การตรวจสอบความแม่นยำของทวิงกลิ้ง อาร์ทิเฟคท์ และปัจจัยอื่น ๆ ที่สำคัญด้วยโมเดลการทำนายเพื่อการวินิจฉัยนิ่วในไต

รุจิลักษณ์ โรจน์ธำรงค์ พ.บ.
กลุ่มงานรังสีวิทยา โรงพยาบาลพระนั่งเกล้า ตำบลบางกระสอ อำเภอเมืองนนทบุรี จังหวัดนนทบุรี 11000

Validation of the Twinkling Artifact and other Significant Factors Using Predictive Model for Diagnostic of Renal Stone

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Abstract

Background: Renal calculi, also known as renal stones, are a significant global health concern. While CT is the preferred method for diagnosing these conditions, it has drawbacks in terms of cost and radiation hazards. Ultrasound imaging is widely used for renal stone screening and initial diagnosis, with CT scans used for confirmation. The presence of the twinkling artifact enhances ultrasound sensitivity for detecting renal stones, but its accuracy should be considered in context. Relying solely on this artifact can lead to overdiagnosis of renal stones during ultrasound exams, resulting in unnecessary CT scans. In 2022, a research publication aimed to enhance the accuracy of the twinkling artifact in diagnosing renal stones. The study introduced the "kidney stone predictive model" as a proposed method to improve diagnostic precision in this area. Objective: To validate the diagnostic performance of the kidney stone predictive model for renal stone diagnosis. Methods: A cross-sectional study examined patients referred for CT scans to investigate kidney stones. On the same day, ultrasound imaging was conducted to document the twinkling artifact and its variability. CT scans were used as the reference standard for stone diagnosis. ROC curves were utilized to analyze the sizes of the twinkling artifact, facilitating calculations of prevalence and diagnostic performance. Results: Out of 82 twinkling artifacts, 37 (45.1%) were confirmed as renal stones by CT scans. The median size was 5.69 mm (±3.48). A twinkling artifact size of 5.0 mm showed overall accuracy of 79.3% sensitivity of 83.8% and specificity of 73.3%. The model demonstrated an accuracy of 82.9%, sensitivity of 75.7% and specificity of 88.9%. No significant differences were observed between the original and validation studies. Conclusions: The kidney stone predictive model demonstrates strong diagnostic performance and moderate interobserver agreement in diagnosing renal stones, making it an effective and accurate diagnostic tool.

Keywords: Twinkling artifact, Kidney stones, Ultrasound

บทคัดย่อ

ภูมิหลัง: ภาวะนิ่วในไตเป็นปัญหาที่พบได้บ่อย การตรวจมาตรฐานสูงสุดคือการทำเอกซเรย์คอมพิวเตอร์ แต่มีค่าใช้จ่ายสูงและคนไข้ได้รับรังสี การทำอัลตร้าซาวด์มีค่าใช้จ่ายต่ำกว่าและคนไข้ไม่ได้รับรังสีจึงเหมาะแก่การนำมาคัดกรองภาวะนิ่วในไตเบื้องต้น ถ้าหากอัลตร้าซาวด์แล้วพบว่าเป็นนิ่ว จะมีการพิจารณาส่งทำเอกซเรย์คอมพิวเตอร์เพื่อประเมินต่อไป ทวิงกลิ้ง อาร์ทิเฟคท์เป็นลักษณะที่พบในการตรวจอัลตร้าซาวด์ที่ช่วยเพิ่มความไวในการตรวจพบนิ่วในไต แต่พบว่าทวิงกลิ้ง อาร์ทิเฟคท์มีความจำเพาะไม่สูงจึงทำให้วินิจฉัยนิ่วในไตจากอัลตร้าซาวด์เพิ่มมากเกิน ส่งผลให้มีการส่งตรวจเอกซเรย์คอมพิวเตอร์เกินจำเป็น ปี 2565 ได้มีการศึกษาเพื่อเพิ่มความแม่นยำในการวินิจฉัยนิ่วจากอัลตร้าซาวด์

