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FULL PAPER

Detection of bladder cancer: comparison of low-dose scans with AIDR 3D and routine-dose scans with FBP on the excretory phase in CT urography

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Objective: To prospectively compare the detection of bladder cancer between low-dose scans with adaptive iterative dose reduction three dimensional projection (AIDR 3D) and routine-dose scans with filtered back projection (FBP) on the excretory phase (EP) in CT urography.

Methods: 42 patients were included. Routine- and low-dose EP were performed in each patient. Routine-dose images were reconstructed with FBP, and low-dose images were reconstructed with AIDR 3D. Two radiologists scored confidence levels for the presence or absence of bladder cancer using a 5-point scale. The CT dose index of each EP was measured, and the dose reduction was calculated.

Results: Sensitivity, specificity and accuracy were 86.4%, 95.0% and 90.5% on routine-dose scans and were 86.4%, 90.0% and 88.1% on low-dose scans, respectively. There was no significant difference (p : not significant, 1.00 and 1.00, respectively). The average CT dose index was 8.07 and 2.63 mGy on routine- and low-dose scans, and the ratio of dose reduction was 67.6%.

Conclusion: The detection of bladder cancer on low-dose scans with AIDR 3D is almost equal to that on routine-dose scans with FBP on the EP, with nearly 70% dose reduction.

Advances in knowledge: Using AIDR 3D, the radiation dose may be reduced on the EP in CT urography for the detection of bladder cancer.

INTRODUCTION

CT urography (CTU) is not the primary methodology for investigation of macroscopic haematuria; moreover, cystoscopy remains the gold standard for making the diagnosis. However, CTU is an excellent technique for the evaluation of calculi and masses in the urinary system performed using the helical scan.^{1–3} The contrast resolution of CTU is superior to that of conventional excretory urography and has become one of the robust imaging tools for the evaluation of the urinary system.² However, CTU results in higher radiation exposure than conventional excretory urography.^{1–4} Therefore, the reduction of radiation dose on CTU is an important problem to be resolved.

Recently, a new method has been developed based on an iterative reconstruction algorithm, which enables the reduction of radiation dose without degenerating image quality.^{5–7} Adaptive iterative dose reduction three dimensional projection (AIDR 3D) is one of the iterative reconstruction algorithms that reduce image noises and

streak artefacts in the reconstruction domain approved by the Toshiba Medical Systems Corporation. In a previous report,⁸ low-dose CTU using AIDR 3D offered diagnostic acceptability comparable with that of routine-dose CTU with filtered back projection (FBP) with about 70% dose reduction on the excretory phase (EP). On the other hand, there has been no report evaluating the detection of bladder cancer in CTU using AIDR 3D. If we can detect bladder cancer on low-dose scan with AIDR 3D, the radiation dose can be reduced.

The purpose of this study was to evaluate the detection of tumours of the urinary bladder with low-dose scans with AIDR 3D comparing with that of routine-dose scans with FBP on the EP in CTU.

METHODS AND MATERIALS

In this study, informed consent was obtained from all patients before they entered the study. The institutional review board of Osaka Medical College approved the study.

Table 1. Sensitivity, specificity and accuracy for the detection of bladder cancer on routine- and low-dose scans

Dose	Sensitivity	Specificity	Accuracy
Routine dose	86.4% (19/22)	95.0% (19/20)	92.9% (38/42)
Low dose	86.4% (19/22)	90.0% (18/20)	88.1% (37/42)
<i>p</i> -value	NS	1.00	1.00

NS, not significant.

The numbers in parentheses were used to calculate percentages.

Patients

Between August 2012 and April 2013, we enrolled 59 consecutive patients who met 4 inclusion criteria: the presence of macroscopic haematuria or bladder cancer; age over 40 years; the absence of contraindications to the use of iodinated contrast material; and a serum glomerular filtration rate of over $45 \text{ ml min}^{-1} 1.73 \text{ m}^2$. Exclusion criteria included patients treated for bladder cancer after CTU and before pathological diagnosis ($n = 10$) and clinical follow-up of less than 1 year with patients of no pathological diagnosis ($n = 7$). Therefore, our final analysis included 42 patients (32 males, 10 females; mean age, 68.6 years; range, 46–89 years; mean weight, 59.2 kg; range, 45–76 kg).

