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Original Article

The use of an artificial neural network in the evaluation of the extracorporeal shockwave lithotripsy as a treatment of choice for urinary lithiasis

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Lithotripsy complications

Abstract *Objective:* Artificial neural networks (ANNs) are widely applied in medicine, since they substantially increase the sensitivity and specificity of the diagnosis, classification, and the prognosis of a medical condition. In this study, we constructed an ANN to evaluate several parameters of extracorporeal shockwave lithotripsy (ESWL), such as the outcome and safety of the procedure.
Methods: Patients with urinary lithiasis suitable for ESWL treatment were enrolled. An ANN was designed using MATLAB. Medical data were collected from all patients and 12 nodes were used as inputs. Conventional statistical analysis was also performed.
Results: Finally, 716 patients were included in our study. Univariate analysis revealed that diabetes and hydronephrosis were positively correlated with ESWL complications. Regarding efficacy, univariate analysis revealed that stone location, stone size, the number and density of shockwaves delivered, and the presence of a stent in the ureter were independent factors of the ESWL outcome. This was further confirmed when adjusted for sex and age in a multivariate analysis. The performance of the ANN at the end of the training state reached 98.72%. The

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four basic ratios (sensitivity, specificity, positive predictive value, and negative predictive value) were calculated for both training and evaluation data sets. The performance of the ANN at the end of the evaluation state was 81.43%.

Conclusion: Our ANN achieved high score in predicting the outcome and the side effects of the ESWL treatment for urinary stones.

1. Introduction

Numerous multivariate computational programs have been widely used over the past decades in medicine, mainly in the oncology field. The aim is clear, to help diagnose and stage cancers and other medical conditions in various ways, as well as estimate the prognosis of critical diseases. These clinical decision tools are utilised to categorise patients by developing patterns and envisaging outcomes given a set of "inputs". These "inputs" may consist of specific patients' or disease characteristics, making the generated outcome thus more accurate than other analogous statistical procedures. These multivariate programs substantially increase the sensitivity and specificity of the diagnosis, classification, and the prognosis of a medical condition [1].

Artificial neural networks (ANNs) are simplified models mimicking the central nervous system. They are networks with highly interconnected neural computing and the capability to react to input signals, learning to adapt to the environment. It is supported that these models offer the most promising integrated approach to constructing truly intelligent computer systems. It has been demonstrated that ANNs can be effectively used as computational processors in a variety of tasks such as speech and visual image recognition, classification, data compression, forecasting, simulation (modeling), and adaptive control. They demonstrated desirable characteristics absent in conventional computing systems, such as high performance when associated with noise or incomplete input standards, high error tolerance, high parallel computing rates, generalization, and adaptive learning. A typical network consists of one set of sensory units that form the input layer, one or more hidden layers with computational connections, and an output layer with calculation nodes [2].

Urinary lithiasis is a common problem worldwide with an increasing trend due to climate change, lifestyle modifications, and diet [3]. Most patients with stone disease have identifiable risk factors; it is noticeable though there is a high stone recurrence rate, reaching approximately 50% at 10 years and 75% at 20 years [4]. Therapy may be quite problematic sometimes, needing for repeating maneuvers, either non-invasive or invasive, with increasing risk of medical complications. Among the therapeutic alternatives, extracorporeal shockwave lithotripsy (ESWL) is a non-invasive method and represents the first choice for urinary lithiasis under specific conditions. The outcome of the ESWL depends on several parameters, such as stone location, stone size, stone composition, and body mass index (BMI), making this therapeutic option quite challenging [5].

So far, different statistical models have been used to evaluate ESWL as a therapy procedure with inconclusive results. Since ESWL is a non-invasive technique, the probability of disintegrating a stone avoiding side effects is the cornerstone of all mathematical or computational methods. In this study, we constructed an ANN to evaluate several parameters of ESWL, such as the outcome and safety.

2. Patients and methods

The database of the ESWL Department of the University Hospital of Larissa, Greece, was used for constructing the ANN. In total, 716 consecutive patients, 404 males and 312 females, with renal and ureteral stones that were treated by ESWL entered our study. All patients met the lithotripsy criteria, *i.e.*, a single stone less than or equal to 1.5 cm in the maximal diameter, no anatomical abnormalities (*i.e.*, horseshoe kidneys, retrocaval ureter, ureteropelvic junction obstruction, congenital or acquired ureteral stenosis, and congenital or acquired vesico-ureteral obstruction), and no signs of urinary tract infection.

