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● *Original Contribution*

# CLINICAL SIGNIFICANCE OF TWINKLING ARTIFACT IN THE DIAGNOSIS OF URINARY STONES

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**Abstract—The twinkling artifact is a color Doppler artifact, but it could be used in the confirmation of urinary stones. Conventionally, gray-scale criteria (echogenic foci with acoustic shadowing) is used in the diagnosis of urinary stones, but unfortunately, its reliability is very low. If the color Doppler twinkling artifact is applied in conjunction with other provocative measures, then its overall reliability exceeds 95%. To determine the clinical significance of twinkling artifact in the diagnosis of urinary stones, this cross-sectional observational study was conducted at Gilani Ultrasound Center, Lahore, Pakistan. For the determination of clinical significance, 1350 patients were recruited for this study. All the patients had renal stones of variable size and location. All the patients were evaluated with gray-scale sonographic criteria, and then color Doppler was applied to look for the twinkling artifact. The findings were confirmed with other imaging modalities (*i.e.,* plain X-ray, computed tomography scan, *etc.*, or during patient follow up). Sensitivity and specificity of the gray-scale ultrasound criteria in the detection of urinary stones was 96.1% and 57.9%, respectively, while the sensitivity and specificity of the color Doppler twinkling artifact in the detection of urinary stones was 100.0% and 97.4%, respectively. It was concluded that the application of twinkling artifact is useful in the confirmation of urinary stones, but specifically, it is of great diagnostic value in the small (less than 5 mm) renal stones and stones adjacent to a strong reflector (*i.e.,* ureteric stones or stones in the prostatic urethra). (E-mail: raham.bacha@rsmi.uol.edu.pk) © 2019 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

*Key Words:* **Twinkling artifact, Urinary stone, Ureteric stone, Renal stone, Acoustic shadowing.**

## INTRODUCTION

A urinary stone is a potential cause of a clinical emergency, and sometimes it can lead to urinary tract infection, hypertension, chronic kidney disease and end-stage renal disease (Petrucci et al. 2018). On the basis of chemical composition, there are various type of urinary stones, including calcium oxalate, calcium phosphate, uric acid and struvite. But amongst them, calcium oxalate accounts for about 70%−80% of all urinary stones (Waikar et al. 2019). Urinary stone disease in human beings is one of the oldest known clinical problems that has compelled people to think about its pathogenesis, but the exact mechanism of its formation is still unknown (Nirumand et al. 2018). Researchers are not only engaged in determining the mechanism of urinary stone formation but also remains busy in devising different methods for its diagnosis (Manzoor et al. 2018). Historically, multiple imaging modalities were used for the diagnosis of urinary stones, but most commonly, computed tomography, sonography and plain film X-ray remain the main focused imaging modalities. Magnetic resonance imaging is also used for the diagnosis of urinary stones from time to time, but because of its lack of availability, expensiveness and time consumption, it has remained very limited (Yuzlan and Hamid 2018). The contrast resolution and imaging field of view reproducibility (re-opinion by an expert) of computed tomography is better than other imaging modalities. In this same way, plain film radiography is also better in some cases. But these modalities work by using X-ray radiation for imaging; therefore, their potential for bioeffects is much greater (Bacha and Gilani 2017). In contrast to other imaging modalities, ultrasound is a non-invasive, inexpensive, readily available and relatively quick procedure

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that requires no special preparation and is safe for the diagnosis of renal stones (Bacha et al. 2017).

