

Multidetector Computed Tomography Urography Using Single and Triple Bolus Contrast Media Injections in Upper Urinary Tract Diseases

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Abstract

Background: Upper urinary tract diseases often present with flank pain and hematuria which is commonly investigated using plain radiography, IVU, ultrasound, CT, and MR urography. MDCT is the preferred imaging modality due to its high sensitivity, but it has limitations like radiation exposure and protocol variability. MR urography offers a radiation-free alternative but is limited by availability, difficulty in detecting stones, and artifacts. Efforts are ongoing to optimize MDCT protocols to reduce radiation and improve diagnostic accuracy. **Material and Methods:** A prospective randomized comparative study of MDCT Urography in upper urinary tract diseases using single and triple bolus contrast media injections was done. Ninety-nine patients were screened over 20 months. Computerized random number tables were used to allocate patients to each protocol. Qualitative and quantitative (Hounsfield units) comparisons were performed for the upper urinary tract, renal parenchymal enhancement, and renal vessels. **Results:** Seventy-three patients' data were analyzed. Triple bolus reduces the radiation dose ~ 50% compared to the conventional single-bolus protocol. A single bolus is better ($p < 0.001$) than a triple bolus for intrarenal collecting system and ureteric opacification. Triple bolus is best for renal vein opacification ($p < 0.001$). **Conclusion:** Triple bolus is better for renal vein opacification. single bolus is better for opacifying the collecting system. No statistically significant difference in renal parenchymal enhancement was noted between the protocols.

Keywords: Split bolus, Triple bolus, Multidetector Computed tomography, Urography.

Received: 02 January 2026

Revised: 25 January 2026

Accepted: 13 February 2026

Published: 25 February 2026

INTRODUCTION

Flank pain and hematuria are common presentations of upper urinary tract diseases. The primary imaging modalities for evaluation include plain radiography, intravenous urography, ultrasound, and Computed tomography urography (CTU).^[1] Among these, multidetector Computed Tomography (MDCT) is the preferred investigation for urinary tract pathologies. However, MDCT urography has limitations, including exposure to ionizing radiation and a lack of standardized protocols. Typically, multiphasic computed tomography (CT) protocols are used for suspected renal or collecting system lesions, leading to high cumulative radiation doses. While single and split (double) bolus protocols are widely employed, the triple bolus technique is less commonly used. Several studies have demonstrated that the split bolus technique significantly reduces radiation exposure, but the potential benefits of the triple bolus approach remain unclear. Magnetic resonance urography (MRU) offers an alternative but has limitations, including limited availability, difficulty detecting calcifications and calculi, susceptibility to artifacts, and incompatibility with metallic implants.^[2] Ongoing efforts focus on minimizing radiation exposure while optimizing MDCT urography protocols. Given the lack of a standardized protocol, our study aims to compare single-bolus and triple-bolus CTU techniques to determine an optimal approach that reduces

radiation exposure and improves diagnostic accuracy.^[3]

MATERIALS AND METHODS

The study was approved by the Institutional Ethics Committee [AIIMS/IEC/18/168] and conducted in accordance with the principles of the Declaration of Helsinki. The patients were scanned on a 128 Slice Dual Source (Siemens Somatom Definition Flash) with a pressure injector 'Imaxeon Salient 2014A Version 1.5.6'.

Study population: Patients referred to the Department of Radiology at AIIMS, Rishikesh, for MDCT urography were assessed according to the inclusion criteria over 20 months from January 2018- August 2019 [Figure 1]. Randomization was performed using computer-generated random numbers (1–100), with numbers 1–50 assigned to the single-bolus protocol and 51–100 to the triple-bolus protocol. The numbers were written on

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DOI:

10.21276/amit.2026.v13.i1.379

How to cite this article: Kumar S, Chauhan U, Mittal A, Saxena S, Puri S. Multidetector Computed Tomography Urography Using Single and Triple Bolus Contrast Media Injections in Upper Urinary Tract Diseases. Acta Med Int. 2026;13(1):501-507.

concealed slips by a research assistant not involved in patient care and placed in a jar. Sequential allocation was performed by the radiographer at the time of scanning. Radiologists interpreting the images were blinded to the protocol assignment. 17 patients were excluded from the study because they did not meet the inclusion criteria. As this was a pilot and feasibility study, no formal a priori power calculation was performed, and a pragmatic minimum of 30 patients per arm was targeted. We acknowledge this as a limitation; the study was not prospectively powered to detect a specific effect size with defined alpha and beta error rates.

