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The Use of Artificial Neural Networks in Decision Support in Vesicoureteral Reflux Treatment

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Key Words
Vesicoureteral reflux · Treatment outcome · Decision-making · Neural networks

Abstract
Aim: To develop a prediction model based on artificial neural networks (ANN) for the treatment selection in vesicoureteral reflux (VUR). ***Methods:*** A total of 96 children with VUR (145 ureteric units (UU)) were treated at our institution during 2004–2006. An ANN based on quick propagation architecture was created with the commercially available software package. The patients' age and sex, the cause and grade of VUR, the affected ureter, the type of treatment (conservative, subureteric injection, or open surgery), existence of renal scar on DMSA, follow-up times and the number of injections were used as variables. These data were also transferred to a statistical software package and regression analysis was done. ***Results:*** In all, 105 UU showed no reflux, 5 UU showed improvements in reflux grade (considered only in the conservative management group), and the remaining 35 UU showed persistence. In the training group (n = 99), ANN showed 98.5% sensitivity, 92.5% specificity, 97% positive predictive value, and 96% negative predictive value in predicting treatment outcome. ***Conclusions:*** We have demonstrated that ANN can accurately predict the resolution of VUR, and thus could be useful in daily clinical practice. This approach would allow urologists to aid in the decision-making process of VUR treatment.

Introduction

Vesicoureteral reflux (VUR) is a very common urological anomaly in children. Therapeutic options of VUR comprise conservative management, including antibiotic prophylaxis, and interventional approaches (i.e. endoscopic subureteral injection, open or laparoscopic surgical correction of reflux), in isolation or combined. However, controversy remains regarding the selection of optimal therapeutic options of children with VUR [1–3]. The choice of treatment modality is based on the presence of renal scars, grade and laterality of reflux, age, sex, bladder capacity and function, patient compliance and parental preference [4].

Currently, antibiotic prophylaxis is generally used as the initial therapy of grade I–III reflux [1]. Open surgery is recommended for children who develop breakthrough infections despite antibiotic prophylaxis, have reflux that fails to resolve, or have reflux of grade IV or V [1, 5]. Although there is not yet a prospective trial proving that endoscopic therapy is equally effective as the conservative management, endoscopic subureteral injection offers the advantage of enabling treatment of the underlying anatomical defect while avoiding the morbidity of open surgery [6].

Artificial neural networks (ANNs) are computational methodologies that perform multifactorial analyses, inspired by networks of biological neurons. These algorithms can be trained to recognize complex patterns in

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Table 1. Patient demographics

Average age, years	5.1 ± 3.7 (range 4 months to 14 years)
Sex	
Male	44
Female	52
Ureters treated	145
Cause (UU)	
Primary	82
Secondary	63
Bladder instability	20
Neurogenic bladder	32
Duplicity	2
PUV	6
Ureterocele	3
Renal scarring (UU)	70

UU = Ureteric units; PUV = posterior urethral valve.

Table 2. Reflux resolution according to grades and treatments

	Ureteric units	Corrected units
Grade I	13	13 (100%)
Grade II	32	27 (84%)
Grade III	49	34 (69%)
Grade IV	36	22 (61%)
Grade V	15	9 (60%)
Total	145	105
Treatment		
Conservative	31	25 (80%)
Subureteric injection	74	47 (64%)
Open surgery	40	33 (83%)

data sets. They have an advantage over conventional statistical methods in that they are not constrained by predefined mathematical relationships between dependent and independent variables and are thus able to model complex non-linear parameters. In recent decades ANNs have become widely adopted in various industries due to their ability to solve tasks that are hard or impossible to solve using other conventional methods. At the same time, several urologic applications for ANNs have also been reported. A particular research interest has been focused on several subspecialty areas, including male infertility [7], uro-oncology [8, 9], endourology [10], and uropathology [11].

In the present study, we aimed to create an ANN to aid in treatment selection for VUR.

Patients and Methods

A total of 96 children with VUR (145 ureteric units (UU)) were treated at our institution during 2004–2006. Patient demographics are presented at table 1. Treatment options were conservative management, including antibiotic prophylaxis (n = 31 UU), endoscopic subureteral injection (n = 74 UU), and open surgery (n = 40 UU). Antibiotic prophylaxis was used as the initial therapy of grade I–III reflux. Endoscopic subureteral injection and ureteric reimplantation were carried out for children who develop breakthrough infections despite antibiotic prophylaxis, have reflux that fails to resolve, or have reflux of grade IV or V. Deflux (Q-Med Scandinavia Inc., Sweden) was used as injection material for all subureteral injection procedures. Surgical techniques used were Politano-Leadbetter in 21 patients and Lich-Gregoir in 19 patients. Patients treated with subureteric injection or ureteric reimplantation were evaluated with renal ultrasonography after 1 month and voiding cystography after 3 months. Patients treated with antibiotic prophylaxis were followed by urinalysis and culture monthly and voiding cystography every 6 months. Treatment outcomes were classified as two groups. Resolution was defined as the complete absence of VUR, and persistence as any grade of reflux even when it was minimal. For patients treated with antibiotic prophylaxis, improvement was defined as the decrease in the reflux grade.