Currently, ultrasound is the imaging modality of choice for the diagnosis of urinary stones, but there are still some limitations that restrict it from being gold standard in this context (Brisbane et al. 2016, Manzoor et al. 2018). Low contrast resolution, limited field of view, some of the artifacts and operator dependency are the most pronounced limitations of sonography (Altaf et al. 2019). But some of the provocative measures, real-time dynamic evaluation, panoramic view reconstruction, color and power Doppler, 3-D and 4-D imaging and elastography in this state-of-the-art modality maintain its supremacy over the other imaging devices (Lu et al. 2019). The reliability of gray-scale ultrasound was calculated to have a sensitivity and specificity of 81% and 100%, respectively, for renal stones and 93% and 100%, respectively, for hydronephrosis. The sensitivity of ultrasound in the detection of ureteric stones was 46%, while hydroureter was 50%. It was concluded that the diagnostic efficacy of sonography is better for hydronephrosis and gradually decreases for renal stones, hydroureter and ureteric stones (Lu et al. 2019). The gray-scale sonographic criteria for renal stones is an echogenic focus having acoustic shadowing that depends on the stone's size and the transducer frequency (Sim 2018). Of all the renal stones that have no acoustic shadowing, some of the small renal stones have either no acoustic shadowing or a faint shadow that could not be accounted for on a gray-scale image (Simon et al. 2017). The sensitivity of gray-scale criteria for detecting urinary stones is almost 100% for stones more than 5 mm in size, but it is very poor for stones less than 4 mm (Sim 2018).

The application of color Doppler and the generation of the twinkling artifact by the urinary stones is not only useful for the confirmation of large urinary stones but also of great value in the diagnosis of those small stones, which could usually be missed by the conventional gray-scale sonographic criteria (Gliga et al. 2017). The twinkling artifact could be generated by many pathologic and normal anatomic structures in the human body, such as calcification in the thyroid, liver, vessel wall, uterine fibroid, *etc.*; bowel gases; foreign body (surgical clips, staples and intrauterine contraceptive devices); the balloon of a foley catheter; and the majority of the urinary stones (Bacha et al. 2019). A number of articles have already been published in the literature regarding the phenomena of twinkling artifact and the factors effecting it (*i.e.,* size, chemical composition and location of the urinary stone, as well as the machine settings, such as pulse repetition frequency, Doppler frequency, focal point, *etc*). But in the present study, we tried to apply color Doppler to detect the twinkling artifact in a very large number of individuals in our population to achieve a maximum reliability and reduce sample size−related error.

## MATERIALS AND METHODS

We conducted a cross-sectional observational study over a long period of time (6 y) from May 5, 2013 to June 20, 2019 at Gilani Ultrasound Center, Lahore, Pakistan. A total of 1350 patients were conveniently recruited with their consent. The study aimed to compare the reliability of gray-scale sonographic criteria and color Doppler twinkling artifact in the diagnosis of urinary stones in different parts of the urinary tract (*i.e.,* kidneys, ureters, bladder and prostatic part of the urethra) with optimum machine settings. The purpose of the large sample size and the long study time was to minimize systematic errors and random errors. The observed stones were followed and confirmed with either surgery, computed tomography or collection of the extracted stone by the patient during micturition, and this group was termed as confirmed positive urinary stones. The other group was termed as confirmed negative, had no history of any urinary stones and were examined with ultrasound, but no evidence of any stone was found in the urinary tract. For patients whose stones were obscured by bowel gases, some additional provocative measures were followed such as graded compression, intake of excessive water and an approximately 15 min walk to settle/ avoid the gases and visualize the stone, especially in the ureters. Approval was received from the institutional review board and the Ethical Committee of the University of Lahore because the study was performed on human patients. A single ultrasound unit Toshiba Xario (Toshiba Medical System) with convex transducer frequency ranging from 3−6 MHz was used for this study. The procedure and aim of the research was explained to the patients, and signed written informed consent was obtained. The American Institute of Ultrasound in Medicine guidelines for abdominal scanning were followed in this study, as is routinely observed in this department (Cohen et al. 2008). The privacy of the patient was kept on a top priority. A single accredited sonologist evaluated the entire urinary tract with gray-scale sonography, and then color Doppler was applied to observe twinkling artifact generated by the stone. Additional variables, like patient age, sex and family history, were also noted. Microsoft Word and Excel 2016 were used for the collection and organization of data, and the Statistical Package for the Social Sciences (SPSS) version 24 (SPSS 24, IBM, Armonk, NY, USA) software was used for the evaluation of data and formation of graphs. The results were summarized in the form of graphs and tables. Specificity and sensitivity were calculated with a $2 \times 2$ contingency table, and

Table 1. Comparison of men and women with and without urinary stones

| Sex x Confirmed Cross-tabulation | | Confirmed: No stone | Confirmed: Urinary stone* | Total |
|---|---|---|---|---|
| Sex | Female | 252 (18.67) | 247 (18.29) | 499 (36.96) |
| | Male | 435 (32.22) | 416 (30.81) | 851 (63.04) |
| Total | | 687 (50.89) | 663 (49.11) | 1350 (100) |

* Data are presented as no. (%).

comparison of means of the urinary stones at different anatomic regions were measured with an independent sample *t*-test. Descriptive data is explained in the form of frequency, mean and standard deviation.

