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ORIGINAL PAPER

Utilizing artificial neural network system to predict the residual valve after endoscopic posterior urethral valve ablation

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Summary

Purpose: To build, train, and assess the artificial neural network (ANN) system in estimating the residual valve rate after endoscopic valve ablation and compare the data obtained with conventional analysis.
Methods: In a retrospective cross-sectional study between June 2010 and December 2020, 144 children with a history of posterior urethral valve (PUV) who underwent endoscopic valve ablation were enrolled in the study. MATLAB software was used to design and train the network in a feed-forward backpropagation error adjustment scheme. Preoperative and postoperative data from 101 patients (70%) (training set) were utilized to assess the impact and relative significance of the necessity for repeated ablation. The validated suitably trained ANN was used to predict repeated ablation in the next 33 patients (22.9%) (test set) whose preoperative data were serially input into the system. To assess system accuracy in forecasting the requirement for repeat ablation, projected values were compared to actual outcomes. The likelihood of predicting the residual valve was calculated using a three-layered backpropagating deep ANN using preoperative and postoperative information.
Results: Of 144 operated cases, 33 (22.9%) had residual valves and needs to repeated ablation. The ANN accuracy, sensitivity, and specificity for predicting the residual valve were 90.75%, 92.73%, and 73.19%, respectively. Younger age at surgery, hyperechogenicity of the renal parenchyma, presence of vesicoureteral reflux (VUR), and grade of reflux before surgery were among the most significant characteristics that affected postoperative outcome variables, the need for repeated ablation, and were given the highest relative weight by the ANN system.
Conclusions: The ANN is an integrated data-gathering tool for analyzing and finding relationships among variables as a complex non-linear statistical model. The results indicate that ANN is a valuable tool for outcome prediction of the residual valve after endoscopic valve ablation in patients with PUV.

KEY WORDS: *Artificial neural network; Artificial intelligence; Children; Outcome; Posterior urethral Valve; Residual valve.*

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INTRODUCTION

Posterior urethral valve (PUV) is the most common cause of congenital bladder outlet obstruction in males, with various outcomes, from exceedingly severe phenotypes with prenatal death to live-born individuals with acceptable renal function (1). Despite being an uncommon congenital abnormality (prevalence 1-9/100,000), it represents approximately 17% of pediatric *end-stage renal disease* (ESRD) (1, 2). The current definitive treatment of choice is endoscopic PUV ablation; however, roughly 10% to 30% of patients require a second surgery to achieve adequate valve ablation (3, 4). Any partial outlet obstruction could cause anatomical and functional deterioration in the detrusor muscle of the bladder wall if it is not released quickly enough (5). This indicates the importance of close follow-up after valve ablation (5).

It might be challenging to assess the result of endoscopic valve ablation. While some investigators suggest that *voiding cystourethrogram* (VCUG) confirms the adequacy of valve ablation, others offer cystoscopic procedures.6-8 The disadvantages of VCUG are transient dysuria, hematuria, and toilet anxiety. On the other hand, the invasive nature and the need for admission and anesthesia are the main disadvantages of the cystoscopic procedure (4, 6).

Distinguishing prognostic factors for residual valves after endoscopic valve ablation can aid in developing a better algorithm for managing PUVs and achieving purposeful follow-up for high-risk patients (4).

As a result, new prediction techniques are required to allow for better patient diagnosis and follow-up (9). A study conducted by *Shirazi et al.* to investigate the patients with a higher risk for residual valves after PUV ablation found that younger age at surgery time, hyperechogenicity of renal parenchyma, presence of vesicoureteral reflux, and grade 4 or 5 reflux before surgery were associated with residual valves and need for repeated ablation (4).

The most commonly used form of *artificial intelligence* (AI) in medicine is *artificial neural networks* (ANNs) that mimic interconnected brain synapses and networks taught by analyzing input and output databases (10, 11). The system learns to identify variables influencing outcomes, and as more data is incorporated, self-optimization matures, resulting in more accurate predictions and higher accuracy rates for specific outcomes (12).

In the present study, we aimed to investigate the efficacy of ANNs as an intelligible interface to predict the rate of the residual valve after endoscopic valve ablation in children with PUV.

