
Total		8	20%

Among study population of 40 having carcinoma UB, on CT, 25% were wrongly staged with 5% having downstaging and 20% having upstaging on histopathology pT staging(taking histopathological staging as standard reference for our study).

DISCUSSION

Aim of our study was to study role of CT in staging of bladder mass lesion and correlate it with histopathology for which we did CT of our study population of UB carcinoma preoperatively and then patients underwent for TURBT/TUR biopsy / Radical cystectomy. CT 'T' staging compared with pathological pT staging in histopathological specimen / soft tissue biopsy (send after TURBT/TUR biopsy / Radical cystectomy) which was considered as the standard reference for our study and then compared the data.

CT is most useful in identifying tumours that have macroscopically invaded through the serosa into the perivesical fat (T3b) and invaded adjacent organs (T4).[23] Inflammation or desmoplastic reaction, particularly soon after biopsy, and can cause a false-positive diagnosis of extravesical extension.[26] Similarly, loss of fat planes between a bladder tumour and adjacent organs can lead to a false-positive impression of organ invasion. CT cannot be used to reliably differentiate tumour confined to the mucosa (T1) from tumour that has invaded the muscularis propria (T2), this is because the layers of the bladder wall and the attenuation of tumour and bladder wall are usually difficult to differentiate.[26] Although it has been suggested that retraction of the bladder wall is an indirect sign of T2b muscle-invasive disease.[19] Some investigators have evaluated presence of hydronephrosis independently predicted non-organ-confined disease.[20]

Table 4- Result For Ct 't' Staging Of Carcinoma Ub

Parameter	T1	T2	T3	T4
Sensitivity	77.8%	60.0%	76.9%	87.5%
Specificity	87.1%	83.3%	96.3%	100.0%
Positive Predictive Value	63.6%	54.5%	90.9%	100.0%
Negative Predictive Value	93.1%	86.2%	89.6%	96.9%
Accuracy	85.0%	77.5%	90.0%	97.5%

Table 5- Result For Ct Muscle Invasive And Locally Invasive Carcinoma UB

Parameter	Muscle Invasive (T2,T3,T4) Vs Non Invasive(T1)	Locally Invasive (T3,T4) Vs Non Locally Invasive (T1,T2)
Sensitivity	87.1%	85.7%
Specificity	77.8%	100%
Positive Predictive Value	93.1%	100%
Negative Predictive Value	63.6%	86.4%
Accuracy	85.0%	92.5%

In our study, 45% have nodal metastasis present on CT and 8 % have distance metastasis, most commonly to liver. In our study population of 40 having carcinoma UB, on CT, 25% were wrongly staged with 5% having downstaging and 20% having upstaging on histopathology pT staging.

In a study of population of 26 of UB carcinoma by Ibrahim Ilker Oz[13] sensitivity of CT examination in the detection of perivesical fatty tissue invasion was 83.3%, and specificity was found to be 100% and accuracy of 83.5%.

Mirmomenet al[21] conducted a review of CT staging studies and demonstrated 49–93% accuracy in detecting perivesical invasion with tumours staged ≥T3[21]

Kim J. K. et al. established perivesical invasion with a high accuracy of 93% with multidetector CT[15]

In our study, CT in detection of perivesical fat has sensitivity, specificity and accuracy is 85.7%, 100%, 92.5% respectively which is consistent with previous studies.

There are some early models using machine learning that may help stratify tumours into stage <T2 and stage ≥T2, which may increase CT utility in this arena of local staging in the future, but currently, this differentiation requires further investigation and validation prior to clinical implementation and acceptance[22]

The results of our study and previously published studies suggest a high reliability of CT imaging for the diagnosis and proper staging of bladder carcinoma. In addition, CT images can provide information regarding lesion size, number, and location to surgeons who perform conventional Cystoscopy.

Cystoscopy and TUR biopsy are considered invasive technique which may be risky particularly in patients with bleeding disorders.[24]CT is non-invasive/ minimally invasive procedure, hence the main purpose of this study was to

assessrole of CT scan in UB carcinoma staging and selection of appropriate management modality. Cases with muscle invasive bladder carcinoma (MIBCs) are treated with neoadjuvant chemotherapy, radical cystectomy, and lymphadenectomy while in non-muscle invasive bladder carcinoma (NMIBCs) transurethral resection + chemo/immunotherapy are to be considered.[25]

In our study diagnosis of muscle invasive(T2,T3,T4) from non muscle invasive(T1) on CT has sensitivity, specificity, positive predictive value, negative predictive value and accuracy, 87.1%, 77.8%, 93.1%, 63.6% and 85.0% respectively.

In our study CT having sensitivity, specificity closely correlating with HPE finding after TURBT and thus we can say, CT is reliable enough to use for choosing appropriate management modality for muscle invasive and non muscle invasive bladder tumour moreover it's a non invasive procedure.

CT and magnetic resonance imaging (MRI) are the imaging modality for diagnosis and staging of urinary bladder cancer. MRI has many advantages including multiplanar imaging, better detection of tumours, better soft tissue characterization, and superiority in evaluation of pelvic organs invasion.[14] MRI has superiority over CT in local staging, especially in superficial and multiple lesions but in perivesical fat tissue invasion and regional or distant lymph node metastases, these two imaging methods have a similar accuracy.[15]

FDGPET/CT is superior in the detection of distant organ and lymph node metastasis while contrast MRI is prominent in performing T-staging or evaluating the local spread.[12]

El-Assmyet al[16] found that DWI had a significantly higher rate of correct primary staging as compared with T2-weighted images.

Abou-El-Ghar et al[17] The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of DW-MRI regarding the degree of muscle invasion of urinary bladder carcinoma were 98.5%, 93.3%, 100%, 92.3%, and 97% respectively.

Multi-parametric MRI that includes dynamic contrast-enhanced MRI and diffusion-weighted MRI is considered as the imaging modality of choice in tumour staging and perivesical invasion, with a reported accuracy of 87%[18]

MRI and FDG-PET/CT are more expensive than CT and not widely available and affordable while CT is widely available and thus its role is staging of UB carcinoma and choosing appropriate modality is evaluated in our study and found to be significant.

CONCLUSION

Cystoscopy and TUR biopsy for staging bladder carcinoma are invasive techniques which may be risky particularly in patients with bleeding disorders. Multi Detector Computed Tomography (MDCT) is a safe, and non-invasive method in early detection and staging of urinary bladder carcinoma for choosing appropriate management modality, moreover, MDCT is widely available and affordable in comparison to MRI and FDG-PET/CT.

The results of our study and previously published studies suggest a high reliability of MDCT imaging for the diagnosis and proper staging of bladder carcinoma for choosing appropriate management modality. In addition, MDCT images can provide valuable information regarding lesion size, shape, number, and location to surgeons who perform conventional cystoscopy.

LIMITATIONS

- Small study population of 40 patients only, accuracy of results can be increased through meta analysis or multi-center studies in which more patients are included.
- Late presentations of patients with advanced bladder tumour as majority were referred from primary and secondary health care, may have affected the results and specificity, positive predictive value, negative predictive value and accuracy of MDCT may be better because of the higher stage of presentation in the present study.

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