## RESULTS

We recruited 1350 patients, including 663 (49.12%) patients with confirmed urinary stones and 687 (50.89%) patients without urinary stones. The mean age of the patients with and without urinary stones was 37.56 ± 18.46 y and 37.39 ± 18.34 y, respectively. The number and percentage of men and women was 851 (63.03%) and 499 (36.96%), respectively, and the mean age of the men and women was 38.95 ± 17.881 y and 34.94 ± 18.987 y, respectively. Details about the patients is given in Table 1. A significant relationship was found between the size of urinary stone and age of the patient, with a $p$ value of 0.039. The mean stone size with standard deviation and the range and occurrence in various parts of the urinary tract are given in detail in Table 2. Comparison of the mean stone size with standard deviation, minimum, maximum and frequency in various parts of the urinary tract and presence of the acoustic shadow and twinkling artifact are given in Table 3. Sensitivity and specificity of the gray-scale ultrasound criteria in the detection of urinary stones was 96.1% and 57.9%, respectively. Meanwhile, the sensitivity and specificity of the color Doppler twinkling artifact in the detection of urinary stones was 100.0%% and 97.4%, respectively, as shown in Figure 1.

## DISCUSSION

Doppler ultrasound has mainly been used for the evaluation of cardiovascular pathologies. However, similar to gray-scale sonography, various artifacts are encountered during Doppler scanning, which deteriorate the imaging quality and diagnosis (Mazoor et al. 2017; Abbasi et al. 2018). Among these artifacts, the color Doppler twinkling artifact is considered a useful diagnostic sign for the reliable evaluation of stones in the urinary tract (*i.e.,* kidney, ureter, bladder and urethra) as shown in Figures 2−4. The twinkling artifact was found in multiple rough-surfaced strong reflectors (*i.e.,* calcified lesions in the liver, gallbladder adenomyomatosis, hepatic bile duct hamartoma, encrusted indwelling urinary stents, bowel gas, metallic foreign bodies, gallstones and choledocholithiasis, chronic pancreatitis and urinary stones) (Bacha et al. 2019). Ultrasound is very useful because it is non-invasive, non-ionizing, easy to use and less time consuming, *etc.*, and color Doppler twinkling artifact is used to confirm urinary stones (Hassan et al. 2019, Manzoor et al. 2019). Urinary stones were more common in men compared with women, either because of the length of the urethra or hard work in warm, like forming or labor, etc. leading to excessive sweating. Whatever the cause may be, men are more prone to develop urinary stones compared with women (Manzoor et al. 2018). A study was conducted on a huge

Table 2. Comparison of the mean stone size with standard deviation, range and occurrence (number/percentage) in various parts of the urinary tract

| Location of stone | Number (%) | Mean stone size (mm) | Std. Deviation | Minimum | Maximum |
|---|---|---|---|---|---|
| Kidney | 213 (32.13) | 8.93 | 3.37 | 3.47 | 22.28 |
| Proximal part of ureter | 133 (20.06) | 8.12 | 2.23 | 5.00 | 14.98 |
| Ureterovesical junction | 130 (19.6) | 8.61 | 2.46 | 4.33 | 19.08 |
| Bladder | 61 (9.2) | 10.24 | 3.87 | 5.00 | 23.35 |
| Iliac crossing | 57 (8.59) | 7.98 | 1.56 | 6.10 | 13.00 |
| Mid part of the ureter | 45 (6.79) | 7.58 | 1.89 | 5.12 | 14.00 |
| Prostatic urethra | 24 (3.62) | 7.83 | 2.41 | 4.00 | 11.80 |
| Total | 663 (100) | 8.61 | 2.88 | 3.47 | 23.35 |

Std. deviation = standard deviation.

