ORIGINAL PAPER

UROLITHIASIS

Could twinkling artifact be a parameter in predicting the success of shock wave lithotripsy? A prospective study

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Introduction It is important to predict success before the treatment of urolithiasis. We aimed to predict the success of shock wave lithotripsy (SWL) by comparing twinkling artifact (TA) revealed through colour Doppler ultrasonography (CDUS) with stone density in non-contrast computed tomography (NCCT).

Material and methods Eighty patients who underwent SWL between January 2021 and January 2022 were included in the study. Patients with stones of 5–20 mm in the renal pelvis and proximal ureter at NCCT were included. Patients' demographics, Hounsfield units (HU) in NCCT, and TA grades in CDUS were recorded. The stone-free rate after SWL, additional treatments, overall success rates, and the association between TA and success rates were evaluated.

Results The mean age was 47.41 ±15.08 years. The mean BMI was 24.49 ±3.67 kg/m^2. Twenty-three (28.8%) patients were TA grade 0, 33 (41.2%) patients were grade 1, and 24 (30%) were grade 2. The mean HU of TA grades 0, 1, and 2 of stones were 628 ±107, 864 ±123, and 1166 ±292, respectively. The HU increased along with the increase in the TA grade of the stone (p <0.01). The mean number of SWL sessions was 2.26 ±0.75 in patients with TA grade 0, and 2.92 ±0.40 in patients with TA grade 2. The mean number of SWL sessions increased along with the increase in TA grade (p <0.01). The stone-free rate decreased as the TA grade increased. Stone diameter and TA were the only predictors of SWL success.

Conclusions We think that TA may be useful in predicting SWL success.

Key Words: twinkling artifact ‹› kidney stone ‹› shock wave lithotripsy ‹› color Doppler ultrasonography

INTRODUCTION

Urolithiasis is a common systemic disease all over the world. According to the European Association of Urology (EAU) guidelines, shock wave lithotripsy (SWL), ureterorenoscopic lithotripsy, retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL) are the treatment options for stones of different localization and size [1]. SWL is a minimally invasive treatment as the first choice, especially for stones less than 2 cm; however, it has limitations that affect the success rate. One of these limitations is the degree of hardness depending on the chemical structure of the stone. Although there is no precise imaging method that shows the hardness of the stone, the most widely used imaging method is the Hounsfield unit (HU) score in non-contrast computed tomography (NCCT) [2]. Furthermore, recent studies have shown an association between twinkling artifact (TA), which is a sonographic finding, and the chemical composition of the stone and the stone size [3]. The TA (also known as the twinkling sign, twinkle artifact, colour comet-tail artifact, or Doppler twinkling) was first described by Rahmouni et al. [4] to diagnose kidney stones. It comprises red and blue pixel combinations that rapidly change behind a strong reflecting object (e.g., a kidney stone), which is like a turbulent blood flow. This phenomenon is thought to be secondary to intrinsic machine 'noise' within the colour Doppler circuitry of the ultrasound device [5]. There are few studies showing that TA is one of the factors predicting the fragility of stones and the success of SWL [6, 7]. In this study, we aimed to show the effect of TA in predicting SWL success by comparing it with HU.

MATERIAL AND METHODS

The study was approved by Kutahya Health Sciences University Ethics Committee on 30.09.2020 with the decision number 2020-05/04. Following the Ethics Committee approval, 80 patients who had undergone SWL due to kidney stones in the urology clinic of our tertiary referral centre between January 2021 and January 2022 were included in the study. The patients with stones in the renal pelvis and proximal ureter with a diameter between 5 and 20 mm detected by NCCT who agreed to have SWL and consented were included in the study. Patients with body mass index (BMI) over 30 kg/m^2, patients with congenital renal anomalies, and those who had open stone surgery were excluded from the study. The urinary tract infection was evaluated with urine culture before SWL for all patients. In case of bacterial growth, adequate antibiotic treatment was prescribed. SWL treatment was performed after urine culture sterility. Age, gender, stone size, hydronephrosis grade, body mass index, HU, and TA of stones were recorded. The stone size was calculated by multiplying the largest axis diameters of the stone that cut each other perpendicularly (mm^2) [8]. NCCT imaging parameters were 120 kV, 300 mA, slice thickness of 5 mm, and reformatting thickness of 1.25. The mean density of the stones was measured as HU in the ROI (region of interest) that covered the entire area of the stone in the tomography section in the abdominal window (WC: 40, WW: 400) where the kidney stone showed the largest area on the axial plane. TA was assessed by CDUS (Logiq 5, GE Medical Systems, Milwaukee, USA). A 3.5-MHz convex probe was used during the examination. Because ultrasonography is an individual decision-dependent imaging technique, patients were evaluated by 2 experienced radiologists. The absence of a TA signal was considered as grade 0, grade 1 was defined as the presence of the artifact but with partial acoustic shadowing, and grade 2 was considered as the presence of the artifact covering the whole acoustic shadowing.

