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Sonographic Detection of Renal and Ureteral Stones. Value of the Twinkling Sign

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ABSTRACT

Purpose: To compare the detection of urinary stones using standard gray scale ultrasound for diagnostic accuracy using the color Doppler "twinkling sign".

Materials and Methods: Our study population consisted of forty-one patients who demonstrated at least one urinary stone on unenhanced CT evaluation of the kidneys or ureters. Each patient was evaluated using gray scale ultrasound and color Doppler imaging by an observer who was blinded to the CT results.

Results: Seventy-seven stones were present in 41 patients, including 47 intrarenal stones, 5 stones in the renal pelvis, 8 stones at the ureteropelvic junction, 5 ureteral stones and 12 stones at the ureterovesical junction. Based upon gray scale sonography the diagnosis of stone was made with confidence in 66% (51/77) of locations. Based upon Doppler sonography using the twinkling sign, the diagnosis of stone was made with confidence in 97% (75/77) of locations. Clustered ROC analysis demonstrated that the Doppler twinkling sign (Az = 0.99) was significantly better than conventional gray scale criteria (Az = 0.95) for the diagnosis of urinary stones (p = 0.005, two-sided test).

Conclusions: The color Doppler twinkling sign improves the detection, confidence and overall accuracy of diagnosis for renal and ureteral stones with minimal loss of specificity.

Key words: *urolithiasis; ultrasound; Doppler; computed tomography*
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INTRODUCTION

Detection of urinary stones on ultrasound (US) may be problematic when the stones are obscured by ultrasonic beam-attenuating tissue, such as renal sinus fat, mesenteric fat, and bowel, or when their posterior acoustic shadowing is weak (1-3). Despite the technical advances of US, radiologists have difficulty confirming or excluding the presence of urinary stones when the gray-scale findings are indeterminate.

The twinkling sign is a color-flow US artifact described behind calcifications and presenting as a random color encoding in the region were shadowing would be expected on gray-scale images (4). Recent studies have reported that the twinkling sign may be useful for detection of urinary stones (5-7).

The present study compares standard gray scale ultrasound with color Doppler ultrasound (twinkling sign) for the detection of urinary stones, initially diagnosed by unenhanced computed tomography (CT).

MATERIALS AND METHODS

Patients

Forty-one patients (24 males, 17 females; mean age: 50 ± 8.7 years, range: 19-74 years) with urinary stones (52 renal stones, 25 ureteral stones) were included in our study. All patients were evaluated for the presence of urinary stones by unenhanced spiral computed tomography (CT), which served as the "gold standard" for the diagnosis of urinary stones (8). In addition, plain abdominal radiography was performed in all patients. Our study had Institutional Review Board Approval and written informed consent was obtained from all patients prior to the US studies.

Ultrasound Technique

US examinations were done within 24 hours after CT. US examinations were performed by one of two experienced radiologists (A.K; F.F.), who were blinded to the CT findings. Gray-scale, color and power Doppler US, and pulsed-wave spectral Doppler US were performed in all 41 patients. All studies were performed with the Acuson Sequoia 512; (Acuson, MountainView, Cal.) with a transmit frequency of 2.5 to 6.0 MHz. Gray-scale US criteria included visualization of a hyperechoic structure with posterior acoustic shadowing within the kidney and/or the ureter. For visualization of posterior acoustic shadowing, focal zones were positioned at the depth of the stone, or slightly deeper than the stone.

Color Doppler US was performed using a red-and-blue color map and power Doppler US using a pink color map with a standardized Doppler protocol to detect the twinkling artifact. For color Doppler, gain was set to the point just below the threshold for color noise and the pulse repetition frequency (= velocity scale) was set to 64 cm/sec to eliminate color flow signals from renal blood flow. The color window size was adjusted to cover the whole renal sinus. Doppler imaging began with continuous sweeps of the renal sinus in the longitudinal and transverse planes. For investigation of the ureter, the color window size was adjusted for each part of the ureter as it was visualized. Evaluation of the ureter began with the UPJ (ureteropelvic junction). The course of the ureter was follow caudally from the UPJ to image the proximal ureter. The mid-ureter was examined at the level where the ureter crossed the iliac vessels. The distal-ureter was evaluated through a full urinary bladder. Whenever a twinkling sign was present, a Doppler spectrum was obtained to exclude arterial or venous flow. At each level, gray scale evaluation was followed by color and power Doppler imaging for a twinkling sign. For each kidney/ureter unit, gray-scale and Doppler findings were recorded at 8 locations: intrarenal upper pole, intrarenal mid-sinus, intrarenal lower-pole, renal pelvis, UPJ, mid-ureter, distal-ureter and ureterovesical junction. Each location was evaluated whether or not there was a stone appearance for each gray-scale and Doppler (color and power).