Table 3. Comparison of the mean stone size with standard deviation, range and occurrence in various parts of the urinary tract

| Comparison of mean stone size in various parts of the urinary tract | Acoustic shad | Number (%) | Mean stone size (mm) | Std. Deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|
| Acoustic shad from the kidney stones | No | 21 (3.17) | 4.97 | 1.27 | 3.47 | 8.40 |
| | Yes | 192 (28.96) | 9.36 | 3.25 | 3.80 | 22.28 |
| Twinkling artifact from the kidney stones | No | 2 (0.30) | 7.05 | 1.91 | 5.70 | 8.40 |
| | Yes | 211 (31.83) | 8.95 | 3.38 | 3.47 | 22.28 |
| Acoustic shad from stones at the proximal part of the ureter | No | 98 (14.78) | 7.37 | 1.75 | 5.00 | 13.32 |
| | Yes | 35 (5.28) | 10.25 | 2.08 | 5.05 | 14.98 |
| Twinkling artifact from the stones in the proximal part of the ureter | No | 5 (0.75) | 7.84 | 2.59 | 5.00 | 11.00 |
| | Yes | 128 (19.31) | 8.14 | 2.23 | 5.00 | 14.98 |
| Acoustic shad from the stones at the ureterovesical junction | No | 98 (14.78) | 7.37 | 1.75 | 5.00 | 13.32 |
| | Yes | 35 (5.28) | 10.25 | 2.08 | 5.05 | 14.98 |
| Twinkling artifact from the stones at the ureterovesical junction | No | 5 (0.75) | 7.84 | 2.59 | 5.00 | 11.00 |
| | Yes | 128 (19.31) | 8.14 | 2.23 | 5.00 | 14.98 |
| Acoustic shad from the stones in the urinary bladder | No | 1 (0.15) | 9.25 | 0.00 | 9.25 | 9.25 |
| | Yes | 60 (9.05) | 10.25 | 3.90 | 5.00 | 23.35 |
| Twinkling artifact from the stones in the urinary bladder | No | 3 (0.45) | 6.91 | 2.03 | 5.73 | 9.25 |
| | Yes | 58 (8.75) | 10.41 | 3.88 | 5.00 | 23.35 |
| Acoustic shad from the stones at the iliac vessels crossing | No | 53 (7.99) | 7.79 | 1.43 | 6.10 | 13.00 |
| | Yes | 4 (0.60) | 10.55 | 0.81 | 9.80 | 11.30 |
| Twinkling artifact from the stones at the iliac vessels crossing | No | 2 (0.30) | 9.00 | 1.41 | 8.00 | 10.00 |
| | Yes | 55 (8.30) | 7.94 | 1.57 | 6.10 | 13.00 |
| Acoustic shadow from the stones at the mid part of the ureter | No | 40 (6.03) | 7.33 | 1.66 | 5.12 | 13.80 |
| | Yes | 5 (0.75) | 9.61 | 2.60 | 7.40 | 14.00 |
| Twinkling artifact from the stones at mid part of the ureter | No | 1 (0.15) | 8.60 | 0.00 | 8.60 | 8.60 |
| | Yes | 44 (6.64) | 7.56 | 1.91 | 5.12 | 14.00 |
| Acoustic shadow from the stones in the prostatic urethra | No | 9 (1.36) | 5.88 | 1.21 | 4.00 | 7.70 |
| | Yes | 15 (2.26) | 9.00 | 2.19 | 5.12 | 11.80 |
| Twinkling artifact from the stones the prostatic urethra | No | 24 (3.62) | 7.83 | 2.41 | 4.00 | 11.80 |
| | Yes | 0 (0.00) | 0.00 | 0.00 | 0.00 | 0.00 |

shad = shadowing; Std. deviation = standard deviation.

number of patients (5661) to evaluate the relationship of urinary stones with sex. Among the patients, 40.9% were women and 59.1% were men (Şahin et al. 2019). It was also obvious from the present study that men develop more urinary stones compared with women (Table 1). Urinary stones could be found in any part of the urinary tract. A two-stage model was formulated for the formation of urinary stones. According to that model, stones are generated because of the deposition of crystals in the collecting system, which then travel to the ureters,