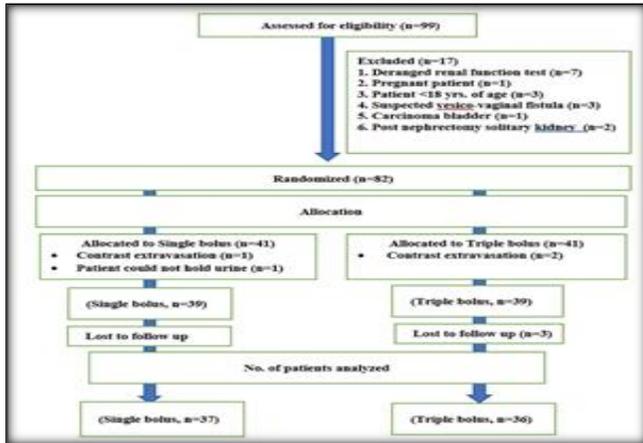


Figure 1: Enrolment of Patients

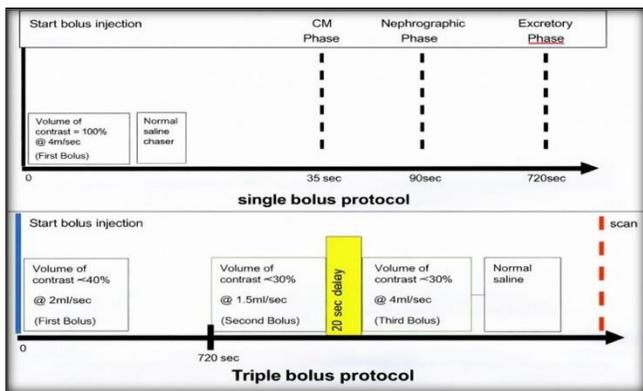


Figure 2: Protocol Design

Study Inclusion Criteria: All patients aged ≥ 18 years presenting to the Department of Radiology for MDCT urography were eligible.

Study Exclusion Criteria: Patients who had contraindication for furosemide and contrast injections, suspected or diagnosed urinary bladder tumour, solitary kidney, lactating or pregnant patients, congestive heart

failure, and chronic renal failure.

Patient Preparation: Nil per oral for at least 6 hours before the procedure and well hydrated before the procedure. Each patient was asked to take 800 millilitres (ml) of water orally about 60 minutes before the scan and to have their bladder half full during the scan, so they could be comfortable during the examination. Contrast Media Dose: 2ml/Kilogram Non-Ionic Water Soluble Iohexol Injection 350 mg/ml (Upper limit-130millitre) (ml). Intravenous 10 mg furosemide was given slowly over 1 minute, 2-3 minutes before the contrast media injection.^[4]

Single bolus and triple bolus protocols are shown in [Figure 2]. Non-contrast computed tomography (NCCT) was acquired in both protocols. Contrast was followed by a 30ml normal saline chaser at 3ml/sec in both single- and triple-bolus protocols. Then an immediate scan was acquired within 5-10 seconds.^[5]

Parameters of MDCT Urography Image Acquisition

Field of view for protocols: All patients were scanned from the diaphragm to the pubic symphysis. Care dose 4D was kept active in all acquisitions. Parameters used are as follows Tube voltage for NCCT=100kilovoltage (kv), contrast enhanced CT (CECT)=120kv, tube current milliampere seconds (mAS) for NCCT=150, CECT =110, Pitch NCCT=0.6, CECT =0.8, Slice thickness NCCT/CECT= 5mm, Reconstructed slice thickness NCCT/CECT=1mm, Rotation time NCCT/CECT=0.5s, Collimation NCCT=1.2mm, CECT =0.6mm, and filter NCCT/CECT =I30medium smooth. Dual energy was not used in our study.