The SWL procedure was performed using an Elmed COMPLIT® lithotripsy (ELMED Medical Systems, Ankara, Turkey) device. SWL was performed in up to 3 sessions. The number of shocks was 1500–2500, and the shock intensity was 14–22 kV with a frequency of 90 shock waves per minute for each session. The treatment was planned to be at least 7 days between 2 sessions. Analgesia was provided through intramuscular injection of diclofenac sodium of 75 mg to patients who had pain during SWL. The stone-free status following SWL was assessed by NCCT in the first month. The presence of a stone at and over 4 mm was considered a residual stone, and smaller stones were considered clinically insignificant residual (CIRF) stones. The overall success rate was assessed after all the additional treatments. The success rate after SWL, additional treatments, overall success rates, and the association between TA and success rates were evaluated prospectively.

Statistical Package for Social Sciences (SPSS) for Windows 22.0 (SPSS Inc., Chicago, IL, USA) software was used for statistical analysis. The Kolmogorov-Smirnov/Shapiro-Wilks test was used to test if the data presented normal distribution. The number, percentage, mean, and standard deviation expressions were used for descriptive statistics. The chi-square /Fisher's exact test was used to compare the categorized data. The chi-square/Fisher's exact test, Student's t-test, and Mann-Whitney U tests were used for the analysis of univariate analyses. Any p-value below 0.05 was accepted as statistically significant.

RESULTS

The eighty patients included in the study consisted of 54 (67.5%) males and 26 (32.5%) females. The mean age was 47.41 ±15.08 years. The mean BMI was 24.49 ±3.67 kg/m^2. The mean stone size was 79.51 ±33.4 mm^2 (Table 1). The stone density was 887.01 ±278.55 HU overall. The mean number of SWL sessions was 2.414 ±0.79. No residual fragment was observed in 28 patients after SWL; however, clinically insignificant residual fragments (CIRF, <4 mm) were observed in 7 patients. Residual fragments were detected in 45 patients. The mean residual stone size was detected as 4.61 ±5.16 mm. Semirigid URS was performed on 15 patients, RIRS was performed on 10 patients, and micro-PNL was performed on 4 patients for residual stone treatment. Overall stone-free status was observed in 64 patients (80%) after the additional procedures; however, residual fragments were observed in 16 patients (20%) (Table 2). There were no complications reported.

The TA grades were grade 0 in 23 (28.8%) patients, grade 1 in 33 (41.2%) patients, and grade 2 in 24 (30%) patients. The mean HU of TA grade 0, 1, and 2 stones were 628 ±107, 864 ±123, and 1166 ±292, respectively. It was detected that HU significantly increased along with the increase of TA grade (p <0.01) (Figure 1). The mean number of SWL sessions was 2.26 ±0.75 with grade 0 TA, and 2.92 ±0.40 with grade 2 TA. It was detected that the average number of SWL sessions increased along with the increase in TA grade (p<0.01). The stone-free rate following SWL decreased as the TA grade increased (p = 0.001). Residual fragments were observed in 2 cases with TA grade 0 stones and in 5 cases with TA grade 1 stones. Residual fragments were observed in 9 cases with TA grade 2 stones. There was no statistically significant difference between TA and overall stone-free status (p = 0.829) (Table 3).