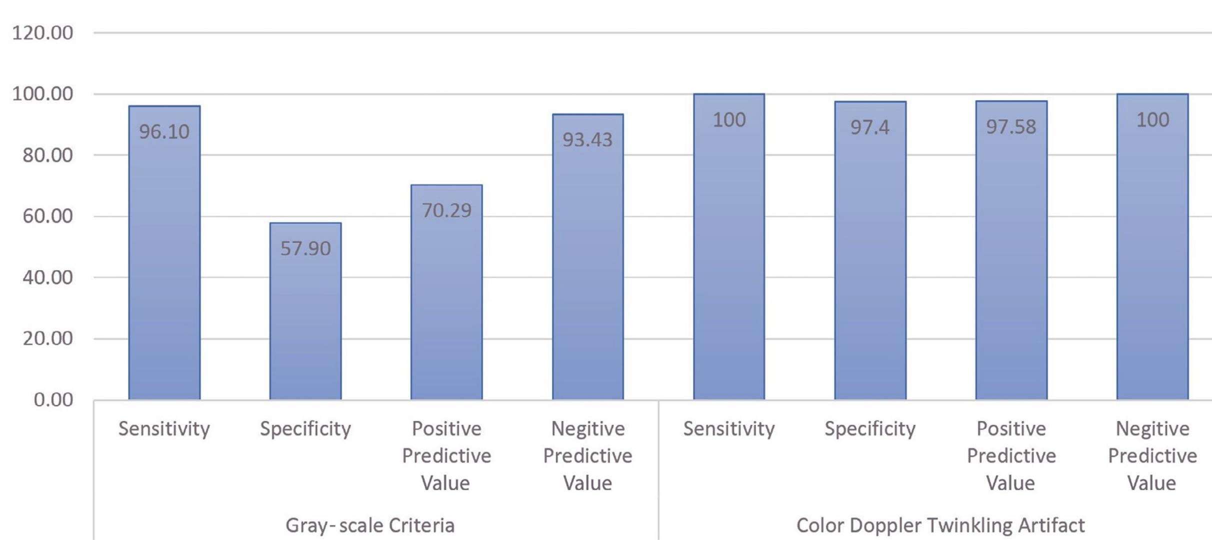


Fig. 1. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the gray-scale criteria and color Doppler twinkling artifact for the detection of urinary stones.