CT urography technique

We obtained the unenhanced, urothelial and EP scans for all patients on a 320-row detector CT scanner (Aquilion ONE™; Toshiba Medical Systems Corporation, Tokyo, Japan) at the following settings for all scans: rotation time, 0.5 s; detector collimation, $64 \times 0.5 \text{ mm}$; helical pitch, 53; tube voltage, 120 kV; and variable tube current determined with auto exposure control (AEC). The current tube was adjusted to 10–550 mA with AEC. The unenhanced and urothelial phases were acquired from the diaphragm to the symphysis pubis, and the EP was acquired from the top of the kidney to the bottom of the urinary bladder. Patients were instructed to hold their breath with tidal inspiration during scanning. 540 mgI kg^{-1} of iohexol (Omnipaque™; Daiichi Sankyo, Tokyo, Japan) was administered into the right antecubital vein using a power injector (Dual Shot GX; Nemoto-Kyorindo, Tokyo, Japan). The contrast injection time was 50 s (contrast injection rate: $1.6\text{--}3.2 \text{ ml s}^{-1}$). The urothelial phase acquisition was started 100 s and EP acquisition 15 min after the administration of the contrast material.

On the EP, we acquired two scans, respectively, and the patients were asked to roll twice on the CT table before the first scan of the EP to obtain uniform contrast density in the bladder on the EPs. In 21 cases, we acquired low-dose EP with AIDR 3D immediately after routine-dose EP; in the other 21 cases, we acquired routine-dose EP immediately after low-dose EP with AIDR 3D. The mean interval between the acquisitions at the two scans was 18 s (range, 15–20 s). To determine the radiation dose, we used standard deviation (SD). SD is the standard deviation of the CT values. After setting the SD, the tube current was determined automatically with AEC. We performed EP acquisitions with $\text{SD} = 20$. On low-dose scans, we chose a setting of 75% reduction ratio of the radiation dose under AIDR 3D. On the EP, the images were reconstructed with FBP on routine-dose scans and with AIDR 3D on low-dose scans. The slice thickness and reconstruction intervals were 1.0 mm for the axial images. From the axial images, coronal images were obtained with a slice thickness and reconstruction interval of 3.0 mm.

Data analysis

Using the picture archiving and communication system, we reviewed all images on a liquid crystal display monitor with a spatial resolution of 1536×2048 pixels.

Because small tumours may be obscured by dense contrast material on images with soft-tissue window settings, wide window settings were used in the reading. Two radiologists with 10 and 6 years' of experience in abdominal CT, who were blinded to clinical information, performed independent visual evaluations. The two radiologists evaluated the axial and coronal images on the EP. The readers recorded their assessments independently and then by consensus. We evaluated low-dose

Figure 1. A 50-year-old male who underwent CT urography for the staging of bladder cancer. The score was 5 on both routine- and low-dose scans. Urothelial carcinoma was confirmed by histological analysis. (a) Routine-dose image; (b) low-dose image.

Figure 2. A 75-year-old male who underwent CT urography for suspicion of recurrence of bladder cancer. The score was 5 on both routine- and low-dose scans, and all tumours could be detected on the low-dose image as well as on the routine-dose image. Urothelial carcinoma was confirmed by histological analysis. (a) Routine-dose image; (b) low-dose image.

scans before routine-dose scans in all patients. The interval between the two sessions was 1 month.

Lesions considered suspicious for bladder cancer on the EPs included one or more masses of any size, or focal wall thickening. The readers scored for the presence or absence of bladder cancer and assigned the following confidence level to their observations in each patient: 1, definitely absent; 2, probably absent; 3, equal; 4, probably present; and 5, definitely present. If we considered that tumours may be present but the contrast material was not filled in the urinary bladder at all owing to hydronephrosis, we categorized as possibly present (Score 3). Lesions scored as 4 and 5 were considered positive results, and lesions with scores of 1–3 were considered negative.

The reference standard for comparison was pathological analysis. A CTU was considered true positive only if the CTU abnormality correlated with the pathological finding. A false-positive (FP) CTU occurred if we evaluated as positive on CTU, but bladder cancer was not confirmed on pathology or there was no evidence of bladder cancer on cystoscopy or on urine cytology at least 1 year of follow-up. A true-negative CTU occurred if we evaluated as negative on CTU, and bladder cancer was not confirmed on pathology or there was no evidence of bladder cancer on cystoscopy or on urine cytology at least 1 year of follow-up. A false-negative (FN) CTU occurred if we evaluated as negative on CTU, but urothelial carcinomas were confirmed on pathology.

In patients with bladder cancer, two radiologists recorded the number of tumours in each patient. If the number of tumours in the urinary bladder was more than 4, we recorded this as >4. Discrepancies were resolved by consensus. In addition, one radiologist measured the maximum diameter of the largest tumour on the axial images in each patient except for patients of FN results.