Factors affecting the SWL success were also analysed. In the univariate analysis stone largest diameter (mm), stone size (mm²), TA, and HU had a significant effect on the SWL success. In the multivariate analysis, 3 significant factors of univariate analysis (either stone largest diameter or stone size) were included. Stone's largest diameter and TA were the only predictors for SWL success (Table 4, Figure 1).

Table 1. *Patient and stone characteristics*

	(n = 80)
Age (years) (mean ±SD)	47.41 ±15.08
Gender (n) (%)	
Male	54 (67.5)
Female	26 (32.5)
Side (n) (%)	
Right	39 (48.8)
Left	41 (51.2)
BMI (kg/m²) (mean ±SD)	24.49 ±3.67
Stone size (mm²) (mean ±SD)	79.51 ±33.4
Number of stones (n) (%)	
Single	75 (93.8)
Multiple	5 (6.2)
Number of stones (mean ±SD)	1.11 ±0.5
Stone localization (n) (%)	
Renal pelvis	51 (63.75)
Proximal ureter	29 (36.25)
Grade of hydronephrosis (n) (%)	
No	45 (56.2)
Grade 1	28 (35)
Grade 2	6 (7.5)
Grade 3	1 (1.2)

n – number; BMI – body mass index; SD – standard deviation

Table 2. *Twinkling artifact grades, Hounsfield units scores, and post-treatment results of stones*

	(n = 80)
Stone-free rate (n) (%)	35 (43.8)
Residual stone size (mm) (mean ±SD)	4.61 ±5.16
Auxiliary procedure (n) (%)	
Semi-rigid URS	15 (18.75)
RIRS	10 (12.5)
PNL	4 (5)
Overall stone-free rate (n) (%)	64 (80)
Stone Hounsfield Unit (mean ±SD)	887.01 ±278.55
Twinkling grade	
Grade 0	23 (28.8)
Grade 1	33 (41.2)
Grade 2	24 (30)

n – number; URS – ureteroscopy; RIRS – retrograde intrarenal surgery; PNL – percutaneous nephrolithotomy; SD – standard deviation

DISCUSSION

SWL is considered an important treatment option because of its high success rate and minimally invasive method when compared to other methods in the treatment of urolithiasis. However, many studies have shown that PCNL and URS have a higher stone-free rate than SWL [9]. There are some limitations to the success rate of SWL such as stone characteristics (size, location, composition, number), lithotripter type, and kidney anatomy. Therefore, it is important to identify potential predictors of SWL outcomes and define the ideal treatment option for each patient. Stone fragility is one of these parameters. The most important factor determining the stone's fragility is its composition [10]. Stone analysis is an important step in deciding the type of treatment. However, it is not possible to make a stone analysis without the stone fragments. Therefore, methods

Table 3. *Comparison of twinkling artifact grade with Hounsfield Units and the effect of twinkling artifact grade on the number of shock wave lithotripsy sessions and success rates*

	(n = 80)	p-value
Mean Hounsfield Unit (±SD)		
Twinkling grade 0	628 ±107	<0.001*
Twinkling grade 1	864 ±123	
Twinkling grade 2	1166 ±292	
Mean ESWL session (±SD)		
Twinkling grade 0	2.26 ±0.75	<0.001*
Twinkling grade 1	2.15 ±0.87	
Twinkling grade 2	2.92 ±0.40	
Stone-free rate (n) (%)		
Twinkling grade 0	17 (73.9)	0.001*
Twinkling grade 1	12 (36.4)	
Twinkling grade 2	6 (25.0)	
Overall stone-free rate (n) (%)		
Twinkling grade 0	2 (12.5)	0.829*
Twinkling grade 1	5 (31.25)	
Twinkling grade 2	9 (56.25)	

*One-way ANOVA, n – number

Table 4. *Factors affecting shock wave lithotripsy success – logistic regression analysis*

