Predicting the Efficacy of Repeated Shockwave Lithotripsy for Treating Patients with Upper Urinary Tract Calculi Using an Artificial Neural Network Model

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Purpose: To establish a prediction model for repeated shockwave lithotripsy (SWL) efficacy to help choose an appropriate treatment plan for patients with a single failed lithotripsy, reducing their treatment burden.

Patients and Methods: The clinical records and imaging data of 304 patients who underwent repeat SWL for upper urinary tract calculi (UUTC) at the Urology Centre of Shiyan People's Hospital between April 2019 and April 2023 were retrospectively collected. This dataset was divided into training (N = 217; 146 males [67.3%] and 71 females [32.7%]) and validation (N = 87; 66 males [75.9%] and 21 females [24.1%]) sets. The overall predictive accuracy of the models was calculated separately for the training and validation. Receiver operating characteristic (ROC) curves were plotted, and the area under the ROC curve (AUC) was calculated. The normalized importance of each independent variable (derived from the one-way analyses) in the input layer of the artificial neural network (ANN) model for the dependent variable (success or failure in repeat SWL) in the output layer was plotted as a bar chart.

Results: This study included 304 patients, of whom 154 (50.7%) underwent successful repeat SWL. Predictive models were constructed in the training set and assessed in the validation set. Fourteen influencing factors were selected as input variables to build an ANN model: age, alcohol, body mass index, sex, hydronephrosis, hematuria, mean stone density (MSD), skin-to-stone distance (SSD), stone heterogeneity index (SHI), stone volume (SV), stone retention time, smoking, stone location, and urinary irritation symptom. The model's AUC was 0.852 (95% confidence interval (CI): 0.8–0.9), and its predictive accuracy for stone clearance in the validation group was 83.3%. The order of importance of the independent variables was MSD > SV > SSD > stone retention time > SHI.

Conclusion: Establishing an ANN model for repeated SWL of UUTC is crucial for optimizing patient care. This model will be pivotal in providing accurate treatment plans for patients with an initial unsuccessful SWL treatment. Moreover, it can significantly enhance the success rate of subsequent SWL treatments, ultimately alleviating patients' treatment burden.

Keywords: artificial neural network model; mean stone density; repeated shockwave lithotripsy; stone heterogeneity index; stone volume; upper urinary tract calculi

INTRODUCTION

The prevalence of urinary lithiasis varies significantly from 1% to 13%worldwide. Its prevalence is lower in Asia (1%–5%) than in North America and Europe.[1] Upper urinary tract calculi (UUTC) account for 70% of all urinary stones and have a high recurrence rate of 40% and 60% at five and nine years, respectively.[2] These stones can lead to complications such as pain, hematuria, obstruction, and infection, significantly impacting patients' quality of life.[3] However, removing the stones may reduce recurrence.[4]

While various treatment options are available for UUTC, shockwave lithotripsy (SWL) and ureteroscopy are two of the most important methods. While the success rate of SWL is low (46.7% after a single session), it remains popular with patients because it is cost-effective, anesthesia-free, and non-invasive.[5,6] However, in cases where the initial SWL treatment fails, patients often require surgical intervention or repeat SWL to remove the stone, leading to increased treatment time and costs. The probability of renal injury also increases with the number of SWL sessions, with minimal additional benefits observed after two SWL sessions targeting the same stone site.[7]

Heviaa et al. investigated the predictive factors of SWL for stone treatment, such as maximum density, maximum diameter, and pyelocaliceal location,[8] and established logistic regression models based on them. Similarly, Zihao et al. considered stone length, course (days), patient age, stone width, and pH value as important predictors and developed an ANN model.[9] However, these studies did not encompass a comprehensive range of influencing factors. Factors such as mean stone

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Received October 2023 & Accepted April 2024