Radiation dose

For the estimation of radiation dose on the EP, CT dose index ($CTDI_{vol}$), dose-length product (DLP) and effective dose on routine- and low-dose scans were recorded from the dose page from the picture archiving and communication system. The

average dose reduction from routine-dose scans to low-dose scans was calculated from $CTDI_{vol}$.

Statistical analysis

The sensitivity, specificity and accuracy of routine- and low-dose scans for the detection of bladder cancer were determined by comparing the results of consensus readings with the final diagnosis, and differences were evaluated by using Fisher's exact test. Differences between routine- and low-dose EPs for detection of bladder cancer were also analysed by the area under the receiver operating characteristic curves (A_z) for the score of the two scans. For statistical analyses, a p -value of <0.05 was considered statistically significant.

Figure 3. Receiver operating characteristic curves of routine- and low-dose scans. The area under the receiver operating characteristic curves for routine-dose (continuous line) and low-dose (dashed line) scans in the detection of bladder cancer was 0.915 and 0.901, respectively.

Figure 4. An 83-year-old female who underwent CT urography with the symptom of haematuria. (a) We considered as post-inflammation state on the routine-dose image (scored 2). (b) We considered as bladder cancer on the low-dose image (scored 4).

Interobserver agreement for 5-point scores related to each patient was determined using kappa statistics. Kappa values of <0.20 indicated poor agreement, values of $0.21\text{--}0.40$ indicated slight agreement, values of $0.41\text{--}0.60$ indicated moderate agreement, values of $0.61\text{--}0.80$ indicated good agreement and values >0.81 indicated excellent agreement. Statistical analyses were performed with SPSS® v. 17.0 (IBM Corp., New York, NY; formerly SPSS® Inc., Chicago, IL).

RESULTS

Detection of bladder cancer

Of 42 patients, 22 patients had pathologically proven bladder cancer. In the remaining 20 patients, inflammation was pathologically confirmed in 1 patient; there was no evidence of bladder cancer on cystoscopy and on urine cytology in 7 patients; and there was no evidence of bladder cancer on urine cytology in 12 patients. Sensitivity, specificity and accuracy for the detection of bladder cancer on low-dose scans [86.4% (19/22), 95.0% (19/20) and 90.5% (38/42), respectively] were not significantly lower than the corresponding values on routine-dose scans [86.4% (19/22), 90.0% (18/20) and 88.1% (37/42), respectively] (p ; not significant, 1.00 and 1.00, respectively) (Table 1, Figures 1 and 2). The Az values for detection of bladder cancer on low-dose scans (0.901) was not significantly different from those on routine-dose scans (0.915) ($p = 0.263$, Figure 3). In one patient of FP results on both routine- and low-dose scans, haematoma was confirmed on cystoscopy. In one patient of FP with result only on low-dose scan, we considered this as post-inflammation state on routine-dose scan (scored 2) instead of bladder cancer (scored 4) on low-dose scan (Figure 4) on the EP. There was negative finding on urine cytology and at 1.5 years of follow-up. In three patients of FN results on both routine- and low-dose scans, there was carcinoma *in situ* (CIS) in two patients, which appeared as only redness on cystoscopy; the contrast material did not flow into the urinary bladder owing to hydronephrosis in one patient. The interobserver agreement for scores was moderate for both routine- ($\kappa = 0.505$) and low-dose scans ($\kappa = 0.571$).

In patients with bladder cancer, the number of tumours was 0, 1, 2, 3, 4 and >4 in 3, 12, 1, 1, 1 and 4 patients, respectively, on both routine- and low-dose scans, and there was no difference

between routine- and low-dose scans. In patients with positive findings in CTU, the mean maximum diameter of the largest tumour was 32.8 mm (range, 5.7–101.3 mm).

Radiation dose

The results are shown in Table 2. The average CTDI_{vol}, DLP and effective dose for scans obtained at routine-dose scans with FBP were 8.07 mGy (range, 4.6–17.1 mGy), 320.7 mGy cm (range, 171.0–689.5 mGy cm) and 4.81 mSv (range, 2.57–10.34 mSv), respectively. For scans obtained at low-dose EP with AIDR 3D, the average CTDI_{vol}, DLP and effective dose were 2.63 mGy (range, 1.2–5.2 mGy), 103.0 mGy cm (range, 45.9–209.8 mGy cm) and 1.55 mSv (range, 0.69–3.15 mSv), respectively. The average dose reduction was 67.6% for CTDI_{vol}.