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender	0.44	0.165–1.195	0.108			
Age	0.99	0.962–1.021	0.544			
BMI	0.94	0.829–1.062	0.316			
Stone localization	1.28	0.992–1.648	0.057			
Stones' largest diameter (mm)	0.76	0.627–0.913	0.004	0.78	0.636–0.960	0.019
Stone size (mm^2)	0.98	0.969–0.998	0.030			
Stone number	0.38	0.068–2.149	0.276			
Twinkling artifact grade	0.34	0.174–0.657	0.001	0.39	0.194–0.781	0.008
Hounsfield unit	0.99	0.995–0.999	0.006			

BMI – body mass index

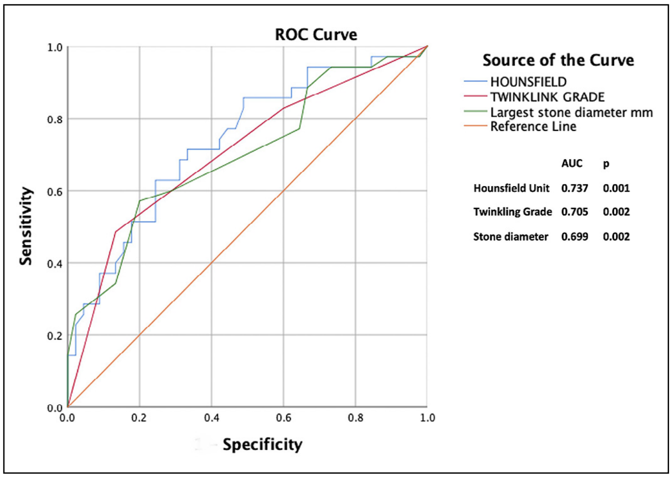

Figure 1. *ROC (receiver operating characteristic) curve of factors affecting shock wave lithotripsy success.*

predicting the SWL success are essential. Although methods such as the degree of opacification of the stone on direct X-ray and molecular concentration measurements in serum and urine are used, there is not an ideal marker. For this purpose, correlations between radiological properties and compositions of stones were investigated in the literature to estimate the effectiveness of lithotripsy before the procedure. The NCCT was frequently used for this purpose, and HU was specially assessed. NCCT enables measurement of the density of the stone by HU to predict its hardness. Patel et al. [11] reported a significant difference between the mean HU values of calcium oxalate, uric acid, and struvite stones in their in vivo studies. Nakada et al. [12] reported no significant difference between the mean HU values of calcium oxalate, uric acid, and struvite stones, in contrast to Patel et al. In particular, kidney stones over 5 mm are observed with echogenic focal lesion and distal acoustic shadowing using US devices. Recent studies found a strong association between the size and density of a stone detected in NCCT and the presence/absence of posterior acoustic shadow detected by US [13, 14]. There are also studies reporting that there is a close association between TA and posterior acoustic shadowing, and TA has greater diagnostic value in kidney stones [15]. In this study, we found a positive correlation between HU and TA, which was used to predict treatment in patients who underwent SWL. In addition, the success rate of SWL decreased with an increase in TA grade in the study.

The HU value of the stone calculated by NCCT is an important factor in predicting the fragility of the stone before SWL. Stones with more than 1000 HU are more resistant to SWL [16]. Alan et al. [6] did not detect any significant association when they compared the TA and HU values of urinary stones in their study. Hassani et al. [17] did not find any significant correlation between the TA grades of calcium-containing and non-calcium-containing stones in an in vitro study. It is revealed in the present study that there is a positive correlation between HU – which indicates the hardness of the stone – and TA. It should be noted that the differences in HU value may be due to the method of measuring the CT attenuation value of the urinary stone or the difference in the CT acquisition protocol. In the present study, the TA grade 0 stones presented lower HU, and the success rate was higher after SWL. The success rate after SWL decreased along with the grade increase of TA. In the multivariate analysis of our study, TA was found to be an independent predictor of SWL success, while HU was not. El-Nahas et al. [16] revealed that one of the factors predicting SWL success was HU. Similarly, in our study, a positive correlation was found between TA and HU in univariate analysis. However, in multivariate analysis, we found that the HU value was not as effective as TA in predicting SWL success. In our opinion, this shows that TA can be as effective as HU (which has been shown to be effective many times in the literature) in predicting the success of SWL. We think that the correlation between TA and HU and its effect on predicting SWL success can be revealed in future studies with a large number of patients.