Materials and methods

Study design

In a retrospective cross-sectional study, 144 children who were diagnosed with PUV and had undergone endoscopic bladder neck resection and valve ablation between June 2010 and December 2020 in the referral centers (*Nemazi Teaching Hospital and Shahid Faghihi Teaching Hospital, Shiraz, southern Iran*) were selected to participate in this study. The ethics committees of Shiraz University of Medical Sciences approved this project (approval code# IR.SUMS.MED.REC.1399. 585), and it was carried out in compliance with the Helsinki Declaration. All patient's parents or legal guardians provided written informed consent before enrolment.

Surgical intervention

All primary PUV ablations were performed by a single experienced pediatric urologist (*Prof. Shirazi*). The valves were carefully ablated at the 5, 7, and 12 o'clock positions using an electrical Bugbee, and the visual assessment of the valve destruction ascertained the endpoint of ablation. Then, a urethral catheter was left in place and removed 48 hours later. Patients were discharged with oral antibiotics.

Postoperative follow-up for residual valve assessment

The possible presence of residual valve remnants was assessed by careful clinical, radiological and endoscopic evaluation (13). For that, the patients were assessed with *ultrasonography* (US) every 3 to 6 months, VCUG 3 months after valve ablation, and a control cystoscopy three to 12 months later, and if a residual valve was found, a second valve ablation was performed (4, 14). Clinically, a persistent symptom of poor stream, nocturnal enuresis in older than 5 years, and persistent or worsened VUR or worsened hydronephrosis in the serial US were also considered.
Slight residual valves that did not cause renal impairment or *urinary tract infections* (UTIs) were excluded (15).

Data collection

All the data used in this study, including preoperative and postoperative parameters, are summarized in Table 1.

Design, training, and validation of the ANN system

We designed and trained the network with MATLAB software (*Mathworks, Natick, MA*) using a feed-forward back-propagation error adjustment scheme (16, 17). The data were separated into training and test sets to fit the ANNs (Figure 1).

Training set

The network training set accounted for 101 (70%) of the study data. The architecture of the education network consists of three layers: input, hidden, and output. The number of nodes in the input and output layers corresponds to the number of predictor and response variables. The number of hidden layer nodes was determined by trial and error. The level criterion below the characteristic performance curve (ROC) was used to find the best network structure. Finally, after selecting the best architecture, the network was evaluated and validated in second-stage data that did not play a role in the network training phase.

Test set

The network test set accounted for 43 (30%) patients. The final response variable or the final output of the model was a two-state variable with the levels of 0-no residual valve and 1-had residual valve. The number of input variables was 24, the same as the independent variables. After selecting the input and output variables, a three-layer perceptron network (with an observer) was used, with one neuron in the output layer and 24 neurons in the input layer. According to the training data set and independent input variables, 320 combinations were

Table 1.
Variables considered for analysis.

Postoperative variables	Preoperative variables
History of enuresis	Age (Months)
Blood pressure (mm Hg)	Birth Weight (Low, Normal)
History of urinary incontinence	Time of diagnosis (Prenatal, Postnatal) Time to PUV ablation (Months)
Presence of VUR (Grad) in VCUG	Grade of VUR in VCUG
Urinary bladder trabeculation (Mild, Moderate, Severe) in US	Urinary bladder trabeculation (Mild, Moderate, Severe) in US
Bladder diverticula in US	Bladder diverticula in US
Blood Creatinine level(mg/dL)	Blood Creatinine level (mg/dL)
Degree of HDN (Mild, Moderate, Severe) in US	Degree of HDN (Mild, Moderate, Severe) in US
Loss of cortico-medullary differentiation	Loss of cortico-medullary differentiation in US
Renal cortical thickness (mm) in US	Renal cortical thickness (mm) in US
Size of bladder wall thickness (mm) in US	Size of bladder wall thickness (mm) in US History of recurrent UTI Proteinuria in urine analysis Urine culture Scar in renal DMSA scan

PUV: Posterior urethral valve; DMSA: Dimercaptosuccinic acid; HDN: hydronephrosis; VUR: Vesicoureteral reflux; VCUG: voiding cystourethrogram; UTI: urinary tract infection; US: Ultrasonography.

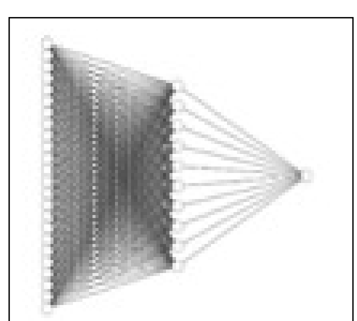


Figure 1.
Schematic design of artificial neural network.

Table 2.
Selecting the best neural network model for the recurrent data.