US findings were evaluated by consensus interpretation of the two radiologists (AK, FF). The gray-scale US appearance of urinary stones was analyzed for size, echo difference between stone and adjacent tissue, and posterior acoustic shadowing. Stone size was determined on gray-scale US alone. The location of the stones was determined either on gray-scale US or color Doppler US findings. Echo difference between stone and adjacent tissue was recorded as marked, slight, or indistinct. Posterior acoustic shadowing was noted as absent, weak or strong. On color and power Doppler images, the presence, appearance, and intensity of the twinkling sign was assessed. The intensity of the color signal was recorded as 0 (= absent), 1 (= weak, present) and 2 (= strong, present). Furthermore, the length of the twinkling sign was classified and a length of > 1 cm was defined as 2 (= strong present). At pulsed-wave spectral Doppler US, the pattern of the spectrum was analyzed.

Computed Tomography Technique

All patients underwent an unenhanced helical CT examination using a Somatom Plus 4 unit (Siemens, Erlangen, Germany). Single breathhold, continuous, transverse helical acquisition was performed from the top of the kidneys to the base of the bladder with a 5-mm collimation, a 2:1 pitch, 120 kVp, 280 mAs, and a reconstruction at 2.5-mm intervals. No oral or intravenous contrast was administered. A typical examination lasted less than 30 seconds. The images were analyzed at a workstation that was capable of reconstruction processing. An independent radiologist reviewed each CT examination for the presence of stones in the kidneys and ureters. Each stone was classified as located in one of the eight previously described positions.

Statistical Analysis

The ultrasound findings were compared with the findings on unenhanced CT. Stone size was measured on axial CT images (maximum transverse diameter) and compared with the size measured on gray-scale US (maximum transverse diameter).

In order to compare the detection rate of urinary stones by gray- scale and Doppler imaging we used ROC analysis. Given the clustered nature of our observations (2 kidneys per patient with 8 locations per kidney/ureter) imaging findings were not independent for each patient. We therefore used a clustered ROC analysis for this comparison with 16 clustered observations per patient (9). In these few cases when two stones were detected by US at a single location (n = 3) the finding was tabulated as a single observation. The confidence of diagnoses was made according to the greatest confidence among the stones in that location for each gray- scale and Doppler sonography. A p-value of less than 0.05 was considered statistically significant (10).

RESULTS

The 77 urinary stones had a mean size of 0.5 cm ± 0.3 on unenhanced CT. The mean size of the 52 renal stones was 0.5 cm ± 0.2 (range, 0.3 - 1.0 cm) and of the 25 ureteral stones was 0.4 cm ± 0.3 (range, 0.3 - 1.0 cm). Forty-seven renal stones (90%) were located in calices and 5 in the renal pelvis (10%). Eight ureteral stones (32%) were located at the UPJ, 2 (8%) in the mid-ureter, 3 (12%) in the distal-ureter, and 12 (48%) at the ureterovesical junction.

On gray-scale US 43 of 77 urinary stones (56%) showed marked echo difference (30 renal stones, 13 ureteral stones), 8 urinary stones (10%; 5 renal stones, 3 ureteral stones) showed slight echo difference, and 26 urinary stones (34%; 17 renal stones, 9 ureteral stones) showed indistinct echo difference (= no definite criteria for a urinary stone), respectively. Forty-six urinary stones (60%) showed strong posterior acoustic shadowing, and 5 urinary stones (7%) had weak posterior acoustic shadowing. The mean size of the 51 urinary stones detected on gray-scale US was 0.7 cm ± 0.5 on. The mean size of the 35 renal stones was 0.7 cm ± 0.5 (range, 0.3 - 1.4 cm) and of the 16 ureteral stones was 0.6 cm ± 0.4 (range, 0.3 - 1.2 cm).