โดยพบปัจจัยที่มีผลต่อการวินิจฉัยและได้เสนอแบบการทำนายร่วมกับ ทวิงกลิ้ง อาร์ทิเฟคท์ขึ้นมา **วัตถุประสงค์:** เพื่อตรวจสอบความแม่นยำของแบบการทำนายร่วมกับ ทวิงกลิ้ง อาร์ทิเฟคท์ เพื่อการวินิจฉัยนิ่วในไต **วิธีการ:** เป็นการศึกษาภาคตัดขวางโดยนำผู้ป่วยที่สงสัยภาวะนิ่วในไต และถูกส่งมาทำเอกซเรย์คอมพิวเตอร์ระบบทางเดินปัสสาวะที่โรงพยาบาลพระนั่งเกล้าตั้งแต่ 1 กุมภาพันธ์ 2566 จนถึง 30 เมษายน 2566 โดยนำผู้ป่วยไปทำอัลตร้าซาวด์ไตในวันเดียวกันกับที่ทำเอกซเรย์คอมพิวเตอร์ นำข้อมูลเกี่ยวกับทวิงกลิ้ง อาร์ทิเฟคท์ที่พบมาเทียบกับผลเอกซเรย์คอมพิวเตอร์ **ผล:** ทวิงกลิ้ง อาร์ทิเฟคท์ 82 หน่วย โดย 37 หน่วย (45.1%) พบว่า เป็นนิ่วในเอกซเรย์คอมพิวเตอร์ ค่ามัธยฐานของขนาด ทวิงกลิ้ง อาร์ทิเฟคท์มีค่าเท่ากับ 5.69 มิลลิเมตร ทวิงกลิ้ง อาร์ทิเฟคท์ที่มีขนาดมากกว่าหรือเท่ากับ 5 มิลลิเมตร มีค่าความแม่นยำ ค่าความไว และค่าความจำเพาะ เท่ากับ 79.3%, 83.8% และ 73.3% ตามลำดับ ส่วนแบบการทำนายมีค่าความแม่นยำ ค่าความไว และค่าความจำเพาะ เท่ากับ 82.9%, 75.7% และค่าความจำเพาะ 88.9% ตามลำดับ ไม่มีความแตกต่างอย่างมีนัยสำคัญของค่าความแม่นยำระหว่างแบบการทำนายในการศึกษาก่อนหน้ากับการศึกษาเพื่อทดสอบนี้ **สรุป:** แบบการทำนายในการวินิจฉัยภาวะนิ่วในไตร่วมกับ ทวิงกลิ้ง อาร์ทิเฟคท์ มีค่าความแม่นยำสูง และใกล้เคียงกับการศึกษาที่เสนอแบบการทำนายนี้ ดังนั้นแบบการทำนายนี้จึงสามารถนำมาใช้ได้

คำสำคัญ: ทวิงกลิ้ง อาร์ทิเฟคท์, นิ่วในไต, อัลตร้าซาวด์

Introduction

Renal stone represents a significant global health issue, with a rising prevalence and incidence rates. The prevalence of kidney stones ranges from 5% to 15% in the world population, and in Thailand, the prevalence stands at 6.6%.[1-3]

Various diagnostic modalities, including plain radiographs, ultrasonography, and computed tomography (CT), are utilized to detect renal stones. CT is considered the gold standard for urolithiasis detection; however, it is accompanied by certain limitations and disadvantages, primarily related to radiation exposure due to the use of x-rays for tissue imaging.[4] Ultrasonography (US), on the other hand, is a safe, cost-efficient, and expedient modality employed for renal stone detection. The detection of small stones (<5mm in size) and obscured echoic stones represents a limitation in the realm of renal stone identification through standard gray-scale ultrasound imaging. Nevertheless, its diagnostic accuracy in identifying lithiasis is inferior to that of non-contrast CT images, particularly for smaller stones.[5]