Many studies investigated the association between the composition of urinary system stones and TA; however, controversial results have been reported. Chelfouh et al. [7] found in their first in vitro study that TA was frequently observed in calcium oxalate dihydrate and calcium phosphate stones, but it was rarely observed in calcium oxalate monohydrate and urate stones. Lee et al. [18] and Louvet [19] could not detect any correlation between TA and stone composition. Furthermore, Moore et al. [20] found in their in vitro study that all oxalate dihydrate and phosphoric acid stones had TA, some oxalate monohydrate and urate stones could have TA, while some stones did not have significant TA. Hassani et al. [17] found that TA could differentiate between calcium oxalate monohydrate and calcium oxalate dihydrate stones; however, it could not differentiate between calcium and non-calcium stones, calcium oxalate, and calcium phosphate stones, or uric acid and cystine stones. Alan et al. [6] reported that TA was detected in almost all of the calcium oxalate dihydrate and calcium phosphate stones, and in more than half of the calcium oxalate monohydrate and uric acid stones. Imamoglu et al. [21] detected in their study that grade 0 and 1 stones were mostly composed of uric acid stones, and grade 2 stones were mostly composed of cystine stones and calcium oxalate monohydrate stones which are hard. Hassani et al. [17] also reported a correlation between TA grade 2 and cystine stones. In our study, we could not include any stone analysis; however, according to our findings, it can be said that the hardness of the stone increases as the TA grade increases because the increase in TA grade is associated with lower SWL success and higher HU.

There may be many reasons why such different results have been revealed in studies in the literature, and the mixed structure of the stones and radiologist-dependent detection of the TA may be among them. Furthermore, there are differences in the grading systems and in the studies. It was also shown that some of the studies were in vivo and some were in vitro [3, 7, 11, 17]. We believe that the reason for failure to achieve homogenization is the fact that the sources, sizes, and surface morphologies of the stones are different [3–6]. Therefore, we investigated the effect of TA in predicting SWL success rates by minimizing other reasons that would affect success rates rather than stone analysis in the design of our study. We would also like to point out that TA may also be observed for reasons such as parenchymal and tumoural calcifications, and incrustation in ureteral double J catheters [22]. In the present study, the evaluation of stones observed in NCCT in terms of CDUS and TA is important to exclude other pathologies. Furthermore, we believe that the similar number of patients in the TA grade groups included in our study is important in terms of the homogenization of the study.

According to these findings, lower HU and grade 0–1 TA are associated with low-density stones. SWL should be considered primarily due to sensitivity. Stones with higher HU and grade 2 TA suggest harder stones that may predict cystine and calcium oxalate monohydrate stones, and SWL success rates are lower. However, it should be noted that some of these may be mixed stones. In line with these results, we detected a significant increase in the number of sessions of SWL along with a grade increase in TA. Therefore, it would be more appropriate to consider a surgical method other than SWL in stones with higher grade TA.

One of the limitations of our study is the lack of analysis of stone composition, although the stones were evaluated with HU and TA. The limited number of patients was another limitation of our study, which might be due to the strict inclusion criteria. However, this study might be an important study in evaluating the relationship between TA and SWL.

CONCLUSIONS

Shockwave lithotripsy is an important treatment option for urolithiasis. We think that TA can be useful in predicting the fragility of stones when applying SWL. Prospective studies with larger patient series are needed to clarify the factors affecting the success and to reveal the association with TA while determining the treatment methods.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis. Eur Urol. 2016; 69: 468-474.

2. Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W. Hounsfield unit density in the determination of urinary stone composition. Urology. 2001; 58: 170-173.

3. Shang M, Sun X, Liu Q, et al. Quantitative Evaluation of the Effects of Urinary Stone Composition and Size on Color Doppler Twinkling Artifact: A Phantom Study. J Ultrasound Med. 2017; 36: 733-740.

4. Rahmouni A, Bargoin R, Herment A, Bargoin N, Vasile N. Color Doppler twinkling artifact in hyperechoic regions. Radiology. 1996; 199: 269-271.

