Original Article

Hybrid CT Urography: Paradigm Shift in CT Radiation Dose Reduction

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ABSTRACT

Introduction: Haematuria is a common clinical finding encountered in day to day practice and can be due to a wide variety of causes viz. urinary tract infection, urolithiasis, malignancies, benign prostatic hyperplasia, trauma, nephropathies, nephritis etc. Though we are armed with a battery of imaging techniques to investigate a case of haematuria, the present study was conducted to describe the clinico-radiological profile of haematuria to compare the diagnostic accuracy and the effective radiation dose in CT urography with hybrid CT urography.

Methodology: A total of 60 patients presenting with haematuria after complete clinical evaluation and routine blood and urine examinations were randomly distributed into two study groups: one group underwent conventional CT urography and the other group underwent hybrid CT urography and the imaging features were observed. Final diagnosis was made on the basis of histopathological findings and clinical follow up. Both the techniques were finally compared for their diagnostic accuracy and radiation dose.

Results: Bladder neoplasms and urolithiasis constituted the most common etiologies in the study population each accounting for 17 cases (28.33%). This was followed by renal cell carcinoma, infection, autosomal dominant polycystic kidney disease, benign prostatic hyperplasia, transitional cell carcinoma, prostatic carcinoma and trauma. Unknown etiology was found in six patients (10%). Diagnostic accuracy of both CT urography and hybrid CT urography was compared and no significant difference was found, however, there was a significant difference in the effective radiation doses between the techniques.

Conclusion: Hybrid CT urography, significantly reduces the radiation exposure to the patient to almost $2/3^{\text{rd}}$ of a

conventional CT urography, while maintaining the same level of diagnostic accuracy.

INTRODUCTION

Haematuria is a common clinical finding encountered in day to day practice and it should not be ignored, because roughly 4% of patients with microscopic haematuria and upto 40% of patients with gross haematuria could be harboring a malignancy.¹ Microscopic haematuria is a more common finding than gross haematuria. The American recommendations define significant microscopic haematuria as three or more RBCs per high power field in a properly collected specimen and in the absence of a benign etiology.² Haematuria can be due to a wide variety of causes viz. urinary tract infection, urolithiasis, malignancies, benign prostatic hyperplasia (BPH), trauma, nephropathies, nephritis etc.

Though we are armed with a battery of imaging techniques to investigate a case of haematuria, CT urography has been found to have the highest degree of sensitivity and specificity.^{3,4} Insufficient data is available in the literature to conclusively indicate whether CT urography has sufficient sensitivity in detecting upper tract urothelial lesions to replace excretory urography (EU) which has higher in-plane spatial resolution. Also, the greater radiation dose of CT compared with EU is another compelling argument in favor of the continued use of radiography which is still considered to be the first line of investigation in cases of haematuria.

Since the initial description of CT urography, many innovative modifications have been employed to optimize protocols. The most commonly used CT urography protocol comprises a three-phase protocol: unenhanced phase, nephrographic phase (following a delay of 90 to 100 seconds after intravenous contrast administration) and pyelographic phase (taken 5 to 15 minutes following

contrast administration). Caoili and colleagues⁵ described a four-phase protocol (two excretory phases at 5 minutes and 7.5 minutes) in an effort to optimize ureteric distension and opacification. However, these techniques render a high radiation dose, are time consuming, and burden the radiologists with an increased number of images. In an attempt to reduce the radiation dose, Chai and colleagues⁶ proposed the use of a split-bolus technique (two doses of intravenous contrast given at an interval of 10-15 minutes) in place of a single intravenous injection to facilitate a two-phase protocol, namely an unenhanced series of images, and a second phase in which nephrographic and pyelographic phases are simultaneously acquired (nephropyelographic phase). Potential disadvantages of the "split bolus" approach have been found, like a small volume of contrast distending and opacifying the collecting systems and ureters, and the potential for streak artefacts from opacified collecting systems during the nephropyelographic phase, which could impact assessment of renal parenchyma. McTavish et al⁷ reported that supplemental infusion of 250 ml of physiological saline immediately after injecting intravenous contrast significantly improved opacification of distal ureters.