Post-processing and image analysis: Coronal and sagittal reformations of the images were performed using maximal intensity projection (MIP), multiplanar reformation (MPR), and volume rendering technique (VRT). The axial and reformatted coronal and sagittal images will be viewed on a workstation for evaluation.^[5]

Image optimization scoring system:

HU measurements were obtained from multiple segments per kidney (calyces, pelvis, ureters). These were analyzed as independent observations. We acknowledge that calyces and ureters within the same kidney and patient are correlated, which violates the assumption of independence for t-tests and ANOVA. Upper urinary tract opacification was evaluated qualitatively and quantitatively.^[5] Qualitative Score 0 - Unopacified; Score 1 - <50%; Score 2 - 51-75% and 76-100% of the ureter opacified^[6]. Quantitative analysis was done on axial images by measuring Opacification in HU (Hounsfield units) with the largest possible manual ROI (Region of interest). For each patient, HU values were averaged for the intrarenal collecting system, renal parenchyma (average of upper, middle, and lower poles), renal artery, and renal vein. [Table 1]

Table 1: shows the different phase of data recording in single and triple bolus protocol

Parameters	Single bolus	Triple bolus
Renal calyces, renal pelvis and ureters	Excretory phase	Post contrast single acquisition
Renal parenchyma	Nephrographic phase	
Renal artery	Corticomedullary phase	
Renal vein	Nephrographic phase	

Renal parenchyma and renal vessels were evaluated qualitatively and quantitatively.^[5] Renal vein and renal artery

were evaluated within first 2cm of the origin from the Aorta with a ROI of 2mm2.

Qualitative evaluation was rated with a three-point scale as Score 1- poor enhancement, Score 2- diagnostically sufficient and score 3- excellent enhancement.

For the quantitative evaluation, the Hounsfield units were measured on non-contrast and contrast-enhanced scans.^[5] Renal parenchymal and renal vessels attenuation (in Hounsfield units) were measured on unenhanced and contrast-enhanced images.

Standard of reference: Follow-up of patients was obtained during the study period. Confirmation was done by histopathology (n=8), laboratory & clinical inputs (n=50), and surgical findings (n=15) by reviewing medical records. The primary outcome of this study was the qualitative opacification and quantitative opacification of the intrarenal collecting system and ureters. Secondary outcomes included renal parenchymal enhancement (averaged HU of the upper, middle, and lower poles), renal arterial and venous opacification, ureteral distention, radiation dose metrics (CTDI and DLP), and interobserver agreement between radiologists, which was assessed using Pearson’s correlation and Cohen’s kappa. These outcomes were selected to comprehensively evaluate both the efficacy of contrast opacification and the quality of image acquisition across the single and triple bolus protocols.

Statistical Methods Planned: Data were entered into Microsoft Excel and analyzed using SPSS version 20 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Between-group comparisons (single vs triple bolus) for categorical qualitative scores were initially assessed using the chi-square test. Because multiple anatomical segments (intrarenal collecting system, upper, middle, and lower ureter, renal parenchyma, renal artery, and renal vein) were measured within the same patient, segment-level observations were not statistically independent. Therefore, a linear mixed-effects model was applied to account for within-patient clustering. Protocol (single vs triple bolus) was treated as a fixed effect, and patient ID was modeled as a random intercept to account for correlation of repeated measurements within individuals. Each patient contributed up to seven segment-level measurements: one value each for intrarenal collecting system, renal parenchyma (averaged

from upper, middle, and lower poles), renal artery, renal vein, and three ureteric segments (upper, middle, and lower).

The intraclass correlation coefficient (ICC) was calculated to quantify the degree of within-patient clustering of segment-level Hounsfield unit (HU) measurements. The presence of moderate ICC values supported the appropriateness of hierarchical modeling over simple independent comparisons. Normality assumptions were assessed visually using histograms and Q–Q plots. Where distributional assumptions were uncertain, non-parametric testing (Mann–Whitney U test) was performed to confirm findings. To control for inflation of type I error due to multiple hypothesis testing across seven anatomical structures, Bonferroni correction was applied, with adjusted significance set at $p < 0.007$. A two-sided p -value < 0.05 was considered statistically significant unless otherwise specified. Qualitative scoring of the intrarenal collecting system, ureters, renal parenchyma, and renal vasculature was independently performed by two radiologists. Because qualitative scores were ordinal (three-point scale), interobserver agreement was assessed using weighted Cohen’s kappa (κ), which accounts for the degree of disagreement between categories. Agreement strength was interpreted according to Landis and Koch criteria: $\kappa < 0.00$ (poor), 0.00–0.20 (slight), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial), and 0.81–1.00 (almost perfect agreement). Because no formal a priori sample size calculation was performed, a post-hoc power analysis was conducted for the primary outcome (qualitative intrarenal collecting system opacification). Based on the observed difference in Score 3 opacification rates between single-bolus (83%) and triple-bolus (63%) protocols, with a two-sided alpha of 0.05 and group sizes of 37 and 36 respectively, the estimated post-hoc power was approximately 72%. For quantitative HU differences in the intrarenal collecting system (mean difference 455 HU), observed power exceeded 90%. These estimates suggest adequate power for large quantitative differences but limited power for moderate qualitative differences. Confidentiality: Participant identities were kept confidential, and all data were coded by numbers known only to the researcher.