Table 1. Types, usage, and duration of drug-assisted lithotripsy

Drug name	Drug type	Dosage	Usage	Duration
Scopolamine	Anticholinergic	250 mL 0.9% NaCl + 10 mg scopolamine hydrobromide	IV QD	7 days
Resorcinol	Benzodiazepines	250 mL 0.9% NaCl + 120 mg Resorcinol	IV QD	7 days
Tamsulosin capsules	Alpha-blockers	0.2 g BID	PO BID	2–4 weeks
Chinese Herbal Stone Removal Soup	Chinese medicine	One dose daily: decoct about 500 mL of water, take in twice; six doses per course of treatment; rest for three days between courses.	PO QD	2 weeks

Abbreviations: Bid, bis in die; IV, Intravenous injection; PO, peros; QD, quaque die.

density (MSD), stone heterogeneity index (SHI), and stone volume (SV) may provide more accurate predictions regarding the effectiveness of SWL.[10] Additionally, there has been limited discussion about the selection of further treatment options after the failure of the initial SWL treatment. Therefore, practical predictive tools are needed to accurately assess the treatment outcomes of repeat SWL.

In recent years, significant advancements in deep-learning technology have led to the development of neural network tools for urolithiasis. These tools are specifically designed to detect ureteral stones and predict their likelihood of spontaneous passage.[11-13] Neural networks function by emulating the human brain's cognitive processes. Like teaching an individual to recognize objects, a neural network learns to classify objects using sophisticated algorithms. This learning process involves training the network with a vast dataset of numerous images and their corresponding labels.[14] One notable advantage of artificial neural networks (ANN) is their exceptional ability to unravel complex nonlinear relationships and draw robust inferences from interdependent variables,[15] making ANNs highly effective in analyzing intricate data patterns within the field of urolithiasis.

This study aimed to develop and validate a clinical model based on an ANN to accurately predict the effectiveness of repeated SWL in treating UUTC. The utilization of an ANN allows for a more comprehensive analysis of the intricate interactions among healthcare risk factors, surpassing the capabilities of traditional statistical methods. This innovative approach aims to enhance the precision and reliability of treatment outcome predictions in patients undergoing repeat SWL.[16,17]

PATIENTS AND METHODS

Study population

Repeat SWL is a second lithotripsy of the site of the first lithotripsy, with a seven-day interval between them.(18) Clinical data were retrospectively collected from 304 patients who underwent repeat SWL for UUTC at the Urology Centre of Shiyan People's Hospital between April 2019 and April 2023. We divided the training and validation sets according to the chronological order of patients' access to the case system, and included 212 patients who accessed the case system from April 2019 to March 2022 in the training set (70%) for modelling, and 92 patients who accessed the case system from April 2022 to April 2023 in the validation set (30%) for modelling. Patients were enrolled in this study if they (a) had UUTC that met the diagnostic criteria and underwent repeated SWL, (b) were aged $\geq$ 18 and $\leq$ 80 years, and (c) had complete clinical, imaging, and follow-up data. The exclusion criteria were: (a) Combined severe cardiovascular disease or on the verge of death, (b) pregnancy, (c) nephrostomy or double "J" tube placement, (c) history of open ureteral surgery or ureteral stenosis, (d) urological malformations (e.g., horseshoe kidneys, renal malrotation, and ectopic kidneys), and (e) lack of a repeat SWL two weeks after the computed tomography (CT) review. In this study, all procedures involving human participants were performed according to the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Hubei University of Medicine (approval number: 2022-RE-031).

Data collection

Clinical case data and medical records were collected retrospectively, and all influencing factors were collected after the first SWL. The collected clinical data included age, alcohol drinking, body mass index (BMI), sex, hydronephrosis, MSD, smoking, urinary irritation symptoms, stone retention time, hematuria, SV, skin-to-stone distance (SSD), stone location, and SHI. MSD is measured primarily by creating an average of the three regions of interest measured in three different views showing the maximum size of the stone in multi-slice CT, without including the adjacent soft tissues on each slice in the axial plane. SHI is defined as the standard deviation of the MSD.[19] SV was calculated using the ellipsoid formula SV = 0.167 × Lwdπ, where L is the longest diameter of the stone, w is the maximum transverse diameter of the stone, d is the depth, and π = 3.14159.[20] Stone retention time is the length of time a stone remains in the urinary tract. SSD is the skin-to-stone distance in the actual lithotripsy path measured on axial images.