DISCUSSION

Bladder cancer is one of the common diseases of older age and is more prevalent among males than females. Commonly, cystoscopy and transurethral resection of bladder tumour are chosen as the initial examination of bladder cancer. CT is usually performed for staging of bladder cancer, and we also evaluate tumours in urinary systems in CT. Metser et al⁹ mentioned that detection of urothelial carcinomas was higher on the urothelial phase than on the EP, and that the EP is not necessary for the evaluation of urinary systems. In addition, we can usually not distinguish carcinomas from haematomas with only the EP. However, according to prior reports,^{10–12} CTU may serve as the

Table 2. The average radiation dose on routine- and low-dose scans

Dose	CTDI _{vol} (mGy)	DLP (mGy cm)	Effective dose (mSv)
Routine dose	8.07	320.7	4.81
Low dose	2.63	103.0	1.55
Dose reduction (%)	67.6		

CTDI_{vol}, CT dose index; DLP, dose-length product.
Dose reduction was calculated with CTDI_{vol}.

primary imaging modality. In addition, Turney et al¹⁰ and Sadow et al¹¹ mentioned that the use of CTU will obviate the need for flexible cystoscopy in patients with a negative CTU for those with macroscopic haematuria. Thus, detection of tumours in the urinary bladder on the EP would be important as well as that in the urothelial phase in CTU.

In this study, there was no significant difference between routine- and low-dose scans for sensitivity, specificity and accuracy for detection of bladder cancer. In addition, there was no significant difference for Az values for detection of bladder cancer between routine- and low-dose scans. On the basis of these results, low-dose scans with AIDR 3D on the EP would be available for the examination of bladder cancer. In one patient of EP results only on low-dose scan, the lesion on routine-dose scan was funicular, in contrast to the lesion on low-dose scan which was mass-like rather than funicular. According to a previous report,⁸ images on low-dose scans with AIDR 3D tend to be blurred compared with that on routine-dose scans with FBP, and this might be the factor. In two patients with CIS, there was only redness on cystoscopy, and there were no obvious irregular surfaces. The EP may not be useful for the detection of CIS. The number of tumours detected on low-dose scans with AIDR 3D was equal to that on routine-dose scans with FBP in all patients with bladder cancer in our study. If we recorded the actual number of tumours in patients with tumours of ≥ 4 , the number of tumours may be different between routine- and low-dose scans. However, we suppose that we may detect the same number of tumours on routine- and low-dose scans when the number of tumours is ≤ 5 .

In a previous report, the average CTDI_{vol} on low-dose scans with AIDR 3D on the EP was 2.7 mGy.⁸ In our study, the average CTDI_{vol} on low-dose scans was 2.61 mGy, which is similar to the previous report.⁸ In a prior article, the radiation dose of excretory urography was about 1.5–3.5 mSv.¹³ In our study, the average effective dose was 1.55 mSv on low-dose scans; thus, radiation dose could be reduced as low as that of excretory urography. Therefore, low-dose scan with AIDR 3D in our study may be useful for CTU instead of excretory urography. Patients diagnosed with bladder cancer usually undergo a staging abdominal CT scan, and the radiation dose is approximately 10–15 mSv for unenhanced and urothelial phases. In these patients, further elevation of radiation dose may result in the risk of cancer. Thus, low-dose scan on the EP would be useful to perform minimal increasing of the total radiation dose.

There are some limitations in our study. First, the number of patients in our study was small. Therefore, studies with larger samples are needed. Second, we did not evaluate tumours dividing into a few groups by tumour size. There was no patient with a tumour of size < 5 mm; thus, we could not make a group of small size tumours. Third, because the number of tumours was not counted on cystoscopy, it was not verified whether the number of tumours on the EP was correct. It is controversial if the number of tumours is equal between that on low-dose scans on the EP and on cystoscopy. In addition, we did not evaluate the 5-point score for per-lesion analysis; thus, it is controversial if all tumours on low-dose scans were detected as clear as those on routine-dose scans. However, because the number of tumours detected on low-dose scans was almost equal to that on routine-dose scan in our study, the results would be feasible. Fourth, 12 patients did not undergo examinations except for CTU and urine cytology. Urine cytology is limited in sensitivity for low-grade non-muscle invasive bladder cancer. This may have subsequent bias on the results, relating to the accuracy of CTU in this study. Finally, we did not evaluate detection of tumours in the upper urinary tract. Because patients with urothelial carcinomas in the upper urinary tracts are quite small, we could not enrol enough number of patients for one study. In the future, evaluation of the number of patients with urothelial carcinomas in the upper urinary tract will be necessary.

In conclusion, detection of bladder cancer on low-dose scans with AIDR 3D is not inferior to that on routine-dose scans with FBP on the EP in CTU. The dose reduction is nearly 70% using AIDR 3D.

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CONFLICTS OF INTEREST

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