The twinkling sign was generated from 75 of 77 urinary stones (97%). One renal stone (2%) and 1 ureteral stone (4%) did not demonstrate this Doppler sign. As described in previous studies, the twinkling sign appeared as a rapidly changing color complex seen persistently behind urinary stones, like a comet's tail.

Fifty-one of 52 of renal stones (98%) and 24 of 25 ureteral stones (96%) demonstrated the signs. Forty-seven of 49 stones (96%) less or equal than 0.4 cm, and 100% of stones (n = 28) with a size greater than 0.4 cm had the twinkling sign (Table-1 and Figures 1-3). Four ureteral stones with indistinct echo difference showed the twinkling sign. Seventeen of 20 urinary stones (85%) with indiscrete posterior acoustic shadowing showed twinkling sign. Sixty (80%) of 75 stones with twinkling sign had signals with strong intensity (Table-2).

Based upon gray-scale criteria 10 false positive stones were suggested within an intrarenal location in while one false positive stone was suggested at a UPJ. One of the false positive intrarenal stones also demonstrated a false positive twinkling sign.

Gray- scale US detected 35 of 52 renal stones (67%) and 16 of 25 ureteral stones (64%). Overall, gray scale US demonstrated a sensitivity of 66% (51/77) while the twinkling sign demonstrated a sensitivity of 97% (75/77) (Table-3). A twinkling sign was present in 51 of 52 (98%) of renal stones and in 24 of 25 ureteral stones (96%). Based upon clustered ROC analysis twinkling sign significantly improved the detection of urinary stones (Az = 0.099) compared

***Table 1** – Comparison of gray-scale ultrasound (US) and Doppler twinkling artifacts of urinary stones based on stone location and stone size.*

Size	Location		Gray-scale US	Twinkling Artifact
	Renal Stones	Ureteral Stones		
≤ 0.4 cm	30	19	29 (59%)	47 (96%)
> 0.4 cm	22	6	22 (79%)	28 (100%)
Total	52	25	51 (66%)	75 (97%)

The stone sizes are based on computed tomography measurements.