The twinkling artifact (TA), also referred to as the color Doppler comet-tail artifact, manifests as a random mixture of red and blue pixels in the high-frequency shift spectrum behind robust, granular, and irregular reflecting interfaces such as crystals, stones, or calcifications.[6] (Figure 1). This sonographic phenomenon has shown potential in aiding the detection of renal stones.[7] However, it has been associated with a high sensitivity for detecting renal stones, albeit with a notable false positive rate.[8] Recent studies have yielded inconclusive results regarding the relationship between stone size and the diagnostic accuracy of the TA for diagnosing kidney stones.[4, 9, 10]

In 2022, Sasiwimonphan et al. conducted an analysis of associated ultrasound findings to enhance the diagnostic accuracy of the TA in kidney stone diagnosis. The study identified factors influencing diagnostic accuracy and proposed a predictive model that utilizes these factors to rate each TA, thereby improving diagnostic precision. This study conducted an initial assessment of diagnostic performance by utilizing patients within the same institute and employing a specific ultrasound machine.[11]

The principal aim of this validation study is to thoroughly evaluate the accuracy, reliability, and generalizability of diagnostic models. By meticulously examining the model's performance across diverse patient cohorts and utilizing ultrasound data from various vendors, the study seeks to attain consistent and precise identification of specific conditions. Furthermore, the evaluation encompasses an examination of various performance parameters and influential factors, yielding valuable insights that inform well-informed decisions and contribute to the development of robust and effective diagnostic approaches. Additionally, this study provides significant insights into the generalizability of the diagnostic models, while also serving as a quality assurance measure. It facilitates comparative analyses, empowering clinicians in their decision-making processes and ensuring the delivery of accurate diagnoses.

Therefore, the objective of this study was to validate the diagnostic performance of the proposed predictive model.

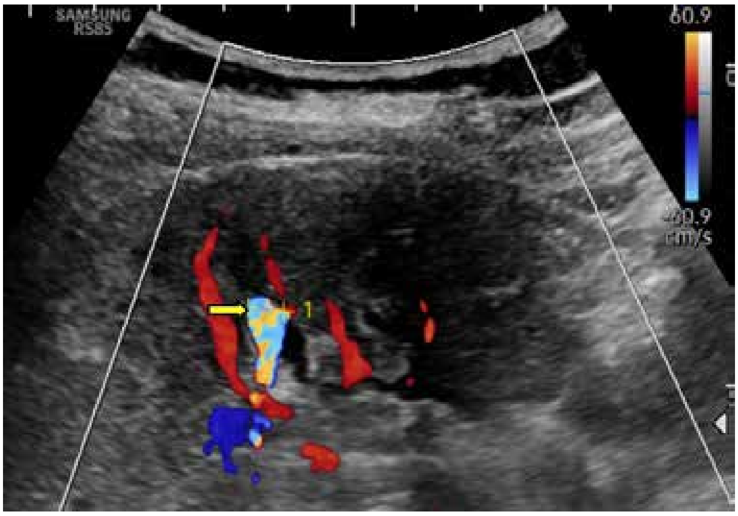

Figure 1. Doppler ultrasonogram showing an area with a twinkling artifact (arrow)

Materials and Methods

Patients

The study protocol received approval from the institutional medical ethics committee of the Pranangklao Hospital. A cross-sectional study was conducted on patients suspected of having kidney stones between February 1, 2023, and April 30, 2023. CT examinations were performed when subsequent sonographic examinations were conducted. During the sonographic examination, the radiologist remained blinded to the CT results.

Achieving appropriate statistical power in diagnostic validation studies necessitates the establishment of an adequate sample size. To determine the suitable sample size for this study, guidance was sought from a statistician and references specific to diagnostic validation studies were consulted. These references offer valuable insights and methodological approaches for sample size determination, thus ensuring the study is adequately powered to detect meaningful differences and relationships. The sample size for this validation study was derived from the methodology outlined in the referenced publication by Bujang et al. (2019)[12] Print with a minimum requirement of 12 positive disease samples and a total minimum sample size of 60.