Motion size	Total squares error	Area below ROC curve	Percentage of correct prediction	Learning rate	Architecture	Row
0.90	33.29	0.836	79.70	0.2	1-4-24	1
0.80	34.08	0.790	72.30	0.2	1-5-24	2
0.85	32.6	0.815	75.50	0.3	1-6-24	3
0.85	36.41	0.821	84.50	0.5	1-7-24	4
0.85	36.73	0.855	77.60	0.2	1-8-24	5
0.80	34.27	0.853	73.40	0.3	1-9-24	6
0.90	31.71	0.903	90.73	0.2	1-10-24	7
0.85	33.47	0.849	74.40	0.4	1-11-24	8
0.80	35.70	0.766	72.30	0.1	1-12-24	9
0.80	34.48	0.792	74.40	0.5	1-13-24	10
0.85	41.96	0.824	75.50	0.3	1-14-24	11
0.90	34.05	0.804	74.40	0.4	1-15-24	12
0.85	33.41	0.827	73.40	0.2	1-16-24	13
0.80	32.29	0.813	72.30	0.1	1-17-24	14
0.85	35.33	0.829	76.70	0.4	1-18-24	15
0.90	38.27	0.798	83.79	0.1	1-19-24	16

AUC: Area under the curve.

based on 4 to 19 nodes in the hidden layer with a size of 0.8 to 0.95 (0.95, 0.9) to model a three-layer perceptron ANN. We evaluated the learning rate of 0.05 to 0.4 (0.4, 0.3, 0.2, 0.1, 0.05) with hyperbolic tangent activity in the hidden layer, sigmoid function activity in the output layer, and post-diffusion learning algorithm. After examining all possible models for the structure of the three-layer ANN, the network with 24 input nodes, 10 hidden nodes, one output node, a learning rate of 0.2, and a motion size of 0.9 with an error propagation algorithm as the best ANN to predict the data. The number of fitted models for each combination was 20; the best model for each structure is shown in Table 2.

Statistical analysis
The mean and standard deviation were used for quantitative variables, and frequency and percentage were used for qualitative variables. To evaluate the predictive accuracy of the system for each postoperative variable, the predicted values were compared with the actual outcomes (observed values), and true positive, false positive, accuracy, and precision rates of the system were calculated for the need for repeated ablation. All statistical analyses were done using SPSS software (*IBM SPSS, version 20, Armonk, New York: IBM Corp*), and the significance level was also considered ($p < 0.05$).

Results
The preoperative characteristics of patients are summarized in Table 3. The mean age at presentation was 8.65 ± 6.12 months. Low birth weight was presented in 0.3% of patients. The prenatal diagnosis of PUV was performed in 81(56.25%) patients. There were 33 (22.91%) patients who required a second valve ablation due to valve remnants. Postoperative data of patients are displayed in Table 4.

Table 3.
Descriptive statistics of preoperative characteristics of the patients.

N (%)	Variables	
8.65 ± 6.12	Age at presentation (years)	
5 (0.3)		Low Birth Weight
81 (56.25)	Prenatally	Time to diagnosis
63 (43.75)	Postnatally	
40 (27.7)	Neonatally	Time of surgery
51 (35.4)	1-3 Month	
14 (9.7)	3-6 Month	
15 (10.4)	6-12 Month	
24 (16.6)	> 12 Month	
69 (47.9)	No	Presence of VUR
15 (10.4)	Left	
23 (16)	Right	
37 (25.7)	Both	
8 (5.5)	1	VUR reflux grad
10 (6.95)	2	
11 (7.6)	3	
19 (13.2)	4	
27 (18.75)	5	
30 (20.8)	Mild	Urinary bladder trabeculation
80 (55.55)	Moderate	
34 (23.65)	Severe	
27 (18.75)		Bladder diverticula
0.748 ± .618		Blood creatinine level (mg/dL)
121 (84)		Prenatal KUB Sonography
31 (21.5)	No	Presence of hydronephrosis
11 (7.6)	Right	
20 (13.9)	Left	
82 (57)	Both	
31 (21.5)	No	Degree of hydronephrosis
18 (12.5)	1	
32 (22.3)	2	
35 (24.3)	3	
28 (19.5)	4	
42 (29.2)		Loss of cortico-medullary differentiation
34 (23.6)	< 3 mm	Size of bladder wall thickness
87 (60.4)	3-5 mm	
23 (16)	> 5 mm	
140 (97.2)		Proteinuria in urine analysis
137 (95.1)		Positive urine culture
83 (57.7)		Renal scar in renal DMSA scan
26.80 ± 18.12	Left	Differential function in renal DMSA scan
29.63 ± 19.75	Right	

AP: anterior-posterior diameter; PUV: posterior urethral valve, DMSA: dimercaptosuccinic acid; VUR: vesicoureteral reflux; UTI: urinary tract infection.