RESULTS

A total of 73 patients’ were evaluated [Table 2], and 73 patient urinary system were evaluated. [Table 3] summarizes the diagnosis of all recruited cases.

Table 2: Patient Demography

Bolus	Male	Female	Mean age	Age range
Single	23	14	44.7	20-74
Triple	20	16	44.8	18-86

Table 3: Final diagnosis of recruited cases

S.no	Diagnosis*	Single bolus	Triple bolus
1	Pelvi-ureteric junction obstruction	1	3
2	Renal stone disease	6	11
3	Malignant mass lesion (Renal cell carcinoma-RCC, Urothelial carcinoma-UC)	10	4
4	Benign mass lesion (Angiomyolipoma-AML, abscess)	2	1
5	Delayed contrast enhancement/excretion	1	0
6	Upper ureteric calculus	1	3
7	Middle ureteric calculus	2	1
8	Distal ureteric calculus	2	5
9	Polycystic kidney disease	1	1
10	Bosniak's cysts	3	3
11	Small kidney	1	1

12	Urinary bladder calculus	2	1
13	Renal parapelvic cyst	1	0
14	Ureterocele	2	0
15	Renal abscess	1	0
16	Pyelitis / Pyelonephritis / Ureteritis	2	5
17	Duplex collecting system	1	2
18	Absent kidney	1	0
19	Ureteric benign stricture (T.B)	1	0
20	Renal calyceal diverticulum	1	0
21	Ureteral injury	0	0
22	Ectopic kidney	0	3
23	Vesicoureteric junction (VUJ) stone	0	2
24	Malrotated kidney	0	1
25	Horseshoe kidney	0	0

* Many patients had more than one finding

In the linear mixed-effects model with protocol (single vs triple bolus) as a fixed effect and patient ID as a random intercept, the estimated fixed-effect coefficient for protocol demonstrated significantly higher attenuation in the intrarenal collecting system with single bolus ($\beta = +448$ HU; 95% CI: 362–534; $p < 0.001$). For the renal artery, the protocol coefficient was +34 HU (95% CI: 15–53; $p < 0.001$), whereas for the renal vein, triple bolus demonstrated significantly higher enhancement ($\beta = -79$ HU for single bolus reference; 95% CI: -94 to -64; $p < 0.001$). The intraclass correlation coefficient (ICC) for segment-level HU measurements was 0.41, indicating moderate within-patient clustering and supporting the appropriateness of hierarchical modeling.

Renal parenchymal opacification: only 1 kidney out of 73 did not show contrast opacification due to a small size and non-excretory status. [Table 4] shows the mean absolute HU values of the renal parenchyma in both protocols.

Renal masses: Twelve kidneys had masses, 8 masses were enhancing, 4 masses had local/distal extension, and 4 masses

had renal vein/inferior vena cava invasion. Vascular invasion was defined by involvement of the inferior vena cava or the renal vein. Two renal masses were enhancing and showed vascular invasion as well.

Collecting system: A total of 73 patients were included in the analysis. Opacification scores (Score 3, 76–100%) in the intrarenal collecting system were achieved in approximately 83% of patients with a single bolus and 63% with a triple bolus. In the ureters, Score 3 opacification was observed in the upper ureter in ~68% of single bolus and ~51% of triple bolus cases, in the middle ureter in 58% of single bolus and ~52% of triple bolus studies, and in the lower ureter in ~57% of single bolus and ~51% of triple bolus cases. Mean HU values for each category are summarized in Table 4, showing higher enhancement in the intrarenal collecting system and renal vessels with the single bolus protocol, while averaged renal parenchyma HU differences were minimal after mixed effect model.