Sonographic technique

Following the CT scan, patients underwent a sonographic scan of the kidneys using an RS85 SAMSUNG ultrasound machine (Gangnam-gu, Seoul, Korea). The examination was performed by a radiologist with six years of experience, utilizing a CA1-7A convex probe with a curved low-frequency (1-7 MHz). A high pulse repetition frequency (PRF) greater than 60 cm/s was applied to suppress background color signals as much as possible. Grayscale and Doppler color images were observed for the presence or absence of hydronephrosis, areas of high echogenicity with associated shadowing, the TA, and other findings as outlined in the model.

Predictive model

Key findings of twinkling artifacts and the final score assessment was recorded. Another radiologist with six years of experience, who was blinded to the CT scan results, reviewed the ultrasound findings and final scores. The final decision was reached through consensus between the two radiologists. The variables in the model are presented in Table 1. The junctional line was defined as the lining interface between the renal cortex and renal sinus. The tail of the positive TA was defined as having a length longer than its width.

Table 1 Twinkling artifact (TA) predicting model for renal stone[11]

Variable	Score
TA Size (>5 mm)	1
Posterior acoustic shadow	2
Long tail of TA	1
Location at junctional line	1
Total score	5

The cutoff scores of 3 or above were positive for stone

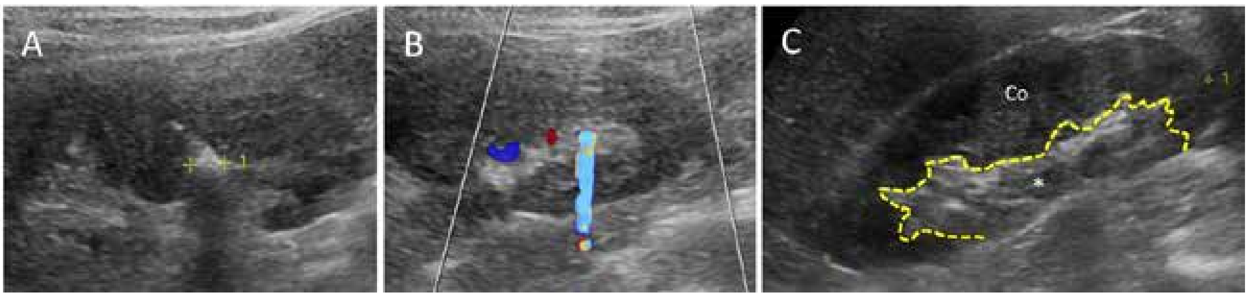

Figure 2. Twinkling artifact (TA) predicting model findings.
(A) Posterior acoustic shadow, lack of signal deep to an imaged tissue interface
(B) The tail of the TA, a length of the TA was longer than its width.
(C) Junctional line, the lining interface (dashed line) between the renal cortex (Co) and renal sinus (asterisk)

Computed tomography technique

CT examinations were performed using the Ingenuity Core128 system (Philips, NV, USA), with a slice thickness/increment of 1.5/1.0 mm and a tube potential of 120 kV. Tube current modulation was employed, and scans were conducted from the top of the kidneys through the base of the bladder (mid-T12 level through the pubic symphysis).

Statistical method

Data analysis was conducted using STATA version 17. Continuous variables were presented as mean ± SD, and categorical data were reported as frequencies and proportions. The optimal cutoff size of the twinkling artifact (TA) was determined using AUC analysis. A significance level of .05 was set for all statistical tests. The interobserver agreement was estimated using intraclass correlation coefficients (ICC). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the model were calculated using the crosstabulation method.

Results

Among the 82 TAs examined, 52 (63.4%) were observed in male patients. The median size of the TAs in color Doppler US was 5.69 mm (+3.48). Kidney stones were detected in 37 TAs (45.12%) based on the CT scan. A posterior acoustic shadow was observed in 21 TAs (25.6%), while 56 TAs (68.3%) were located at the junctional line, and 54 TAs (65.9%) had long tails. The interobserver agreement was calculated to be 0.7.

Table 2 Characteristics of TAs.