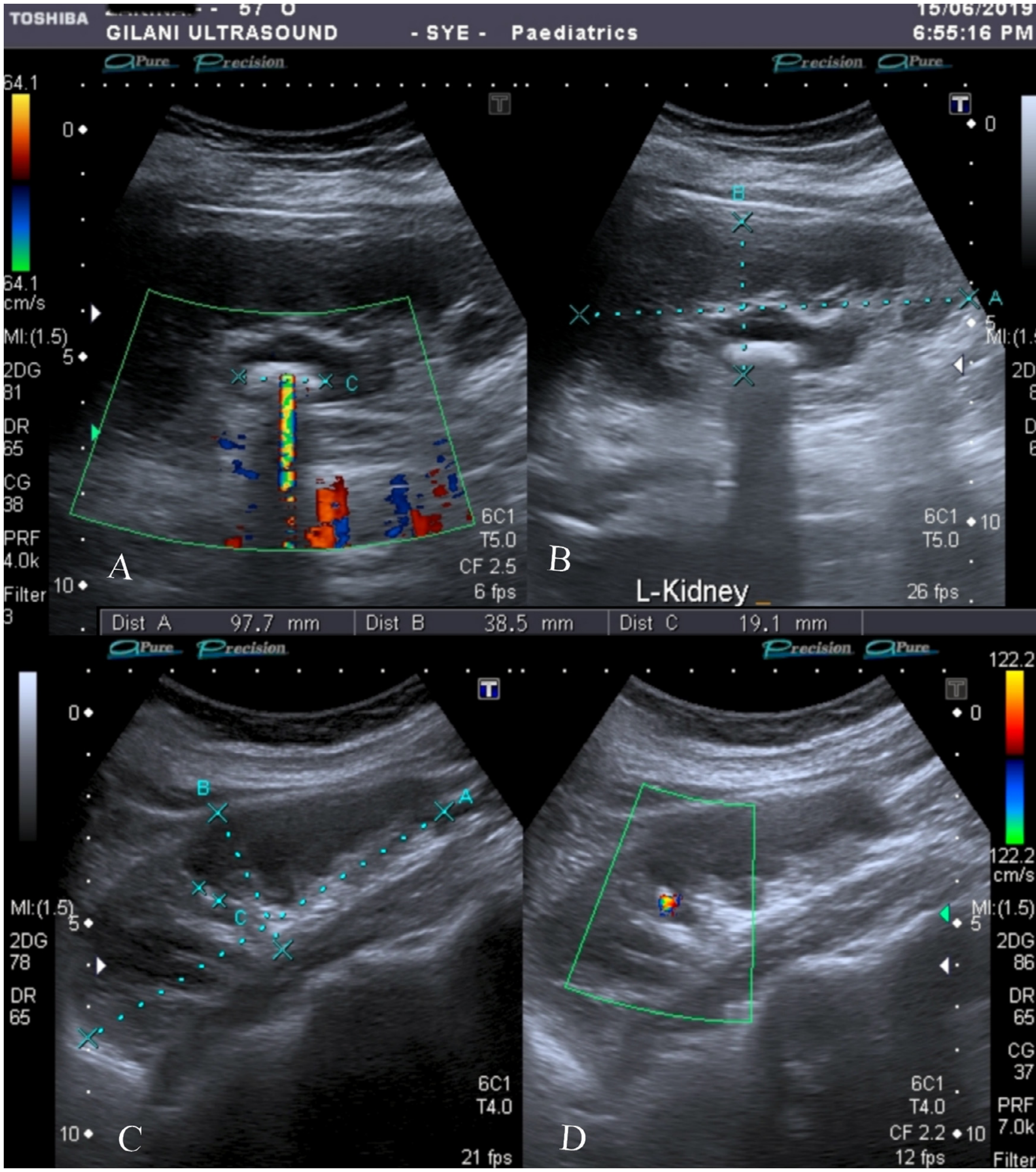


Fig. 2. (a) and (b) are images of the same kidney with and without color Doppler twinkling artifact. This stone has a prominent acoustic shadow because it is large. But (c) and (d) are images in the same kidney of a stone with no acoustic shadow (c), but color Doppler twinkling artifact is present (d).

bladder and urethra (Lovett et al. 2018). According to Yongzhi et al. (2018), urinary stones vary in frequency in various site of the urinary tract (*i.e.,* renal stone 34%, ureteral stone 34.74%, bladder stone 6.20%, urethral stone 1.36% and stones in multiple sites 23.70%). The results of the present study regarding the site of the stones in the urinary tract agree with previous studies (Table 2).

Conventionally, urinary stones in the urinary tract were identified with the gray-scale criteria (highly attenuating echogenic focus with acoustic shadowing). This conventional sonographic criteria was well applicable on large stones (more than 5 mm) because large stones have a clear acoustic shadow (Fig. 2a, 2b) (Bacha and Gilani 2017). But a stone adjacent to a strong reflector (*i.e.,* in the renal sinus, especially in senile patients and patients with chronic renal parenchymal disease) or a stone in the ureter along with gas in the adjacent gut loops have either no or faint acoustic shadow (Fig. 2c, 2d). These stones are often missed when relying only on