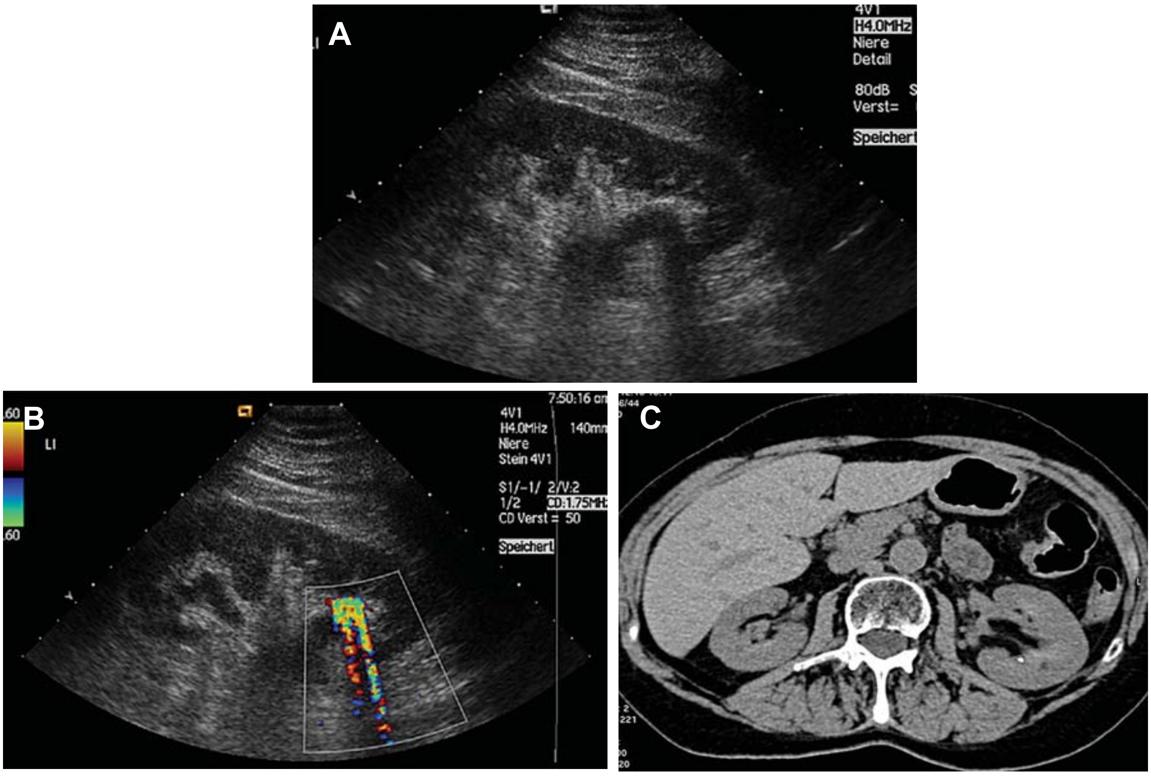

***Figure 1** – Sixty-seven year-old man with 3-mm renal stone. A) Sonogram shows echogenic lesion with indiscrete acoustic shadowing. It is poorly distinguished from adjacent echogenic tissue. Therefore, it is not easy to determine that this lesion is an intrarenal lower-pole stone. B) Color Doppler sonogram shows rapidly changing color band seen persistently behind stone with comet's tail appearance. C) Unenhanced computed tomography with clearly visible intrarenal lower-pole stone of the left kidney.*

with gray-scale US (Az = 0.095), ($p < 0.005$). Table-2 shows the location of urinary stones by size (≤ 0.4 cm and > 0.4 cm; based on CT size measurement) detected with gray-scale US and/or with twinkling sign.

Forty-six of 77 urinary stones (60%) were visible on plain abdominal film. All 46 of these stones showed a twinkling sign. The 2 urinary stones with no twinkling sign were radiolucent on plain abdominal films.