SWL treatment

We used a Shenzhen New Element ZH-VE (CX9002) electromagnetic SWL machine with an ultrasonic localization system for pre-treatment positioning. All patients were treated supine, and UTTC shockwaves were given via the lumbar path. The initial voltage averaged 13 kV (11–15 kV), increasing by 0.3 kV until the maximum voltage the patient thought they could withstand. The number of SWL shocks was no more than 2,500, with a frequency of 60–80 times/min. The interval between the first and repeat SWL was seven days, during which the patients were instructed to drink more than 2 L of water daily. The same team performed the patient's ultrasonic positioning and SWL treatment.

Drug-assisted lithotripsy

We routinely use lithotripsy medications after SWL to promote stone removal.

We currently use scopolamine, resorcinol, tamsulosin capsules, and Chinese Herbal Stone Removal Soup (30 g Ji Nei Jin, 30 g Jin Qian Cao, 20 g Hai Jin Sha, 15 g Bian Xu, 15 g Qu Mai, 15 g Hua Shi, 15 g Che Qian Zi, 10 g Dan Shen, 10 g Wang Bu Liu Xing, 10 g Chi Shao, 12 g Chen Pi, 10 g Zhi Ke, 10 g Mang Xiao, 15 g Niu

Table 2. Multiple imputation methods and the numbers of missing and imputed values.

Variable	Regression type	Missing values	Imputed values
SV	Linear	3	15
MSD	Linear	4	20
Stone retention time	Linear	6	30
Hydronephrosis	Logistic	7	35
SHI	Linear	9	45

Abbreviations: SV, stone volume; MSD, mean stone density; SHI, stone heterogeneity index.

Xi, 6 g Gan Cao, 30 g Hu Zhang, and 3 g Hu Po). The dosage, administration, and duration of these four drugs are shown in **Table 1**.

Study outcomes

Two weeks after hospital discharge, a CT scan was conducted to assess the treatment's effectiveness. In this evaluation, clinically insignificant stone fragments measuring < 4 mm, or as determined by the radiologist through CT analysis, were considered successful outcomes; such patients were included in the repeat SWL treatment group.[21] Conversely, the need for continued SWL or alternative surgical procedures was considered an unsuccessful outcome; such patients were included in the treatment failure group.

Statistical analysis

The dataset was divided chronologically, with 212 patients collected from April 2019 to March 2022 included in the training set and 92 patients collected from April 2022 to April 2023 included in the validation set: a ratio of 7:3. Continuous variables are reported as the mean values ± standard deviation, while categorical variables are presented as the frequency (percentage). The ANN models were developed using the training set and evaluated for their performance using the validation set. Statistical analyses were conducted using SPSS software (version 26.0) and the R statistical software (version 4.3.0). The ANN algorithm was implemented using R's "RSNNS" package. A traditional two-layer multilayer perceptron model was used, incorporating a feed-forward neural network and using the back-propagation algorithm.

Five variables in our dataset had missing data (SHI, MSD, SV, hydronephrosis, and stone retention time), with a missing rate of 9.5%. Among these five variables, SV had three missing values, MSD had four, stone retention time had six, hydronephrosis had seven, and SHI had nine. We used multiple imputation to fill in the missing data.[22] As shown in Table 2, we interpolated the missing values for each variable five times using linear or logistic regression. This method uses the available information from other variables to predict the missing values.[23] Next, the missing values are substituted with the predicted values, creating a complete dataset. The final dataset was obtained by averaging or taking the median of the five imputations and using it as a new dataset for further analysis.

The performance of the developed models was assessed by measuring their accuracy, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC) in the validation set. The AUC was calculated by plotting the true positive rate (sensitivity) against the false positive rate (1 − specificity).