Kawashima et al⁸ comprehensively described the techniques of "combined CT and EU CT urography" (also known as hybrid CT urography) and "CT (only CT) urography". They also mentioned several limitations of "CT (only CT) urography" one of which concerns the

higher radiation dose. However, a comparative study of a hybrid CT urography and a conventional CT urography with respect to their diagnostic accuracy and radiation dose has been lacking. The present study is primarily focused on the radiation aspect of two techniques (viz. hybrid CT urography and conventional CT urography) and an attempt has been made to analyse their diagnostic yield in the day to day clinical setting.

Radiation Exposure Calculation: Standard parameters that have been defined for the purpose of measurement of the radiation exposure to the patients are given in figure 1. Effective dose stands out to be the best parameter that can be used to calculate radiation exposure to the patients. CT dose index (CTDI) is a standardized measure of radiation dose output of a CT scanner which allows the user to compare radiation output of different CT scanners. For helical scanners in current use, the parameter CTDI volume ($CTDI_{vol}$) is the most relevant one. The effective dose (ED), expressed in sieverts (Sv), is used for dose distributions that are not homogeneous (which is always the case with CT); it is designed to be proportional to a generic estimate of the overall harm to the patient caused by the radiation exposure and allows for a rough comparison between different CT scenarios.

Dose length product (DLP): CT scans are performed over a length of the patient. The length of the scan is determined in centimetres (1 inch = 2.54 cm, 1 cm is about 3/8 inch), and the DLP is determined by multiplying the $CTDI_{vol}$ value by the scan length, resulting in the units of

Figure 1: Ionising Radiation - Protection Dose Quantities in SI units.

mGy-cm. DLP value is a more direct indicator of the overall radiation risk of the procedure. A generic method was proposed to estimate effective dose from the DLP of an examination⁹, with the DLP being reported on most of the systems.

METHODS

A total of 60 randomly selected patients presenting with either gross or microscopic haematuria (with three or more RBCs per high power field) were recruited into the study. Patients with a history of prior reaction to contrast, allergy, asthma, cardiac diseases, deranged renal function tests, pregnancy and patients with medical causes of haematuria were excluded. Ethical and Research Committee approval and informed consent were taken prior to the study.

The study subjects were randomly divided into two groups. The protocol of the first group (which underwent CT urography) consisted of an unenhanced CT scan of abdomen, CECT scan after 90 seconds of intravenous administration of contrast (nephrographic phase) and excretory phase CT after eight minutes of contrast injection. The second group underwent hybrid (CT plus EU) CT urography. The protocol included an unenhanced CT scan of abdomen, CECT scan after 90 seconds of IV administration of contrast (nephrographic phase) and excretory urography images acquired at eight and fifteen minutes and finally in full bladder phase.

CT studies were performed on Phillips Brilliance™ 40 slice MDCT scanner (Philips N.V., Amsterdam, Netherlands) or six-slice MDCT Somatom Emotion (M/s Siemens AG Healthcare Sector, Erlangen, Germany). Scans were obtained from dome of the diaphragm to pubic symphysis. Parameters for Phillips Brilliance™ CT consisted of section thickness 2.5 mm, spacing between slices 1.25 mm, Collimation 400×0.6 mm, Pitch 0.6 mm, FOV 400 mm in non-contrast and 550 mm in contrast enhanced CT scans, tube current (mA) 337, kVp 120 and CTDI_{vol} 17.50 mSv. For Siemens Somatom Emotion 6, the parameters used were section thickness 3 mm, spacing between slices 1.25 mm, collimation 400 × 0.6 mm, pitch 0.6 mm, FOV 400 mm in non-contrast and 550 mm in contrast enhanced CT scans, tube current (mA) 195, kVp 130 and CTDI_{vol} 17.03 mSv. The above parameters mentioned are the standard institutional parameters used. Computed radiography was done on GE DX-525 CR system (GE Health care Chicago, Illinois, USA), using a moving grid. CTDI_{vol} were automatically estimated by the

inbuilt software (VB10B) in Siemens Somatom Emotion 6 and software version 2.3.0 in Phillips Brilliance™ CT scanner.

Non-ionic iodinated contrast was used in a dose of 300 mg Iodine/kg body weight. Rate of injection was set at 3-5 ml/sec. Multiplanar 2D and 3D reformation (Maximum Intensity Projection) images were generated on workstations from source images obtained during the excretory enhanced phase. The images were reviewed independently by two radiologists for various findings and image quality and a radiological diagnosis was assigned to each case. Final diagnosis was made on the basis of histopathological finding clinical follow up.