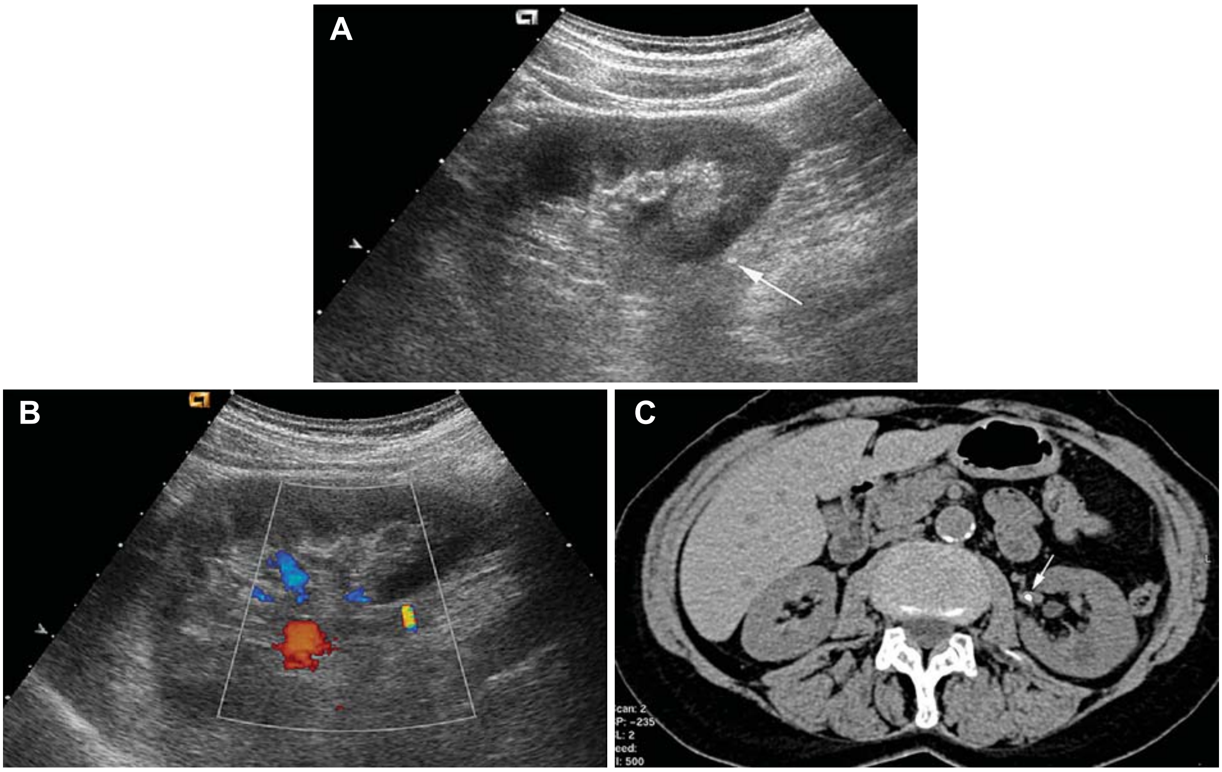

Figure 2 – *Forty-seven year-old woman with 4-mm ureteral stone. A) Sonogram shows echogenic lesion near lower pole of left kidney. It is slightly distinguished from adjacent echogenic tissue and does not show posterior acoustic shadowing. Therefore, it is not easy to determine that this lesion is a ureteral stone. B) Color Doppler sonogram shows twinkling artifact from echogenic lesion. C) Corresponding unenhanced computed tomography with clearly visible ureteral stone on the left side.*

Table 2 – *Comparison of gray-scale ultrasound and Doppler twinkling artifacts of urinary stones.*

	Renal Stones						Ureteral Stones					
Echo Difference	Marked (30)		Slight (5)		Indistinct (17)		Marked (13)		Slight (3)		Indistinct (9)	
Posterior Shadowing	Strong (30)	Weak (0)	Strong (4)	Weak (1)	Strong (0)	Weak (0)	Strong (12)	Weak (1)	Strong (0)	Weak (3)	Strong (0)	Weak (0)
Twinkling Artifact	30 (100%)	0	4 (100%)	1 (100%)	16 (94%)		12 (100%)	1 (100%)	0	3 (100%)	8 (89%)	
Stone Size	0.5 cm ± 0.2 (mean ± SD)						0.4 cm ± 0.3 (mean ± SD)					

The stone sizes are based on computed tomography.

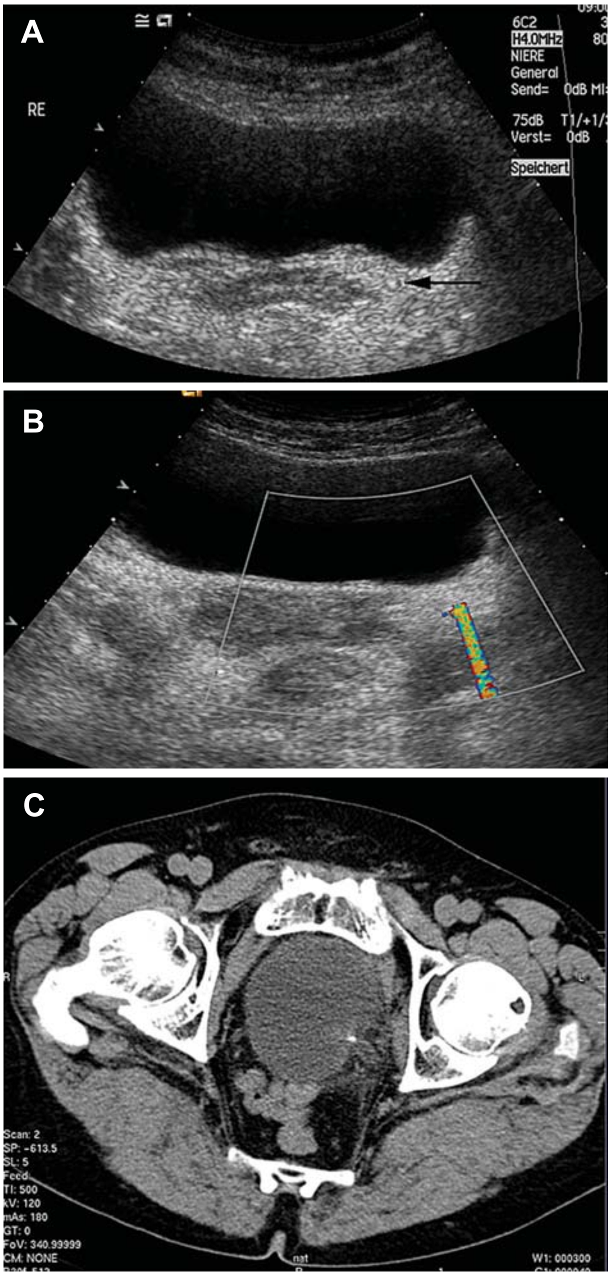

Figure 3 – Forty-six year-old woman with 5-mm stone near ureterovesical junction (UVJ). A) Axial sonogram of bladder shows that left UVJ is swollen and is slightly more echogenic compared with opposite site. However, existence of ureteral stone (arrow) is not definite because of surrounding echogenic tissue and absent posterior acoustic shadowing. B) Color Doppler sonogram shows prominent twinkling artifact from left UVJ area. C) Corresponding unenhanced computed tomography with clearly visible stone at the left UVJ.