RESULTS

Population characteristics

This retrospective study analyzed the clinical data of 336 patients who underwent repeated SWL treatment for UUTC. Six cases with more than 20% missing influencing factors and 26 without CT findings after the initial lithotripsy were excluded based on the predefined inclusion and exclusion criteria, leaving 304 for analysis.

Table 3 shows detailed demographic characteristics of the study population. It comprised 212 (69.7%) males and 92 (30.3%) females. The subjects' mean age was 46.8 ± 12.5 years. Among the subjects, 230 (75.7%) did not drink alcohol, while 74 (24.3%) did drink alcohol; and 83 (27.3%) smoked cigarettes, while 221 (72.7%)

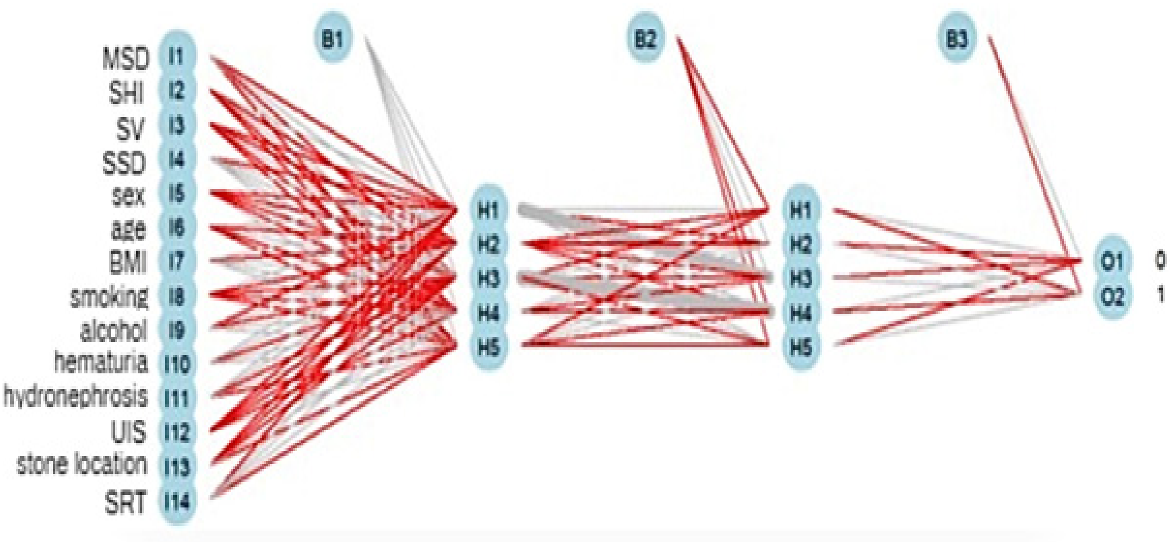

Figure 1. A structural diagram of the ANN model that was used to predict the efficacy of repeated SWL for UUTC.
Abbreviations: BMI, body mass index; SV, stone volume; MSD, mean stone density; SHI, stone heterogeneity index; UIS, urinary irritation symptom; SRT, stone retention time.

Table 3. Subjects' general conditions and stone characteristics.