Variable	n (%), mean ± SD
Male	52 (63.4%)
Age(year)	53.95 ± 14.37
BMI (ml/min/1.73 m^2)	23.54 ± 4.65
TA Size (>5 mm)	43 (52.4%)
Posterior acoustic shadow	21 (25.6%)
Long tail of TA	54 (65.9%)
Location at junctional line	56 (68.3%)
Final score positive (of 3 or above)	33 (40.2%)
Caliectasis	13 (15.9%)
Location at renal cortex	16 (19.5%)
Presented renal stone in CT	37(45.1%)

TA=Twinkling artifact

ROC curve analysis of the sizes of TAs (Figure 3.) revealed the cutoff at 5.0 mm for renal stone with sensitivity 83.8%, specificity 73.3%, PPV 72.7%, NPV 86.8%, accuracy 79.3%.

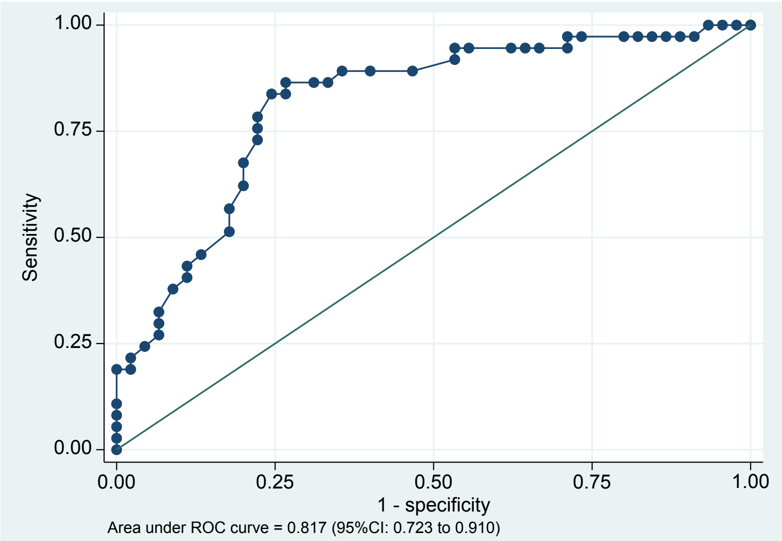

Figure 3. Receiver operating characteristic (ROC) curves for the diagnosis of renal calculus by TA size. AUC=0.817 (95% CI 0.723-0.910)

Table 3 Diagnostic performance of predicting model

	Sensitivity	Specificity	PPV	NPV	Accuracy
TA size>5mm	83.8%	73.3%	72.1%	84.6%	78.0%
Location at junctional line	91.9%	51.1%	60.7%	88.5%	69.5%
Posterior acoustic shadow	48.6%	93.3%	85.7%	68.9%	73.2%
Long tail of TA	78.4%	44.4%	53.7%	71.4%	59.8%
Predictive score (≥3=positive)	**75.7%**	**88.9%**	**84.8%**	**81.6%**	**82.9%**

Table 4 Comparison of diagnostic performances between purposed model study[11] and this validation study

	Purposed model study	Validation study
Sensitivity	75%	75.7%
Specificity	88%	88.9%
PPV	87.5%	84.8%
NPV	75.9%	81.6%
Accuracy	81.1%	82.9%

Furthermore, all 16 TAs located in the renal cortex were negative on the CT scan. Conversely, all TAs with caliectasis showed positive CT results for stone detection.