Table 3 *– Comparison of urinary stone detection with gray-scale ultrasound (US) and Doppler twinkling artifacts.*

	CT	
	Stone	No Stone
Gray-scale US	51	26
Twinkling artifact	75	2

CT = computed tomography; Fisher's exact test, $p < 0.001$.

COMMENTS

Sonographic detection of urinary stones is relative easy for stones with both distinct echogenicity and posterior acoustic shadowing (11). However, in many cases it is difficult to determine whether a urinary stone is present because of its indistinct echogenicity and indiscrete posterior acoustic shadowing. Indistinct echogenicity of stones results from surrounding echogenic tissue, such as prominent renal sinus fat, mesenteric fat, and bowel. When a renal stone is poorly distinguished from echogenic renal sinus fat and has an indiscrete posterior acoustic shadowing, it may be difficult to determine its presence on US. In one prior study, three radiologists interpreted 31 ultrasonograms with a sensitivity of 81% and a specificity of 86% for detecting renal stones (3).

The present study was performed to determine whether the color Doppler twinkling sign might improve the sonographic diagnosis of urinary stones. Almost all stones (97%; 75 of 77) showed a color Doppler twinkling sign and 60 of 75 stones (80%) with twinkling signs had signals with strong intensity. The conclusion of the present study is that the twinkling sign has potential usefulness in clinical practice, especially to confirm the presence of stones with indistinct echo difference and indistinct posterior acoustical shadowing.

Rahmouni et al. found color Doppler twinkling artifacts originating from parenchymal calcifications, including bladder calculi (4). They explained that when the US beam is incident to a rough interface composed of sparse reflectors, a twinkling sign is generated by the phase shifts resulting from multiple reflections in the medium. Because urinary stones become larger particles by aggregation or agglomeration of primary crystal forms, they are predominantly composed of a highly reflecting crystalline aggregate of varying chemical composition with a mucoproteinous organic matrix (12). On the basis of the explanation of Rahmouni et al., the twinkling artifacts from urinary stones are likely to be generated by random strong reflections and multiple inner reflections of the incidental US beam at a rough interface formed by a crystalline aggregate of stones (4). In a phantom study of Lee et al., the twinkling sign originated from a fixed site of each stone during repeated scanning (7). This finding indicates that the twinkling sign is related to some structural factor in the stone.

Rahmouni et al. suggested that the artifact could be influenced by ultrasonic beam attenuation of tissues interposed between the probe and a calcification (4). Lee et al. reported that 4 of 20 renal stones and 2 of 16 ureteral stones did not show any twinkling sign (7). They suggested that ureteral stones may be influenced more than renal stones by ultrasonic attenuation of interposed tissues because the ureter is deep-seated below abundant fatty tissue without a proper acoustic window. In the present study only two urinary stones showed no twinkling sign. Furthermore, Lee et al. reported that they could not find any correlation between the location of stones and the genesis of the signs, which is in line with our findings (7). Our findings suggest, that color Doppler twinkling sign is more affected by the architecture of the stones than by beam attenuation from interposed tissue.

Lee et al. further reported that the location of focal zone can influence the occurrence and intensity of the sign (7). When the focal zone was placed below urinary stones, artificial color signal was prominent and strengthened in our phantom study (results not presented). Our standardized protocol placed the focal zone slightly below the area of interest. Using this focal position we found a twinkling sign in almost all stones (75 of 77). Based on our results we support standardized US settings with the focal depth slightly below the stone of interest.

Lee et al. noted that one of the limitations of their study was that they did not determine whether the detection of the twinkling signs would actually improve the detection of stones. In our study we evaluated the improvement in the detection of urinary stones using the twinkling sign. With CT findings as our “gold standard”, we were able to improve significantly the detection of urinary stones with twinkling sign as compared with gray- scale US ($p < 0.005$). Only two stones (≤ 0.4 cm) did not show a twinkling sign and these stones were not visible on gray-scale US. Both stones were radiolucent and the urine analysis was suggested uric acid stones. This finding is in line with the finding of Chelfouh et al. who reported absence of the twinkling sign from uric acid stones. Based upon our observations, it is possible that the twinkling sign might be helpful in the differentiation of urinary stone composition and morphology. However, this should be evaluated in further studies.