Variable[abc]	Total (n = 304)	Training set (n = 217)	Validation set (n = 87)
Age (years), mean ± SD (range)	46.8 ± 12.5 (34–60)	47.0 ± 12.2 (35–59)	46.1 ± 13.1 (33–59)
Alcohol drinking			
No	230 (75.7%)	159 (73.3%)	71 (81.0%)
Yes	74 (24.3%)	57 (26.7%)	17 (19.0%)
BMI, kg/m^2			
<18.5	124 (40.8%)	89 (41.0%)	35 (40.2%)
18.5-24.9	160 (52.6%)	115 (53.0%)	45 (51.7%)
≥ 25	20 (6.6%)	13 (6.0%)	7 (8.1%)
Sex			
Female	92 (30.3%)	71 (32.7%)	21 (24.1%)
Male	212 (69.7%)	146 (67.3%)	66 (75.9%)
Hematuria			
No	182 (59.9%)	137 (63.1%)	45 (51.7%)
Yes	122 (40.1%)	80 (36.9%)	42 (48.3%)
Hydronephrosis			
No	30 (9.9%)	21 (9.7%)	9 (10.3%)
Yes	274 (90.1%)	196 (90.3%)	78 (89.7%)
MSD (HU), mean ± SD (range)	492.8 ± 186.8 (306–680)	492.8 ± 180.9 (312–674)	492.8 ± 201.9 (219–695)
SSD (mm), mean ± SD (range)	108.4 ± 14.9 (93–123)	108.9 ± 14.6 (94–124)	107.3 ± 15.6 (91.4–123)
SHI		448.8 (377.5–527.1)	457.7 (345.3–562.3)
SV (mm^3)		180.0 (130.0–280.0)	180.0 (130.0–340.0)
Stone retention time (days)	5.0 (1.0–30.0)	15.0(1.0–60.0)	
Smoking			
No	221 (72.7%)	156 (71.9%)	65 (74.1%)
Yes	83 (27.3%)	61 (28.1%)	22 (25.3%)
Stone location			
Left upper ureter	132 (43.4%)	94 (43.3%)	38 (43.7%)
Left kidney	19 (6.3%)	12 (5.6%)	7 (8.0%)
Right upper ureter	140 (46.0%)	104 (47.9%)	36 (41.4%)
Right kidney	13(4.3%)	7 (3.2%)	6 (6.9%)
Urinary irritation symptoms			
No	253 (83.2%)	181 (83.4%)	72 (82.8%)
Yes	51 (16.8%)	36 (16.6%)	15 (17.2%)

Abbreviations: BMI, body mass index; SV, stone volume; MSD, mean stone density; SHI, stone heterogeneity index.
SSD, skin-to-stone distance.
aContinuous variables were compared using an independent samples t-test.
bVariables that were nonnormally distributed, Median, interquartile spacing M (P25, P75) were compared using the rank sum test.
cCount data were expressed as cases (%) and comparison were made using the $\chi 2$ test.

were non-smokers. In addition, 184 (93.4) had a BMI of <24.9 kg/m2, and 20 (6.6%) had a BMI of >25 kg/m2. Moreover, 122 (40.1%) had haematuria, while 182 (59.9%) did not; and 274 (90.1%) had hydronephrosis before surgery, while 30 (9.9%) did not. The subjects' mean MSD was 492.8 ± 186.8 mm and SSD was 108.4 ± 14.9 mm. In addition, 172 (89.4%) had ureteral stones, and 22 (10.6%) had renal stones. Finally, 51