Commercially available software was used for developing this decision-aid model (Alyuda Research, Inc., Los Altos, Calif., USA). An ANN based on quick propagation architecture was created using a 26-13-3 structure. The patients' age and sex, the cause and grade of VUR, the affected ureter, the type of treatment (conservative, subureteric injection, or open surgery), existence of renal scar on DMSA, follow-up times and the number of injections were used as variables. A total of 99 UU were randomly assigned as training set (68.97%), 23 for validation set, and the remaining 22 for selected as test set. These data were also transferred to a statistical software package (SPSS for Windows 11.0) and linear regression analysis was carried out.

Results

The average patient's age was 5.1 years (range 4 months to 14 years). We observed bilateral reflux in 49 patients and unilateral reflux in the remaining 47 patients (145 UU). Reflux resolution according to grades and treatment types are presented in table 2. 68 renal units showed cortical scar on DMSA study (46.9%). We carried out subureteric injection in 74 UU, open surgery in 40 UU, and the remaining 31 UU were followed by conservative management. Mean follow-up time was 28.54 ± 16.83 months. In all, 105 UU showed no reflux, 5 showed improvements in reflux grade, and the remaining 35 units showed persistence. In the training group (n = 99), the success rate of the ANN model on predicting treatment outcome was 98% in resolved units (66/67), 100% in improved units (5/5), and 92% in failed units (25/27). In addition, ANN

showed 98.5% sensitivity, 92.5% specificity, 97% positive predictive value, and 96% negative predictive value. In linear regression, only the number of subureteric injections (correlation coefficient = 0.361; p = 0.007) and follow-up times (correlation coefficient = –0.239; p = 0.006) were found to be statistically significant.

Discussion

Humans have limited ability to evaluate and discriminate complex models, especially multidimensional relationships among variables. Thus, it is often difficult or impossible to discriminate between dependent and independent variables (as age, co-morbidity, prevalence of the disease, clinical and biochemical data). An ANN can correlate different predicting factors, find hidden interactions among variables, predict an outcome for a patient or for groups, classify patients in risk groups, or approximate a function and complete a known pattern. Nearly all published papers on the field of ANN in urology showed a similar or remarkable better performance to multivariate analysis and a significant better accuracy than univariate analysis [8, 12–17]. Thus, we found that ANN showed better performance to conventional statistical analysis for predicting treatment outcome of VUR.

In the present ANN algorithm, supervised learning has been applied for solving this problem. Supervised learning is based on an 'external teacher' that tells the ANN to each input the correct output (nominal variable) and/or the difference to the output (continuous). Thus, ANN changes the weights and learns. In addition, we used Quick Propagation learning algorithm which is general-purpose training algorithm of choice [18].

Serrano-Durba et al. [19] reported an ANN based on multilayer perception architecture to aid in predicting the results of endoscopic treatment for VUR. They compared the results of ANN with conventional statistical methods. Their results showed that ANN gave better values for all the performance variables (sensitivity, specificity, positive and negative predictive values). They created an ANN only to assist in predicting the result of the subureteric injection, whereas, our algorithm was extended to all treatment alternatives of VUR. Thus, the current algorithm offers to aid in selection of best treatment for individual patient.

In the present study, ANN showed better performance than traditional statistical methods. In linear regression, the number of subureteric injections (p = 0.007) and follow-up time (p = 0.006) were found statistically significant. Other parameters, such as the cause and grade of VUR, the treatment type, and the number of injections were not found statistically significant. In the training group, ANN can accurately predict 66 of 67 resolved units (98%) and 25 of 27 failed units (92%). It means that ANN showed valuable performance in predicting treatment outcome, regardless of the treatment type.

Conclusions

In this study, we have demonstrated that ANN can accurately predict the resolution of VUR, and thus could be useful in daily clinical practice. This approach would allow urologists to aid in the decision-making process of VUR. Moreover, ANN may have a role in complementing traditional methods to produce a more accurate prediction of clinical outcome.

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