Echogenic foci with color signs can be seen in the area of the renal sinus and do not always suggest stones. Renal artery calcification should be considered in the differential diagnosis, especially in patients with long-standing diabetes, hypertension, or other systemic diseases associated with atherosclerotic vascular disease (13). Real-time scanning can help differentiate arterial calcifications from renal calculi because arterial calcifications are seen to pulsate. However, twinkling sign may also develop from calcifications of renal tumor, renal cyst, and renal parenchyma. These calcifications usually can be differentiated from renal stones on the basis of their location on real-time scanning and the patient’s history.

We note several limitations of our study. The main limitation of the study is that only 8% of the ureteral stones were located in the mid ureter. Since it is known that this mid-ureteral stones are often the hardest to be localized by sonography, the good results of stone detection by sonography may differ, when more mid ureteral stones would have been included. Further, the US examination was interpreted by conserves review of two radiologists. We have no data about intra- and interobserver-variability. Second, we used only one US unit (Acuson Sequoia 512). As reported by Aytac et al. the twinkling sign depends on the color sensitivity and the acoustic output of the US unit (6). Therefore, with different US units these results might be not reproducible. In spite of these limitations, we conclude that the color Doppler twinkling sign was frequent and characteristic enough to provide a useful additional finding for urinary stones on US.

CONCLUSIONS

The color Doppler twinkling sign improves the detection and confidence of diagnosis for renal and ureteral stones with minimal loss of specificity.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

This is an interesting study with some provocative findings, which should stimulate further research in this diagnostic area. The main limitations of the findings, partly pointed out by the authors, are related to the issues of variability (inter and intra-observer), scanning machine, experience of the observer, availability and comparability in the emergency out-of-hours setting, and the lack of sufficient numbers of patients with stones in the mid-ureter, or distal ureter above the ureterovesical junction and below the iliac vessels, as these are often the hardest to visualize and often confused with pelvic phleboliths. The fact that the color-Doppler studies were always performed after the normal sonography added an element of observer verification bias. The authors also failed to state if there were any differences between color and power Doppler. However, there is sufficient encouragement from the authors' findings to stimulate a multicenter larger double-blinded study with randomization and some negative controls, to define the true diagnostic role of this technique in wider practice, as ultimately, ultrasound is a more observer dependent technique than non-contrast computed tomography.

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REPLY BY THE AUTHORS

For the diagnostic imaging of patients with suspected urinary tract stones, excretory urography has been the gold standard. In recent years unenhanced helical computed tomography (CT) has been introduced as a quick alternative. Additional information regarding renal function may be obtained by combining CT with contrast infusion. As an alternative a plain film of the kidneys, ureters and bladder (KUB) combined with ultrasonography (US) can be used (1).

The major disadvantage of X-ray and CT imaging is the high radiation doses given to the patient during the investigation. In the United States, the number of CT scans has been quadrupled since 1992. Physicians are referring their patients for so many imaging tests that as many as 2% of cancers may be attributable to radiation exposure during CT scanning (2). The cumulative effective doses of radiation from imaging procedures increased with advancing age. In a recent paper about low-dose ionizing radiation exposure from medical imaging procedures, Fazel et al. concluded that the current pattern of use of medical imaging in the United States is exposing many patients to substantial doses of ionizing radiation (3). Therefore, strategies for optimizing and ensuring appropriate use of these procedures in the general population should be developed.

In our opinion, there is an urgent need to reduce radiation exposure in imaging, especially for repeated or redundant imaging like in patients with urinary stones. US has the advantage of being universally available, does not expose the patient to radiation, requires no intravenous contrast medium, and is independent of the kidney function. The present study shows, that the twinkling sign using the color Doppler US improves the detection of urinary stones in comparison with gray-scale US and almost achieves the same results as unenhanced CT. Therefore, in our opinion color Doppler US with the twinkling sign can become a main alternative diagnostic imaging tool for patients with suspected urinary stones or for follow-up and may replace more expensive, invasive or harmful imaging procedures.

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