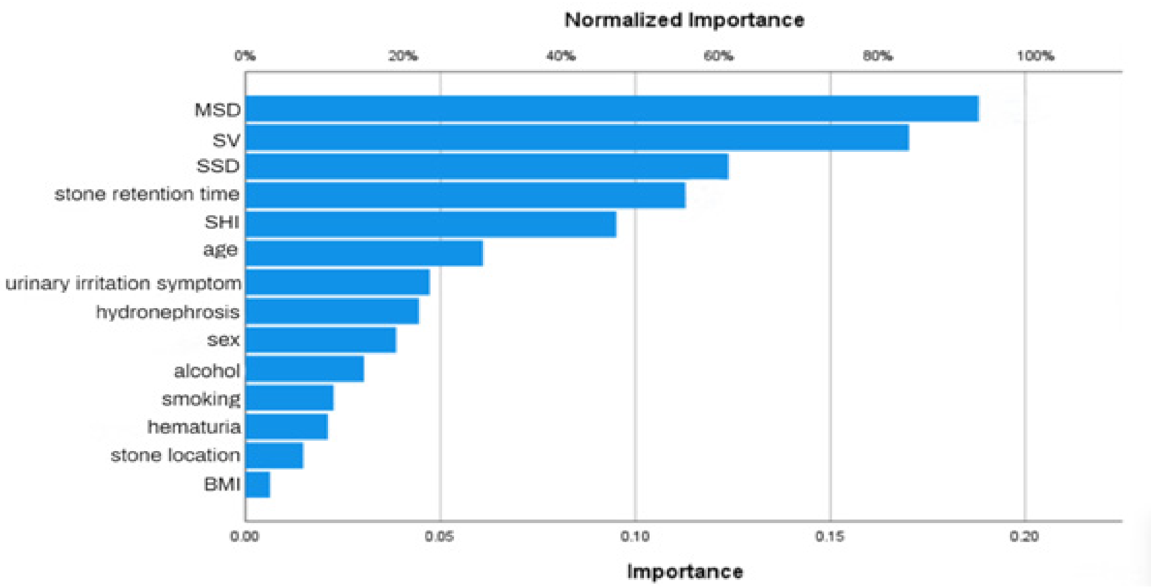

Figure 2. The normalized importance of the independent variables in the input layer for the dependent variable in the output layer of an ANN-based model for predicting the efficacy of repeated SWL for UUTC.

Table 4. Accuracy of the ANN-based predictive model in predicting the efficacy of repeated SWL for UUTC in the training and validation sets.

Set		Failure	Success	Accuracy (%)	AUC[a]	95% CI[b]
Training	Failure	80	26	77.4%	0.852	0.8-0.9
	Success	17	89	81.8%		
	Total	45.8%	54.2%	79.2%		
Testing	Failure	35	9	77.3%	0.763	0.6-0.9
	Success	8	40	77.1%		
	Total	46.7%	53.3%	77.2%		

[a]Area under the receiver operating characteristic curve.
[b]95% confidence interval.

(16.8%) had signs of urinary tract irritation, while 253 (83.2%) did not.

Model development

The model used in this study was a feed-forward neural network that incorporated the back-propagation algorithm. The neural network consisted of multiple layers, each containing a series of neurons known as nodes. The connections between neurons in adjacent layers are represented by weights.

The optimal configuration for the model was determined through iterative experimentation to determine the number of neurons in the hidden layers. The input layer of the ANN model consisted of 14 neurons, including nine stone feature variables and five essential patient information variables. Positive weights are shown by red lines, and negative weights are shown by grey lines. The thickness of these lines reflects the magnitude of the corresponding weights (**Figure 1**). Specifically, the network had two hidden layers, each with five neurons. The neural network used the sigmoid activation function. During the training process, we used R's "neuralnet" library and followed the default algorithm, which trains the network until the total sum of squared errors reaches a certain threshold (default = 0.01), at which point the training process ends.

Importance analysis of independent variables

The importance of each independent variable was examined (**Figure 2**): The ANN model was used to assess the degree of influence of the independent variables in the input layer on the dependent variables in the output layer. The results were visualized as a bar graph showing the normalized importance. They indicated that the five variables with the highest weights were MSD, SV, SSD, stone retention time, and SHI. Specifically, these variables showed the greatest influence, ranked in descending order, with a normalized significance exceeding 50%.

Predictive accuracy analysis

The prediction model achieved a prediction accuracy of 79.2% in the training set (AUC = 0.852, 95% confidence interval [CI] = 0.8–0.9) and 77.2% in the validation set (AUC = 0.763, 95% CI = 0.6–0.9; Table 4). Moreover, the ROC curve (Figure 3) indicated that the constructed ANN-based prediction model had an AUC of 0.852 (95% CI = 0.8–0.9), suggesting a robust predictive ability for the efficacy of repeated SWL in treating patients with UUTC.