The predictive factor for the residual valve in Regression analysis
In multivariate analysis, the factors below were significantly associated with the residual valve and need for repeated ablation: younger age at operation (*odds ratio* [OR] 1.142; 95% *Confidence interval* [CI] 1.006-1.297), high initial serum creatinine (OR: 1.498; 95%CI: 1.089-3.257), increased bladder wall thickness (OR: 1.486; 95%CI: 1.014-2.741), higher postoperative serum creatinine (OR: 1.883; 95%CI: 1.181-4.311), presence of renal cortical thickness (OR: 1.185; 95%CI: 1.004-1.721), presence of severe bladder trabeculation (OR:1.54; 95%CI:1.136-11.281), and presence of reflux grading

Table 4.
Descriptive statistics of postoperative characteristics of the patients

N (%)	Variables	
0.617 ± .429	Blood creatinine level (mg/dL)	
69 (47.9)	No	Presence of hydronephrosis
10 (6.95)	Right	
18 (12.5)	Left	
47 (32.65)	Both	
69 (48)	No	Degree of hydronephrosis
12 (8.3)	1	
21 (14.6)	2	
24 (16.6)	3	
18 (12.5)	4	
138 (95.8)		Urine analysis
136 (94.4)		Urine culture
83 (57.6)	Normal	Blood pressure (mm Hg)
4 (2.8)	Hight	
17 (11.8)		History of urinary incontinency
15 (10.4)		History of enuresis
60 (41.6)	1	Proteinuria in urine analysis
63 (43.7)	2	
21 (14.7)	3	
33 (22.91)	Yes	Remnant valve
111 (77.09)	No	

three (OR: 2.526; 95%CI: 1.208-7.021), presence of reflux grading four (OR: 3.72; 95%CI:1.557-8.899).

ANN model

Three hundred and twenty models were fitted to the 16 structures, as shown in Table 2. We selected model 7 as the best model (green row) among these models. The prediction accuracy was 90.73%, and the area under the ROC curve was 0.903. The accuracy, sensitivity, and specificity of the ANN system for predicting the rate of remanent valves were 90.75%, 92.73%, and 73.19%, respectively (Table 5).

Table 5.
Performance of an artificial neural network system in recurrence.

AUC	Accuracy	Negative predictive value	Positive Predictive value	True negative rate (specificity)	True positive rate (sensitivity)	
0.903	90.75%	97.13%	50.69%	73.19%	92.73%	**Recurrence**

AUC: Area under the curve.

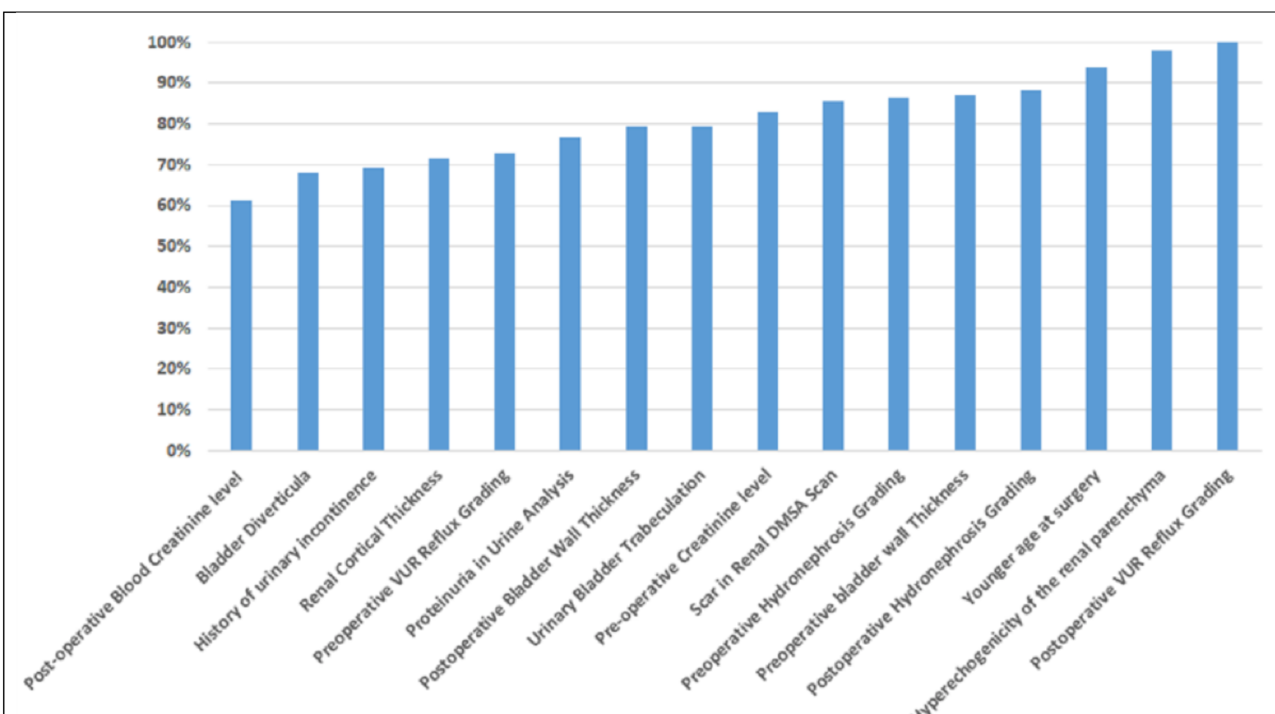
The predictive factor for the residual valve in the ANN model