Data collected were analysed in view of the demographic profile of the patients, clinical, biochemical findings and radiological features. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of radiological diagnosis in respect to final diagnosis were calculated. Area under ROC curves of both groups were compared to find out any significant difference in diagnostic accuracy in both the groups.

RESULTS

In the present study, age of the subjects was in the range of 13 to 78 years with maximum number of patients belonging to the 4th decade (28%). Mean age of the study sample was 44.13 years. There was a definite male predominance, where out of 60 subjects, 44 patients (73.33%) were male and 16 (26.67%) were female. Urinary infection (>5 pus cells/hpf) was found in 12 (20%) out of the 60 subjects. All of the subjects with urinary infection showed presence of *E. coli* in their urine samples.

Radiological diagnosis were reached after thoroughly examining the CT and EU (in cases of hybrid CT) images of the study subjects and on the basis of that a radiologically identifiable disease causing haematuria was assigned to 52 study subjects, while eight subjects were found to be normal. Bladder neoplasms and urolithiasis constituted the most common etiologies in the study population each accounting for 17 cases (28.33%). Together they accounted 56.66% cases. This was followed by renal cell carcinoma (RCC), infection, autosomal dominant polycystic kidney disease (ADPKD), benign prostatic hyperplasia (BPH), transitional cell carcinoma (TCC), prostatic carcinoma, and trauma in the order of decreasing incidence. No cause was found in 6 patients (10%). The frequencies of occurrence of the various causes for haematuria observed in both

2(a)

2 (b)

Axial nephrographic CT image shows a large heterogeneously enhancing mass with necrotic areas arising from the left kidney.

2(c)

2(d)

Coronal MIP images from 8 mins scan showing subtle filling defect in the left renal pelvis. Both the ureters were normal in caliber and outline.

Figure 2: Left sided renal cell carcinoma (RCC).

(A 70 yrs old female patient presenting with haematuria, pain and swelling in left flank. Underwent CT Urography with 6 slice CT scanner, kVp 130, mAs 150. Diagnosed as RCC radiologically. Confirmed on biopsy. Effective radiation dose: 27.33 mSv).

Table 1: Causes of haematuria in study subjects

Causes	CT group	HCT group	Total	p value
ADPKD	3 (10.00%)	1 (3.33%)	4 (6.67%)	0.291
Bladder neoplasm	7 (23.33%)	10 (33.33%)	17 (28.33%)	
BPH	1 (3.33%)	1 (3.33%)	2 (3.33%)	
Infection	1(3.33%)	4 (13.33%)	5(8.33%)	
Prostatic carcinoma	0 (0.00%)	1 (3.33%)	1 (1.67%)	
Renal cell carcinoma	3 (10.00%)	2 (6.67%)	5 (8.33%)	
TCC renal pelvis	2 (6.67%)	0 (0.00%)	2 (3.33%)	
Trauma	1 (3.33%)	0 (0.00%)	1 (1.67%)	
Cause not found	3 (10.00%)	3 (10.00%)	6 (10.00%)	
Urolithiasis	9 (30.00%)	8 (26.67%)	17 (28.33%)	
Total	30	30	60

3(a)

Axial nephrographic CT image shows a heterogeneously enhancing mass arising from the right renal parenchyma with central necrotic areas.

3(b)

Coronal reformatted image in the same patient.

3(c)

Excretory Urography image at 8 mins showing opacification of the right renal mass with compression and distortion of the calyces.

3(d)

EU image at 15 mins showing more intense opacification of the mass.

Figure 3: Right sided renal cell carcinoma.

(A 50 yrs old male patient presenting with haematuria, pain and swelling in right flank, underwent Hybrid CT with 6 slice CT, kVp 130, mAs 150. Diagnosed as RCC radiologically. Confirmed on biopsy. Effective radiation dose: 25.87 mSv).

Table 2: Radiological diagnosis in study subjects

		Final Diagnosis		Total	p value	kappa
Groups		Disease	Non Disease			
CT	Disease	27 (90.00%)	0 (0.00%)	27 (90.00%)	0.0	1.000
	Non Disease	0 (0.00%)	3 (10.00%)	3 (10.00%)		
HCT	Disease	25 (83.33%)	0 (0.00%)	25 (83.33%)	0.0	0.714**
	Non Disease	2 (6.67%)	3 (10.00%)	5 (16.67%)		

Strength of kappa values; *very good ; **good

4(a)

4(b)

Axial nephrographic CT image shows multifocal bladder masses showing heterogeneous enhancement. Few foci of calcifications were also present. No extension noted outside bladder wall.