Table 4: comparison of absolute mean HU values in single and triple bolus

Structure	n (patients)	Single Bolus Mean HU	Triple Bolus Mean HU	Mean Difference (M.D)	Bonferroni-adjusted p-values	95% CI
Intrarenal collecting system	73	595	140	455	<0.001	(360, 550)
Upper ureter	70	493	122	371	<0.001	(278, 462)
Middle ureter	67	512	118	394	<0.001	(300, 487)
Lower ureter	67	439	578	-139	0.93	(-1079, 801)
Renal parenchyma	73	5.2	4.8	0.4	0.51	(-7.2, 19.8)
Renal artery	73	225	189	36	<0.001	(16, 57)
Renal vein	72	126	208	-82	<0.001	(-97, -67)

M.D = Mean difference of Hounsfield units.

Positive values indicate higher HU in the single bolus group, while negative values indicate higher HU in the triple bolus group.

CI = Confidence Interval.

Ureter analysis: 18 ureteral calculi were seen; nine of the calculi were associated with ureteral thickening, and only one, with benign stricture (tubercular etiology), was seen.

Ureteric distention: 140 upper ureter, 134 middle ureter, and 134 lower ureter were compared among different boluses. Upper Urinary Tract distention was evaluated by means of 3 measurements of the maximal short-axis lumen diameter of the proximal, middle, and distal ureters on transverse images. Proximal ureteric diameter was 5.9 mm in a single bolus and 5.2 mm in a triple bolus. The middle ureteric diameter was 5.0 mm in a single bolus and 4.8 mm in a triple bolus. Lower ureteric diameter was 4.6 mm in a single bolus, and 4.2 mm in a triple bolus.

Renal vasculature: Score 3 (excellent opacification) was

achieved in renal arteries in ~83% in single bolus, and ~ 63 % in triple bolus. Score 3 (excellent opacification) was achieved in renal veins in ~19% in single bolus and ~83 % in triple bolus. Mean absolute HU values are shown in [Table 4].

Diagnostically sufficient scores of renal vasculatures: Single bolus protocol patients n=67/73 renal veins were opacified with at least score 2, n=6 were not evaluated due to venous invasion by renal tumor. n=72/72 renal arteries were opacified with a score of at least 2. In triple-bolus patients (n=70/72), 72 renal veins were opacified with a score of at least 2; 1 renal vein was not opacified due to vascular invasion, and 1 was not opacified in a small, atrophic kidney. [figure 3]

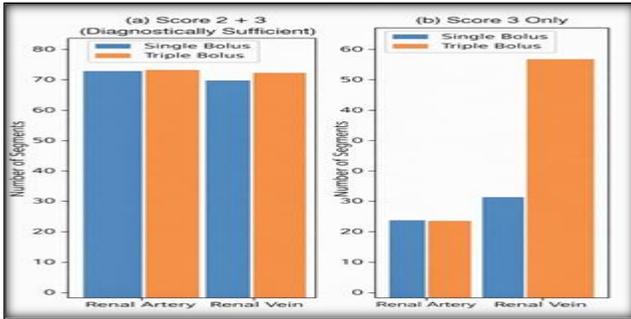


Figure 3 a-b: Comparison of diagnostically sufficient (Score 2 and 3) and score 3 (excellent opacification) of Renal vessels in single bolus and triple bolus shows the renal vein is better opacified in triple bolus protocol.