ESWL was performed using the electromagnetic Dornier lithotripter SII (EMSE 220 F-XP, Dornier MedTech, Munich, Germany) under fluoroscopic or ultrasonographic guidance, as previously described [6]. All parameters of each session were recorded for each case, following the standard lithotripsy protocol. Ultrasonography or computed tomography urography prior to ESWL was used to exclude patients with anatomical abnormalities. Analgesic was applied when needed (fentanyl citrate, 0.05 mg, *i.v.*).

2.1. Statistical analysis

Tables 1 and 2 show patient characteristics and statistical analysis. All variables were assumed to be discrete, and categorical due to the group of data that was limited per category (not infinite). The Chi-square test was used to check categorical variables, with $p<0.05$ considered as statistical significant (Statistical Package for Social Sciences 25.0, IBM Corp., Armonk, NY, USA).

2.2. ANN philosophy

A neural network is a sequence of "neurons" organized in connecting layers [7]. The structure of neural networks was formed by an "input" layer, one or more "hidden" layers, and the "output" layer. The input signal is propagated

Table 1 Characteristics of 716 patients treated with ESWL.

Patient category	Complication after ESWL, n	No complication after ESWL, n	p-Value
Sex			0.470
Male	213	191	
Female	156	156	
Age, year			0.945
$\leq$30	18	29	
31–45	76	69	
46–60	136	117	
$\geq$61	139	132	
BMI, kg/m^2			0.035
<18.50	0	3	
18.50–24.99	104	92	
25.00–29.99	167	166	
$\geq$30.00	98	86	
Stone location			0.311
Right kidney	131	113	
Left kidney	116	121	
Bladder	7	8	
Left ureteral	49	58	
Right ureteral	66	47	
Stone size (diameter), mm			0.541
$\leq$6	42	31	
7–9	89	78	
10–11	78	71	
12–13	59	67	
14–15	44	40	
16–20	47	51	
21–32	10	9	
Comorbidity			0.533
No symptoms	245	215	
One symptom	68	71	
Two or more symptoms	56	61	
Previous ESWL sessions			<0.001
Yes	262	146	
No	107	201	
Analgesia			0.013
Yes	16	31	
No	353	316	
Number of shocks			0.118
2500–3500	349	325	
$\geq$3500	22	20	
Intensity			0.060
<40%	3	2	
40%–60%	78	52	
61%–80%	265	267	
81%–100%	23	26	
Pig-tail existence			0.797
Yes	80	78	
No	289	269	
Hydronephrosis, n			<0.001
Yes	74	137	
No	295	210	

BMI, body mass index; ESWL, extracorporeal shockwave lithotripsy.

Table 2 Statistical analysis of input variables.

Variable	Mean	SD
Age, year	54.70	14.19
BMI, kg/m^2	27.66	4.25
Stone size (diameter), mm	11.50	4.45
Number of shock	3050.54	484.92

BMI, body mass index; SD, standard deviation.

through the network in the forward direction through layers. These neural networks are commonly referred to as multiple layer perceptrons and have been successfully implemented to solve difficult and varied problems through their education in a supervised way, using algorithms, known as error back-propagation algorithms. These algorithms are based on the error-correction learning rule and can be regarded as a generalization of an equally widespread adaptive algorithm filtering, called least mean square algorithm. The process of error back-propagation consists of a forward and a backward passage through the different layers of the network. In the forward passage, an activity pattern (input path) is applied to the sensing connections of the network and its action is transmitted through the layers; eventually an output is produced.

During the forward passage, the synaptic weights are all fixed. On the other hand, during the backward passage, the synaptic weights are all adjusted according to the error-correction rule. In particular, the real network response is subtracted from the anticipated response (target) to deliver the error signal. Then, this error signal propagates back through the layers to the opposite path of the synaptic nodes (error back-propagation). The synaptic weights are adapted in such a way to bring the actual network response closer to the desired response [8,9].

2.3. ANN structure

A high-level programming language and an environment for numerical computation and visualization were developed for a feed-forward error back-propagation neural network using MATLAB (Matrix Laboratory). Data from 716 patients were divided into two sets: A training set of 549 patients and an evaluation set of 167 patients, intending to maintain equal frequency of outcomes in each set. A group of 12 variables, according to patients' characteristics, was defined as input variables (Fig. 1).

Variables such as age, BMI, and stone size contributed to the input layer with their initial values. Other variables such as intensity, stone location, and analgesia had the value of 1 when the category was present and 0 otherwise. "Sex" variable had the value of 1 for female patients and 0 for male. Due to the values of each variable, the input layer of ANN had 20 neurons in maximum (Table 3). Fig. 2 shows how stone location has been labeled with binary values and, as a result, the variable splits into five neurons in input layer. Each neuron corresponds to one organ in the renal system. For example, if a stone exists in right kidney, we set the value at (1, 0, 0, 0, 0). The same method was followed for comorbidity.