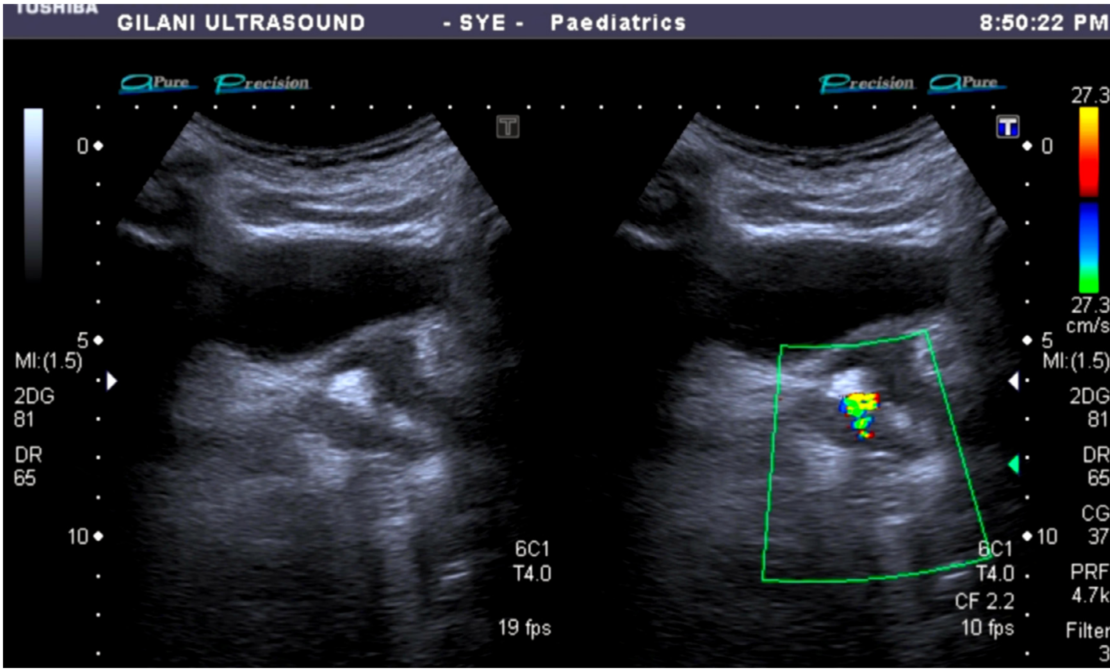


Fig. 3. A stone in the prostatic part of the urethra has a faint shadow because of its position adjacent to strong reflectors (gases in the rectum posterior to the stone), but color Doppler twinkling artifact is able to recognize it.

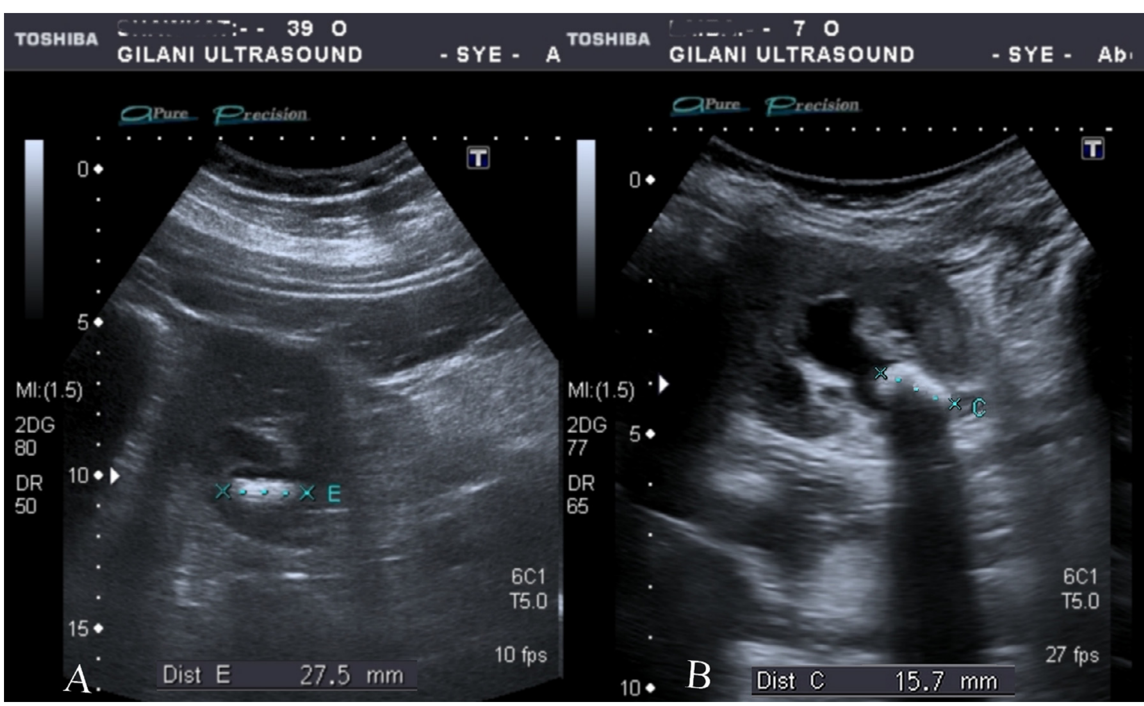


Fig. 4. (a) A 39-y-old man with a renal stone (27.5 mm) that has a faint shadow with optimum machine settings. (b) A 7-y-old boy with a renal stone (15.7 mm) that has a prominent acoustic shadow.