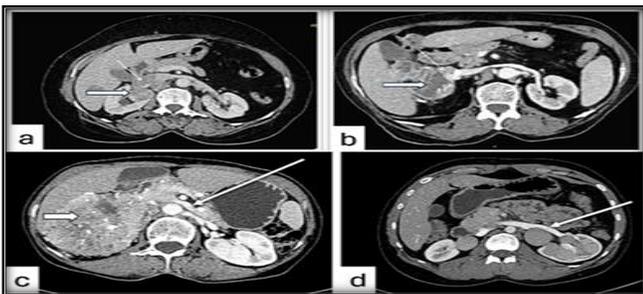


Figure 4: Axial MPR images (a) 65-year-old male patient synchronous MPR axial image shows right renal cell carcinoma, where the broad arrow showing the enhancing renal mass with renal vein/inferior vena cava thrombosis (narrow arrow) in a single bolus protocol. (b) A 40-year-old female patient, MPR axial image shows a heterogeneously enhancing necrotic renal cell carcinoma in the right kidney with renal vein/inferior vena cava thrombosis (narrow arrow) in the triple bolus protocol. (c) 76-year-old male patient. MPR synchronous nephrographic phase axial image shows large, markedly enhancing right renal cell carcinoma with neovascularization (seen as small, intensely enhancing vessels) and renal vein/inferior vena cava thrombosis (long arrow) in a triple-bolus protocol. (d) 49-year-old female patient MPR synchronous nephrographic phase axial image (long arrow) shows markedly opacified left renal vein in triple bolus protocol and mild left hydronephrosis due to ureteric stone (not shown).

Solid masses subgroup analysis: 12 patients had solid masses in a single bolus; 10 patients had renal cell carcinoma (n=2, urothelial carcinoma, n=7, clear cell carcinoma); and n=1, chromophobe cell carcinoma; n=1, angiomyolipoma; and n=1, renal abscess. Figure. 4 show imaging characteristics of renal cell carcinoma on a single-bolus protocol. five patients had solid masses in triple bolus, n= 4, clear cell carcinoma, n=1, angiomyolipoma. All the solid masses were compared for renal parenchymal and vascular

opacification. The renal parenchyma was better opacified in the single-bolus protocol compared with the triple-bolus protocol. The renal artery is better opacified in a single bolus and the renal vein is better opacified in a triple bolus as compared to a single bolus. Renal vein is best opacified in triple bolus (p value < 0.001) as shown in [Figure 4].

Cystic masses analysis: Cystic lesions more than 3 cm were evaluated. Four patients had cystic masses in a single bolus; n=1 had Bosniak's category III cyst 3, n=1 had Bosniak's category II cyst, n=1 had Bosniak's category I cyst, and n=1 had calyceal diverticulum type I. Three patients had cystic masses in the triple-bolus; n=3 Bosniak's category I cysts.

Obstructed segments analysis: Obstructed segments were defined as having hydronephrosis or a ureteric diameter of more than 7mm. 15 segments in a single bolus and 17 segments in a triple bolus were compared. The collecting system is better opacified with the single bolus than with the triple bolus (p-value < 0.001). No significant difference in ureteral distention was seen among different protocols. Figure 5 shows diagnostically sufficient opacification of the collecting system in both single- and triple-bolus protocols.

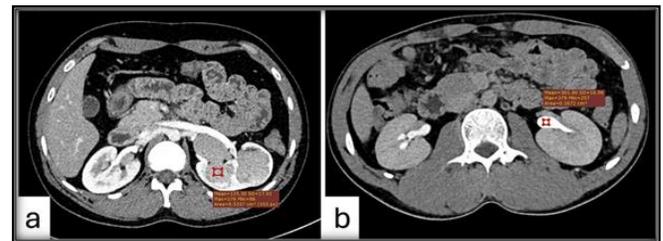


Figure 5: Axial MPR images of (a) a 29-year-old male patient with pelvi-ureteric junction obstruction showing left moderate hydronephrosis with diagnostically sufficient opacification of the left intrarenal collecting system and excellent renal vein opacification in triple bolus protocol. (b) 33-year-old female patient with intense opacification of the bilateral renal pelvis in a single bolus protocol. The patient had a renal cyst in the left kidney (not shown)

Interobserver agreement: Although qualitative scoring demonstrated fair to substantial interobserver agreement ($\kappa = 0.34-0.63$), agreement was only moderate for the collecting system and ureteric segments. This variability likely reflects the subjective nature of semi-quantitative scoring and intermittent ureteric opacification. The moderate reproducibility underscores the importance of standardized scoring criteria and suggests that quantitative HU measurements may provide complementary objective assessment. Cohen's kappa with p-values for each segment are depicted in [Table 5]. No significant difference exists in the qualitative scoring by the two radiologists, and there is fair to moderate agreement between them.

Table 5: Interobserver agreements

Structure	Weighted Cohen's κ	Strength of Agreement*
Collecting system	0.45	Moderate
Upper ureter	0.42	Moderate
Middle ureter	0.34	Fair
Lower ureter	0.37	Fair
Renal parenchyma	0.63	Substantial
Renal artery	0.45	Moderate
Renal vein	0.59	Moderate

*Agreement interpreted according to Landis and Koch criteria.