4(c)

4(d)

EU images at 8 and 15 mins showing well distended contrast filled bladder with filling defects and irregularities in the outline corresponding to the bladder masses. Bilateral ureters were normal in calibre.

Figure 4: Ca urinary bladder.

(A 60 yrs old female patient presenting painless haematuria, underwent Hybrid CT with 40 slice CT, kVp 120, mAs 250. Diagnosed as Ca urinary bladder radiologically. Confirmed on cystoscopic biopsy. Effective radiation dose: 22.48 mSv).

Table 3: Sensitivity, specificity and predictive values for conventional CT Urography and Hybrid CT Urography

Group	Sensitivity	Specificity	PPV	NPV
CT	100.00%	100.00%	100.00%	100.00%
HCT	92.59%	100.00%	100.00%	60.00%

PPV- Positive predictive value; NPV- Negative predictive value

5(a)

5(b)

Axial scan image at nephrographic phase showing a heterogeneously enhancing mass (red arrow) arising from the bladder base. Mild thickening (blue arrow) of the bladder wall was also noted.

5(c)

Coronal reformatted image in the excretory phase showing normal collecting systems.

5(d)

Delayed scan in the full bladder shows a thin Pedicle (green arrow) connecting the mass with the bladder base. Cystoscopic biopsy revealed inverted papilloma.

Figure 5: Inverted papilloma bladder.

(A 55 yrs old male patient presenting with 2 episodes of painless haematuria, underwent CT Urography with 6 slice CT, 130 kVp, 150 mAs. Diagnosed as Ca bladder radiologically. Biopsy revealed inverted papilloma. Effective radiation dose: 42.96 mSv).

6(a)

Axial noncontrast CT image shows bilateral renal and right proximal ureteric calculus. Right PCS and ureter are dilated.

6(b)

Axial noncontrast image showing vesical calculi.

6(c)

6(d)

Axial CT images at 8 mins and 30 mins showing normally functioning bilateral kidneys with delayed excretion in the right kidney.

Figure 6: Bilateral renal with vesical calculi.

(A 55 yrs old male patient presenting with haematuria, pain abdomen and poor stream, underwent CT Urography with 40 slice CT, kVp 120, mAs 250). Diagnosed as bilateral renal calculi with vesical calculi radiologically. Effective radiation dose: 30.45 mSv).

Table 4: Comparison of the area under ROC curve

Groups	AUC	Standard Error	95% Confidence interval	Difference	Significance level
CT	1	0	0.884297 to 1.000000	0.037	0.1495
HCT	0.962963	0.0257	0.822158 to 0.998714		

AUC: Area under the ROC curve

7(a)

Coronal noncontrast CT image shows right renal calculus (red arrow). Right proximal ureter is dilated. left kidney is atrophic.

7(b)

Axial image at nephrographic phase shows dilated proximal right ureter with thickened walls (green arrow) suggesting ureteritis.

7(c)

7(d)

AP and oblique EU images at 15mins and 30 mins respectively showing the right hydroureteronephrosis with narrowing in the middle third of the right ureter likely to be a stricture. Left kidney is small with dilated pelvic calyceal system.

Figure 7: Right renal calculus.

(A 35 yrs old female patient presenting with haematuria and bilateral flank, underwent Hybrid CT Urography with 40 Slice CT, 120 kVp, 250 mAs. Diagnosed as right renal calculus radiologically. Effective radiation dose: 42.1 mSv).

Table 5: Effective radiation doses received by the study subjects

Group		Effective Radiation Dose (mSv)
CT (n=30)	Mean $\pm$ SD	38.47 $\pm$ 7.02
	Median	39.48
	Min-Max	28.29-57.5
	Inter quartile Range	32.440- 43.280
HCT (n=30)	Mean $\pm$ SD	23.56 $\pm$ 3.2
	Median	23.8
	Min-Max	16.02-28.87
	Inter quartile Range	21.460 - 25.870
p value		0

the groups were also compared and there was no significant difference (Table 1). Some of the radiologically interesting cases have been shown in the figures 2-7.