DISCUSSION

The failure of the initial SWL when treating UUTC can lead to prolonged ureteral obstruction, necessitating additional procedures such as repeat lithotripsy or alternative surgical options for stone removal. In clinical practice, many patients opt for repeat SWL due to its cost-effectiveness and avoidance of anesthesia. While some studies have identified independent risk factors and established clinical prediction models for first-time SWL in treating UUTC, these models do not apply to patients undergoing repeat SWL. Therefore, there is a pressing need to develop an ANN-based predictive model specifically for repeat SWL in treating UUTC. Such a model would assist physicians in selecting appropriate treatment options, reducing patients' treatment burden and hospital stay.

ANNs have proven effective in addressing various clinical challenges.[24] These networks offer distinct advantages, including an ability to perform nonlinear operations and identify the significance of variables.[25] In our study, we developed an ANN model incorporating influential factors such as SHI, MSD, and SV. This model enabled us to predict the SWL outcome of patients whose initial SWL had failed more accurately. In our ANN model, the MSD, SV, SSD, stone retention time, and SHI variables had importance scores exceeding 50%. Stone surface area, SV, and longest stone diameter are three measures of stone burden.[26] The longest stone diameter is currently the most used measure of stone burden in clinical practice. However, two stones with equal longest diameters may have a tenfold difference in SV. Therefore, SV is a more suitable measure of the stone burden than the one-dimensional longest diameter of a stone. It more accurately represents the stone burden by combining the stone's longest diameter, largest cross-section, and depth.[26] Stone burden is greatly important in predicting the outcome of SWL treatment, correlating negatively with SWL success.[27] Numerous studies have examined using CT attenuation values to predict SWL success, with most utilizing the mean Hounsfield Unit (HU). Ouzaid et al. identified a threshold of 970 HU for predicting SWL success. Additionally, per the American Urological Association guideline, patients with MSD values higher than 900–1000 HU tended to have fewer successful SWL outcomes.[28,29] In our study, the cutoff was determined to be 486 HU. Discrepancies among these studies can be attributed to variations in CT protocols, inclusion criteria, or measurement techniques.

A recent study demonstrated that SHI is a representative measure of stone variability and can be a valuable parameter for assessing the degree of stone fragility.[30] Consequently, it can complement clinical decision-making by supplementing known predictive variables such as stone size and density. Jing et al. observed that only 37.4% of renal stones were pure, while most showed a mixed composition (62.6%), with calcium oxalate being the most frequently observed component.[15] Therefore, SHI can reflect changes in both stone composition and internal structure, capturing morphological heterogeneity.[30]