the gray-scale criteria (Roberson et al. 2018). Small stones may pass without causing symptoms, but stones of >5 mm can cause blockage of the ureter, which can result in severe pain. Sometimes these small stones can lodge in the narrow part of the urinary tract to cause an obstruction with related signs and symptoms (Hemminki et al. 2018). An overview was conducted by Brisbane et al (2016) to compare the results of the gray-scale ultrasound, color Doppler twinkling artifact and computed tomography. It was seen that the sensitivity and specificity of ultrasound was 84% and 53%, respectively. It was concluded that ultrasonography should be considered the standard-of-care, first-line imaging modality for all patients with potential nephrolithiasis when a strong suspicion of stones exists. It was also observed that gray-scale sonographic criteria were more useful in children (age <18 y) and thin individuals (body mass index <30 mg/kg$^2$) (Brisbane et al. 2016). In the present study, the sensitivity and specificity of gray-scale sonography in the diagnosis of urinary stones agree with the data already published in the literature. We observed that the size of the urinary stones had a strong correlation with patient age, with a $p$ value of 0.039. The stone's mean size increased with age as the stone gradually grew because of the accumulation of crystals. It was also observed that the acoustic shadow was prominent in younger and thin individuals, but the acoustic shadow was either absent or faint in obese individuals. In Figure 4, the acoustic shadows of a renal stone of a 7-y-old boy and a 39-y-old man were compared. It is obvious that the stone's acoustic shadow in the boy is far better than that of the adult.

The application of color Doppler to observe the twinkling artifact produced by the urinary stone increased the reliability of ultrasound in the diagnosis of urinary stones. Liu et al. (2019) compared the reliability of twinkling artifact with gold standard computed tomography. It was observed that the sensitivity and specificity of color Doppler twinkling artifact was 96.98% and 90.39%, respectively, while the positive predictive value and negative predictive value of the color Doppler twinkling artifact was 99.77% and 41.23%, respectively. In the present study, the sensitivity, specificity, positive predictive value and negative predictive value are each more than 95%, as shown in Figure 1. This increase in the overall reliability is brought about by the application of an additional provocative techniques (machine settings to high pulse repetition frequency/scale) (Bacha et al. 2019). The diagnostic accuracy of gray-scale acoustic shadowing and twinkling artifact were compared in a study by Wang et al. (2019). They included 117 patients with urinary stones confirmed with computed tomography. Three groups of physicians examined the patients and concluded that twinkling artifact was more consistent and had better diagnostic sensitivity than that of shadowing for the diagnosis of ureteral stones. The stone size was also observed to have a close keen impact on both twinkling and acoustic shadowing, with a $p$ value $< 0.001$ (Wang et al. 2019). In the present study, the conventional gray-scale criteria and application color Doppler twinkling artifact was compared in different parts of the urinary tract (Table 3). It was observed that many stones were missed in the ureters, especially in the mid part of the ureter, because of excessive amount of gases by gray-scale ultrasound, but these were found by the application of twinkling artifact along with some provocative measures (*i.e.,* preparation of the patient, graded compression use of high pulse repetition frequency/scale and reexamining the patient in suspicious cases after a walk of about 15 min). Color Doppler twinkling artifact along with other provocative measures increases ultrasound's reliability to more than 90% in the visualization of urinary stones.

## CONCLUSION

The application of twinkling artifact is useful in the confirmation of urinary stones, but specifically, it is of great diagnostic value in the small (less than 5 mm) renal stones and in the stones adjacent to a strong reflector, such as, ureteric stones or stones in the prostatic urethra.

*Conflict of interest disclosure*—The authors declare no competing interests.

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