Younger age at surgery, hyperechogenicity of the renal parenchyma, presence of VUR, and grade of reflux before surgery were among the most significant characteristics that affected postoperative outcome variables, the need for repeated ablation, and were given the highest relative weight by the ANN system (Figure 2).

Discussion

In this study, we developed and utilized an ANN system to predict residual valve and ablation needs after endoscopic PUV ablation. The accuracy and sensitivity ranged from 90.75% to 92.73%, proving that ANN is a valuable

Figure 2.
The ANN main factors that predict the residual valve.



tool for the prediction of the residual in PUV patients. Endoscopic primary valve ablation is the ideal initial surgical therapy for PUVs; however determining the absence of remaining valve remains necessitates meticulous examination. Some prescribe VCUG for adequacy, while others advise cystoscopy follow-up. Both procedures offer advantages and downsides, such as transitory dysuria, enuresis, hematuria, and toileting anxiety, as well as the necessity for general anesthesia for cystoscopy. The high incidence rate of remaining leaflets necessitates post-ablation assessment (18).

In this study, to reduce the impact of technical aspects of the first PUV ablation in the presence of remaining valves, all procedures in the research were carried out by the same surgeon with an experienced pediatric urologist with more than 20 years of experience in the pediatric urology field. Additionally, as the VCUG alone was insufficient to exclude residual valve tissue (positive and negative predictive values of 56% and 50%, respectively) (7), so cystoscopy was routinely performed on the patients.

The reported recurrence rate of residual valves was 10%-30% in most studies.13,19 In the same line with previous studies, the recurrence rate in this study was 22.91%. A higher recurrence rate was reported in some studies, such as the study carried out by *Nawaz et al.*, who reported 78% residual valves during the follow-up cystoscopy. 8 The high rate of residual valves may be attributed to the use of routine follow-up cystoscopy after primary valve ablation.

Previous studies have primarily examined the correlation between preoperative factors and postoperative kidney function (20, 21), with limited attention given to the risk of residual remnants valve risk in PUV patients (4). In this study, factors significantly associated with residual valve and need for repeated ablation in regression analysis include younger age at operation, high initial serum creatinine, increased bladder wall thickness, higher postoperative creatinine, renal cortical thickness, severe bladder trabeculation, and advanced reflux grading (three or four). Similarly, *Shirazi et al*. evaluated the relationship between preoperative findings and residual obstructive leaflets after valve ablation. The authors found that younger age at PUV ablation, increased renal echogenicity, and the high VUR grade were significantly associated with the presence of residual valves (4). In *Nabil et al.'s* study, the authors found that age at presentation and substantial *post-void residual volume* (PVR) were highly associated with the presence of residual valves (22). *Motiwala et al.*, in their study, recommend using the urethral ratio and bladder wall thickness to assess residual valves (23). Premature birth, prenatal diagnosis, and loss of corticomedullary differentiation unilaterally or bilaterally were all associated with meaningfully higher rates of CKD, ESRD, and the need for many corrective surgeries in PUV patients, according to *Bilgutay et al.* Furthermore, symptomatic presentation, recurrent UTI, and pre-operative and postoperative high VUR were associated with the need for many corrective surgeries but not poor renal outcomes (24). In contrast, some studies mentioned that age of presentation or ablation, urinary diversion, and the bladder neck incision did not significantly affect the outcome of PUV management (24, 25). Nevertheless, assessing the efficacy of the PUV ablation procedure is not uniform and has some drawbacks (4). Additionally, bladder dysfunction after primary valve ablation is caused by the gradual deterioration of bladder contractility due to secondary lower urinary tract obstruction and eventually to myogenic bladder failure (24, 25).