Radiation dose reduction: Dose-length product (DLP) values were recorded for each acquisition phase and summed per patient. Effective dose was estimated using the ICRP Publication 103 conversion coefficient for the abdomen and pelvis ($k = 0.015 \text{ mSv} \cdot \text{mGy}^{-1} \cdot \text{cm}^{-1}$). The mean DLP for the single-bolus protocol was $1578 \pm 312 \text{ mGy} \cdot \text{cm}$, corresponding to an estimated effective dose of $23.7 \pm 4.7 \text{ mSv}$. The mean DLP for the triple-bolus protocol was $796 \pm 148 \text{ mGy} \cdot \text{cm}$, corresponding to $11.9 \pm 2.2 \text{ mSv}$. The observed reduction reflects consolidation of imaging phases in the triple-bolus protocol rather than reduction in administered contrast volume. CareDose 4D automatic tube current modulation was active in all scans. No differences in reconstruction algorithms or kernel settings existed between groups. Our triple bolus effective dose of approximately 11.9 mSv is higher than the 9.8 mSv reported by Kekelidze et al. primarily because we acquired a non-contrast CT (NCCT) phase in both protocols, whereas Kekelidze et al. omitted NCCT. For clinical contexts in which NCCT can be safely omitted (e.g., follow-up of known renal masses without suspected calculi), the triple bolus effective dose could be further reduced to an estimated 6–7 mSv, comparable to or lower than the Kekelidze et al.^[5]

DISCUSSION

In this study, seven anatomical structures were compared between single- and triple-bolus CT urography (CTU) protocols. Given multiple hypothesis testing, the family-wise error rate at $\alpha = 0.05$ approaches 30%. After Bonferroni correction (adjusted $\alpha = 0.007$), statistically significant differences persisted for the intrarenal collecting system, upper ureter, middle ureter, renal artery, and renal vein (all $p < 0.001$), whereas the lower ureter and renal parenchyma remained non-significant. Mixed-effects modeling was further applied to account for clustering of multiple segments within individual patients. Although confidence intervals widened modestly, the direction and magnitude of associations remained stable, supporting the robustness of our findings.

Quantitatively, the single-bolus protocol resulted in significantly higher attenuation values in the intrarenal collecting system and proximal ureters ($p < 0.001$). This finding is physiologically expected, as 100% of administered contrast is available for urinary excretion in the single-bolus protocol compared with approximately 30% in the triple-bolus protocol. Dure-Smith et al.^[7] similarly emphasized that excretory phase enhancement depends on the total amount of contrast medium within the urinary tract. However, when assessed qualitatively—arguably the more clinically relevant endpoint—no significant difference was observed between protocols for diagnostic sufficiency of the intrarenal collecting system or ureters, with both achieving adequate opacification for detection of filling defects or urothelial thickening. Although the single-bolus protocol produced substantially higher attenuation values, this quantitative superiority did not translate into improved diagnostic adequacy, suggesting a threshold effect whereby once sufficient opacification for lesion detection is achieved,

further increases in attenuation confer limited additional clinical benefit. These findings are consistent with prior studies demonstrating comparable qualitative performance across single- and split-bolus techniques.^[8-10]