Discussion

Only a few researchers have evaluated the use of the TA for the detection of nephrolithiasis. However, there is evidence that suggests this artifact may substantially improve the ability of physicians to detect nephrolithiasis with US. In the in vitro study of Shabana et al, the TA associated with renal calculi exhibited a noteworthy enhancement in contrast-to-noise ratio when compared to the gray-scale posterior acoustic shadowing.[13] Lithiasis of smaller dimensions (less than 5 mm) may lack posterior shadowing and exhibit comparable echogenicity to the surrounding structures of the kidney, vessel walls, or renal sinus fat. Consequently, the detection of these stones may be compromised, leading to potential failures in identification[5]. Remarkably, the findings of their study unveiled that the utilization of the twinkling artifact in color Doppler ultrasound surpassed the presence of posterior shadowing as a more accurate method for detecting urolithiasis, yielding a detection rate of 97% compared to 66%.[5]

Other scholars have posited that this particular artifact exhibits a significant potential to enhance the detection of renal calculi in comparison to conventional gray-scale ultrasound imaging. TA can be regarded as a significant marker for the presence of urolithiasis[14] and a major diagnosing sonographic finding in this context.[15]

Even more, TA based color Doppler US is preferable for the sensitive detection of very small nephrolithiasis.[16, 17] Park et al, in 318 patients, reported sensitivity and specificity rates for TA of 98 % and 100 % respectively; meanwhile Korkmaz et al reported only 93% sensitivity and Yavuz et al found a PPV of 88.3% for TA.[14, 16, 18] Chelfouh et al noticed an intriguing interrelation emerged between the stone composition and the presence of the TA. Stones primarily composed of calcium oxalate or calcium phosphate exhibited the TA phenomenon, while a majority of stones predominantly composed of calcium oxalate monohydrate or urate did not manifest the TA.[5, 17] This statement elucidates that certain stones have not exhibited the presence of TA during ultrasound examinations.

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. This finding expounds upon the observation that certain TA have not corresponded to the presence of stones in CT imaging. Aytac and Ozcan concluded that TA can assist in differentiating small stones from other echogenic structures.[19]

Real-time scanning proves invaluable in discerning arterial calcifications from renal calculi, owing to the pulsatile nature of the former. Nevertheless, it is important to note that the twinkling sign can also manifest in cases involving calcifications of renal tumors, renal cysts, and renal parenchyma. Distinguishing these calcifications from renal stones can typically be accomplished by examining their location on real-time scanning in conjunction with the patient's medical history. Interestingly, their findings revealed that using twinkling artifact in color Doppler US is more accurate than the presence of posterior shadowing for the detection of urolithiasis (97% vs. 66%).[5]

The predictive model developed by Sasiwimonphan and Rojthamrong aimed to enhance the accuracy of diagnosing kidney stones and improve communication between radiologists and clinicians. The selected variables in the model demonstrated moderate to high associations with kidney stones.[11]

In the aforementioned study[11], the prevalence of stones in the twinkling artifacts (TAs) was reported as 23.4%, whereas in our study, the prevalence was 45.1%. Nevertheless, no significant differences were observed in the diagnostic performances between the original model study and our validation study, indicating a moderate agreement.

The optimal cutoff size for TAs was similar to the prior study, 5 mm. Notably, the area under the curve (AUC) for TA size in our study was higher than in the previous study, with values of 0.817 and 0.679, respectively. Different studies have reported varying sensitivity levels of renal ultrasound for detecting small renal stones (5 mm). Gliga et al. reported a sensitivity of 99%, while Yavuz et al. found a lower sensitivity of 68.1% for the same stone size. These differences may be attributed to the modalities used to confirm the presence of stones.[16, 20]

However, it should be noted that isolated TA has a high false-positive rate when compared with unenhanced CT images.[21] Therefore, simultaneous interpretation of TA and the predictive model is recommended for highly accurate diagnosis of renal stones.

Regarding the physiopathology of stone location, TAs located in the renal cortex do not necessarily indicate the presence of a stone. Our study also revealed that TAs located in the renal cortex were significantly associated with negative CT results, while associated caliectasis correlated with positive CT results. These additional findings can aid in distinguishing true stones.

The present study has limitations including the lack of information on stone composition, a relatively small sample size, and a study population limited to patients referred for CT scans due to clinical indications of stone disease, potentially introducing selection bias.

Conclusion

The results of our study demonstrate that the kidney stone predictive model exhibits high diagnostic performance and moderate interobserver agreement for diagnosing renal stones. Therefore, this model can be effectively applied for the diagnosis of renal stones.

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