5. Laher AE, McDowall J, Gerber L, et al. The ultrasound 'twinkling artefact' in the diagnosis of urolithiasis: hocus or valuable point-of-care-ultrasound? A systematic review and meta-analysis. Eur J Emerg Med. 2020; 27: 13-20.

6. Alan C, Koçoğlu H, Kosar S, Karatag O, Ersay AR, Erhan A. Role of twinkling artifact in characterization of urinary calculi. Actas Urol Esp. 2011; 35: 396-402.

7. Chelfouh N, Grenier N, Higueret D, et al. Characterization of urinary calculi: in vitro study of 'twinkling artifact' revealed by color-flow sonography. AJR Am J Roentgenol. 1998; 171: 1055-1060.

8. Bayar G, Kadihasanoglu M, Aydin M, Sariogullari U, Tanriverdi O, Kendirici M. The effect of stone localization on the success and complication rates of percutaneous nephrolithotomy. Urol J. 2014; 11: 1938-1942.

9. Yamashita S, Kohjimoto Y, Iguchi T, Nishizawa S, Kikkawa K, Hara I. Ureteral wall volume at ureteral stone site is a critical predictor for shock wave lithotripsy outcomes: comparison with ureteral wall thickness and area. Urolithiasis. 2020; 48: 361-368.

10. Dretler SP. Stone fragility - a new therapeutic distinction. J Urol. 1988; 139: 1124-1127.

11. Patel SR, Haleblian G, Zabbo A, Pareek G. Hounsfield units on computed tomography predict calcium stone subtype composition. Urol Int. 2009; 83: 175-180.

12. Nakada SY, Hoff DG, Attai S, Heisey D, Blankenbaker D, Pozniak M. Determination of stone composition by noncontrast spiral computed tomography in the clinical setting. Urology. 2000; 55: 816-819.

13. Dai JC, Dunmire B, Sternberg KM, et al. Retrospective comparison of measured stone size and posterior acoustic shadow width in clinical ultrasound images. World J Urol. 2018; 36: 727-732.

14. Korkmaz M, Aras B, Sanal B, et al. Investigating the clinical significance of twinkling artifacts in patients with urolithiasis smaller than 5 mm. Jpn J Radiol. 2014; 32: 482-486.

15. Mitterberger M, Aigner F, Pallwein L, et al. Sonographic detection of renal and ureteral stones. Value of the twinkling sign. Int Braz J Urol. 2009; 35: 532-541.

16. El-Nahas AR, El-Assmy AM, Mansour O, Sheir KZ. A prospective multivariate analysis of factors predicting stone disintegration by extracorporeal shock wave lithotripsy: the value of high-resolution noncontrast computed tomography. Eur Urol. 2007; 51: 1688-1694.

17. Hassani H, Raynal G, Spie R, Daudon M, Vallée JN. Imaging-based assessment of the mineral composition of urinary stones: an in vitro study of the combination of hounsfield unit measurement in noncontrast helical computerized tomography and the twinkling artifact in color Doppler ultrasound. Ultrasound Med Biol. 2012; 38: 803-810.

18. Lee JY, Kim SH, Cho JY, Han D. Color and power Doppler twinkling artifacts from urinary stones: clinical observations and phantom studies. AJR Am J Roentgenol. 2001; 176: 1441-1445.

19. Louvet A. Twinkling artifact in small animal color-Doppler sonography. Vet Radiol Ultrasound. 2006; 47: 384-390.

20. Moore SL, Somani BK, Cook P. Journey of a cystinuric patient with a long-term follow-up from a medical stone clinic: necessity to be SaFER (stone and fragments entirely removed). Urolithiasis. 2019; 47: 165-170.

21. İmamoğlu Ç, Gül Büyükbayraktar İmamoğlu F, Gök A, et al. Characterization Of Kidney Stones With Imaging Modalities: Twinkling Artifact In Color Doppler Ultrasound And Density In Non-Contrast-Enhanced CT. Tepecik Eğit Hast Derg. 2016; 26: 120-126.

22. Conkbayir I, Yanik B, Senyücel C, Hekimoğlu B. Twinkling artifact in color Doppler ultrasonography: pictorial essay. Tani Girisim Radyol. 2003; 9: 407-410.