The lower ureter demonstrated substantial variability in attenuation with wide confidence intervals and no statistically significant difference between protocols. This heterogeneity likely reflects distal ureteral peristalsis, intermittent opacification, dependent pooling of contrast, and partial obstruction in some patients. Similar limitations in distal ureteral opacification have been reported by McNicholas et al.^[8] Kekelidze et al.^[5] also reported incomplete distal ureteral opacification in 21% of cases despite using a higher fixed contrast dose and delayed acquisition at 510 seconds. Our comparatively lower opacification rates may relate to weight-based dosing (2 ml/kg, maximum 130 ml) rather than the higher total contrast volumes used in other triple-bolus studies. With respect to renal parenchymal enhancement, no significant difference was observed between protocols ($p > 0.05$), consistent with findings by Lee et al.^[11] and Abedi et al.^[12], who reported comparable enhancement characteristics across varying split-bolus ratios and between conventional and triple-bolus techniques. Although renal masses were not the primary focus of this study, all 12 detected masses were correctly characterized, supporting the adequacy of both protocols for parenchymal lesion assessment. In vascular evaluation, renal arterial opacification was significantly higher with the single-bolus protocol ($p < 0.001$), whereas renal venous opacification was significantly better with the triple-bolus protocol ($p < 0.001$). Excellent renal vein opacification was achieved in 83% of triple-bolus cases compared with 19% in the single-bolus group. This likely reflects acquisition timing immediately after completion of the third bolus. Kekelidze et al.^[5], in contrast, reported stronger arterial than venous enhancement, possibly due to differences in scan timing. Despite quantitative differences, diagnostically sufficient vascular opacification was comparable between protocols. It should also be noted that excessively high attenuation with single bolus may obscure subtle filling defects or produce beam-hardening artifacts, as described by O'Connor et al.^[3]. The excretory phase in our protocol was acquired at 12 minutes, whereas Raman and Fishman^[9] recommend imaging approximately 4 minutes after contrast administration for optimal urothelial assessment. The delayed acquisition in our study likely accentuated attenuation differences between protocols. Nevertheless, given the relatively low incidence of upper urinary tract urothelial carcinoma (approximately 7%)^[11] and primary ureteral carcinoma (approximately 1%)^[10], the quantitative superiority of single bolus alone may not justify universal preference in all patients. Overall, no significant qualitative differences were observed between protocols for collecting system, ureteric, or parenchymal opacification. Single bolus provides higher absolute attenuation in the collecting system and renal artery and superior volume-rendered imaging, whereas triple bolus offers improved renal vein opacification. Thus, triple-bolus CTU represents a reasonable alternative to single bolus, particularly when venous evaluation is prioritized or when contrast dose optimization is feasible.

CONCLUSION

In this prospective randomized comparison, single- and triple-bolus CT urography protocols demonstrated comparable qualitative diagnostic adequacy for evaluation of the upper urinary tract. Single bolus resulted in significantly higher quantitative attenuation of the intrarenal collecting system and renal arteries, whereas triple bolus provided

superior renal venous opacification and substantially reduced radiation dose.

Given the absence of major qualitative differences, triple-bolus CTU may serve as a dose-efficient alternative in selected clinical scenarios. Larger adequately powered studies are warranted to confirm these findings and to determine whether quantitative differences translate into improved diagnostic performance.

Table 6: summary of imaging characteristics of single bolus and triple bolus

Parameter	Single Bolus (SB)	Triple Bolus (TB)	Statistical Interpretation
Renal parenchymal enhancement	Comparable	Comparable	No significant difference
Intrarenal collecting system (HU)	Significantly higher	Lower	SB superior quantitatively (p<0.001)
Qualitative collecting system opacification	Comparable	Comparable	No significant difference
Ureteric opacification	Higher HU	Lower HU	SB superior quantitatively (p<0.001)
Ureteric distention	Comparable	Comparable	No significant difference
Renal artery	Higher HU	Lower HU	SB superior (p<0.001)
Renal vein	Lower HU	Higher HU	TB superior (p<0.001)

Implication for clinical practise: The absence of significant qualitative differences between protocols suggests that both single- and triple-bolus CTU provide diagnostically sufficient evaluation of the upper urinary tract in most patients. The single-bolus protocol yields higher absolute attenuation in the collecting system and renal artery, which may be advantageous for detecting subtle urothelial lesions or arterial anatomy. In contrast, the triple-bolus protocol provides superior renal venous opacification while reducing radiation exposure by approximately 50%, making it a reasonable alternative when venous assessment or dose reduction is prioritized. Therefore, protocol selection may be individualized based on clinical indication: single bolus when arterial detail or maximal collecting system attenuation is desired, and triple bolus when venous evaluation or radiation minimization is emphasized.

Limitations

Although clustering was addressed using mixed-effects modeling, segment-level analysis may still overestimate effective sample size. No positional maneuvers or additional delayed scans were performed to enhance distal ureteral opacification. Furthermore, contrast dosing was weight-based rather than fixed at higher volumes as reported in some triple-bolus studies^[5], which may have influenced excretory enhancement.^[12-15]

Larger prospective studies are warranted to validate these findings and refine protocol selection for specific clinical indications

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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