The radiological diagnosis in both the groups was individually assessed against the final diagnosis to find out the kappa values of both the studies (Table 2). In the present study, successful diagnosis on the positive as well as negative cases on CT urography was achieved. However, on hybrid CT urography, two false negative cases were reported. In both the cases, urinary infection was diagnosed on urine examination though imaging wise there were no signs of any urinary infection. Sensitivity, specificity, predictive values were calculated for both the study groups (Table 3).

The area under ROC curve for each group was compared to find out whether there was any significant difference between the two modalities (Table 4). The effective radiation doses received by the subjects during the course of the study were assessed and compared among the two groups. A significant difference was observed between the effective radiation doses in both modalities (Table 5).

DISCUSSION

In an era of ever-increasing CT studies in the medical field, CT urography serves as a highly sophisticated tool in diagnosis of various urological diseases. But it entails an exposure of the patient to a high degree of radiation. The present study was an endeavour to evolve a CT technique with reduced radiation exposure without affecting its diagnostic accuracy. Keng Lim Ng et al¹⁰ reported that the main cause of haematuria in their study

was BPH (22.6%) followed by "no cause found" (22.3%). This was followed by urolithiasis, urinary tract infection, non specific cystitis, bladder tumours, and other genitourinary tumours. Edwards and colleagues¹¹ had reported that in 79.9 % of the cases in their study, no cause was detected. The most common causes in their study were urinary bladder neoplasms (10%), urolithiasis (8.4%), RCC (1.5%), and TCC (0.32%). Thus, though causes of haematuria in the present study did not depict the same pattern of distribution as that of Keng Lim Ng et al,¹⁰ it was in agreement with that of Edwards and colleagues¹¹ except only for the fact that a significantly larger proportion of the study population had no underlying cause.

In the present study, urological malignancy rates were 41.63% and among the positive cases 46.25 % cases were due to urological malignancies. Edwards et al¹¹ reported an incidence of 59.23% for urological malignancies amongst the positive cases. A study reported the incidence of urological malignancies as 16%¹² while an incidence of 3.8% for the same has also been reported.¹⁰ Thus, incidence of urological malignancy rates were highly variable among different studies.

However, most common finding in all the studies was transitional cell carcinoma of urinary bladder followed by renal cell carcinoma. Also in all of the above studies, incidence of malignancy was higher in the older age groups. None of the upper tract malignancies were detected in patients less than 30 years, with no upper tract transitional cell carcinoma detected in those patients less than 50 years in the study. Studies have reported no case of malignancy in those < 50 years old who presented with

microscopic haematuria when compared to 7.5% in those > 50 years of age al.^{11,12} Bhuiyan et al¹³ reported no incidence of malignancy in patients less than 40 years of age. However, in this study, one case of urological malignancy (Bladder Carcinoma) below the age of 30 was reported. Percentages of urological malignancy as etiology in 41-50, 51-60, and 61-70 years of age groups were 43%, 71%, and 70% respectively.

In the present study, the diagnostic accuracy of both CT and hybrid CT urography was statistically compared and p value obtained was 0.1495 depicting no statistical difference in the diagnostic accuracy of the two modalities. Nawfel et al¹⁴ reported effective radiation dose of 15.6 mSv for a three phase CT urography. However, in their study only a limited field size in the renal area for the nephrographic phase was scanned. In a study which estimated effective doses from a four-phase CT urography protocol ranged from 25 to 30 mSv.⁵ Kawashima et al⁸ reported that a single abdominopelvic CT scan delivered an effective radiation dose of 11 mSv. Vrtiska et al¹⁵ reported that the effective radiation dose from triphasic CT urography ranges from 20.1 mSv to 66.3 mSv. No data were available on the effective radiation doses from Hybrid CT urography in any of the previous literature. However, in the study by Vrtiska et al¹⁵, the lowest-dose CT urography protocols used only two CT acquisitions: unenhanced and combined nephrographic and excretory phase along with 3 KUB radiographs, similar to that used in the hybrid CT protocol in the present study. Its effective dose was calculated to be 27.2 mSv. The hybrid CT urography protocol in the present study had mean value of 23.56 mSv. These values are almost comparable with the study of Vrtiska et al¹⁵.

CONCLUSION

Hybrid CT urography which combines CT with excretory urography significantly reduces the radiation exposure to the patient to almost 2/3rd of a conventional CT urography, while maintaining the same level of diagnostic accuracy.

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