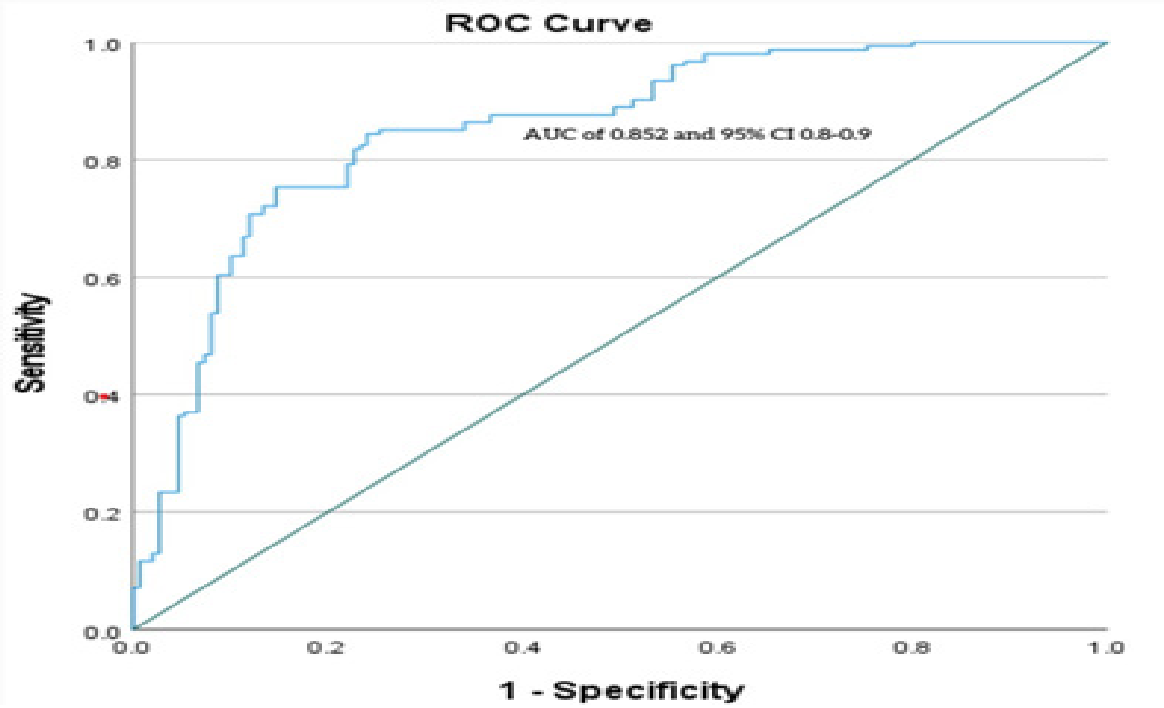

Figure 3. A ROC curve shows the ability of the ANN-based predictive model to predict the efficacy of repeated SWL for UUTC.

Whether SSD independently influences SWL is controversial in many studies. They showed that SWL was likely to fail in patients with an SSD >11 cm.[31] Since then, it has been reported that longer SSD significantly predicts SWL failure not only in patients with lower pole kidney stones but also in those with kidney or ureteral stones.[32,33] In our study, there were more cases of ureteral stones than renal stones. SSD with a cutoff of 10.6 cm was an independent factor in predicting the success of repeat SWL lithotripsy.

The duration a stone remains in place can significantly impact its expulsion.[34] When stones are retained for a short period, they have insufficient time to grow. During this early stage, the stone is typically smaller, softer, and more likely to pass naturally. However, if the stone remains in place for an extended period, it gradually grows and solidifies. Prolonged retention causes the stone to harden, become sharper, and adhere to the urinary tract walls. Consequently, passing the stone becomes more challenging. The stone may obstruct the urinary tract, leading to complications such as urinary tract infections. Therefore, the longer the stone remains in place, the more difficult it becomes to pass. Factors such as the stone's size, location, shape, and characteristics also influence its retention time.[35]

As a retrospective study, we acknowledge certain limitations that should be considered. Firstly, the data collection was conducted only at one urological center, which may restrict the generalizability of our model. Further studies involving multiple centers are needed to validate the applicability of our findings across different populations. Secondly, the accurate measurement of stone surface area and SV requires specialized CT post-processing software, which was unavailable at our hospital during the study period. This limitation may have affected the precision of our measurements for stone surface area and SV. Thirdly, the descriptive parameters used in our study, such as SV, MSD, and SHI, only capture certain aspects of stone properties and may not encompass their full spectrum. Future research should aim to incorporate a more comprehensive evaluation of stone properties. Lastly, due to the limited number of clinical cases included in our study, the predictive accuracy of our model must be further confirmed through analysis of a larger dataset comprising more clinical cases. It is essential to acknowledge these limitations to interpret our results appropriately. Further studies with larger sample sizes and diverse clinical settings are warranted to enhance the robustness and generalizability of our model. Please note that while our model shows promising results, it is important to consider individual patient factors for personalized treatment.

CONCLUSIONS

We have developed and validated an ANN model to predict the effectiveness of repeated SWL in patients with UUTC. Our findings demonstrate that ANNs can reliably predict repeated SWL outcomes in this patient population. Accurately identifying patients suitable for repeat SWL can reduce costs and provide clinicians with a precise treatment plan. We envision that our model can be implemented in clinical practice to influence the treatment decision-making process at an early stage. By doing so, we aim to improve patient care and optimize treatment strategies.

ACKNOWLEDGMENTS

This research was supported by the Natural Science Foundation of Hubei Province of Chian (2022CFB164).

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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