There is a need to develop predictive models to optimize patient selection and patient counseling and to develop further ways to determine the most likely surgical outcomes before surgery is performed. In the study, younger age at surgery, hyperechogenicity of the renal parenchyma, presence of VUR, and grade of reflux before surgery were among the most significant characteristics that affected postoperative outcome variables, the need for repeated ablation and were given the highest relative weight by the ANN system. The advantage of ANN is that it can simply estimate and notify the relative importance of every variable on PUV outcome without the use of invasive methods. The prediction accuracy of the ANN model was 90.73%, and the area under the ROC curve was 0.903. The accuracy, sensitivity, and specificity of the system for predicting the residual valve were 90.75%, 92.73%, and 73.19%, respectively. Using a preoperative and postoperative dataset and a readily available cloud-based predictive analytical platform, we indicated that it could precisely train a model that can predict the rate of remnant leaflets valve after endoscopic valve ablation. Since predicting patient outcomes based on data sets is not a novel concept, constructing and verifying these predictive models necessitates time-consuming calculations and powerful statistical techniques to be carried out by appropriately qualified professionals (26). Moreover, once these calculations were completed and the result was available and ready for presentation, the statistical data set could become out of date (27). Based on recent clinical data, the ANN system can produce these designs in a reproducible manner a few times, allowing for continuous data entry, real-time constant model retraining, and provision of an output to influence clinical decision-making (28). As more input data was fed into the system (24 variables), the system innately augmented the integrated weights between the parameters. As a result, the predicted values were very close to the expected value. However, no studies have been conducted to date to compare the predictive accuracy of ANN versus regression analysis methods in predicting which patients are at high risk of obstructive remnant leaflets after valve ablation in boys with PUV. Previous research on the outcomes of remnant leaflets after valve ablation reported the same predictive accuracy of ANN systems in comparison to statistical models (4, 22, 23). The advantages of the ANN model are that it is the software can be easily used and updated with more preoperative, postoperative, and intraoperative variables in future versions, and the institutes can easily add other features to their software to customize it. However, the disadvantages of the ANN model include the absence of underlying causal relationships between data processing algorithms and clinical realities. Few published data investigated the role of AI in PUV outcomes. For example, *Weaver et al.* used ANNs to predict renal failure in children with PUV using a survival analysis tool. They used deep learning imaging features from US images to predict renal failure accurately. They found that the ANNs model could accurately predict which patients will develop renal failure (29). *Abdovic et al.* utilized ANN to predict the late presentation of PUV in boys with lower urinary tract symptoms. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of ANNs were 92.7%, 100.0%, 89.7%, 80.0%, and 100.0%, respectively (30).

Study limitation
There are several limitations to the study. Firstly, the retrospective nature and low sample size inherently lacked control and randomization. This approach is prone to selection bias and attrition due to loss of follow-up, potentially skewing the results. However, such surveys can aid in the development of a better methodology for the management of PUVs, as well as the achievement of purposeful follow-up for high-risk patients rather than invasive procedures. The assessment of outcomes was also limited, lacking adjustments for critical factors such as depth of incision, surgeon experience, urodynamic evaluation, and needs for anticholinergic therapy. Also, we do not include information on the varied outcomes, such as ESRD, dialysis, and renal transplantation, which can influence the outcome. This omission could lead to an incomplete understanding of the factors influencing treatment outcomes. Therefore, prospective comparative trials will be needed to confirm the predictive value of ANN vs. statistical data mining models and validate the system to decide whether or not to proceed with PUV ablation.

Conclusions
In conclusion, the ANN is an integrated data-gathering tool for analyzing and understanding the relationships among variables as a complex non-linear statistical model. The accuracy and sensitivity in predicting the rate of the residual valve after the endoscopic valve ablation ranged from 90.75% to 92.73%. The results indicate that ANN might be a valuable tool for outcome prediction of the residual valve after endoscopic valve ablation in patients with PUV.

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