After the training process and careful evaluation of the network results, the hidden layer consisted of 20 neurons, giving the best network performance. The output layer consisted of one neuron, giving the value of 1 when complications were present and the value of 0 when there were no complications. Transfer function (from layer i to layer j) and training function were the default functions of MATLAB.

All participants were informed and gave their written consents. The study was approved by the Ethics Committee of the University of Thessaly (349/29.01.2016).

3. Results

In all 716 patients, efficacy and complications of the ESWL were evaluated in a univariate and multivariate analysis, for all the known parameters that affect the lithotripsy treatment. Univariate analysis revealed that diabetes and hydronephrosis were positively correlated to the ESWL complications; previous therapies and analgesia were not found to lead to any side effect. When adjusted for sex and age, multivariate analysis confirmed these results.

Regarding efficacy, univariate analysis revealed that stone location, stone size, the number and density of shockwaves delivered, and the presence of a stent in the ureter were independent factors of the ESWL outcome. These were further confirmed when adjusted for sex and age in a multivariate analysis.

Initially, a data set of the statistically significant variables, as shown from the univariate and multivariate analyses, was chosen to build the neural network. Seven variables (stone location, stone size, the number and density of shockwaves delivered, the presence of a stent in the

Table 3 ANN input data.

Variables	Neuron/ variable, *n*	Input value (neuron)
Sex	1	- Male or female
Age	1	- Positive number
BMI	1	- Positive number
Stone location	5	- Right kidney, left kidney, bladder, left ureter, or right ureter
Stone size	1	- Positive number
Comorbidity	5	- Anticoagulant, heart issues, diabetes, hypertension, or coagulation issues
Previous ESWL	1	- Yes or no
Analgesia	1	- Yes or no
Number of shocks	1	- Positive number percentage
Intensity	1	- Yes or no
Pig-tail existence	1	- Yes or no
Hydronephrosis	1	- 1: For complications; 0: Without complications
Output neuron	1	- 1: For complications; 0: Without complications

ANN, artificial neural network; BMI, body mass index; ESWL, extracorporeal shockwave lithotripsy.

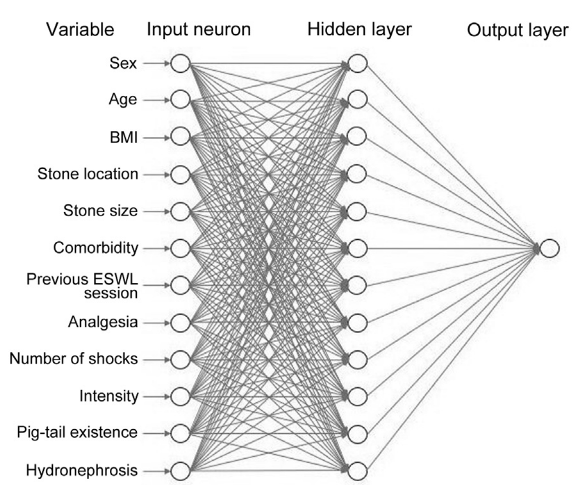

Figure 1 Artificial neural network nodes and connection. BMI, body mass index; ESWL, extracorporeal shockwave lithotripsy.

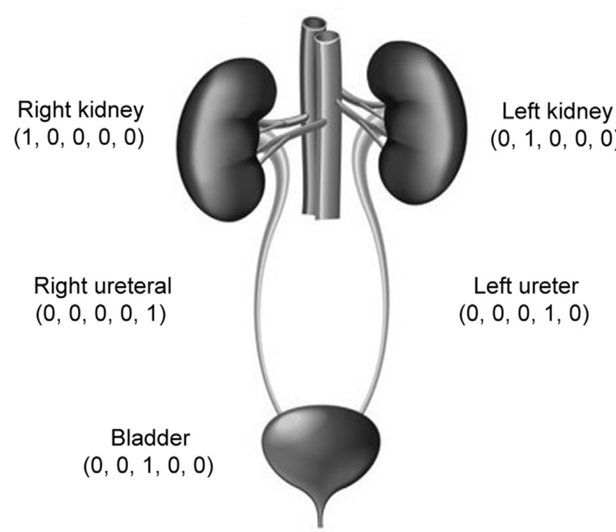

Figure 2 Stone location. Numbers (1, 0) were used in the ANN to denote the presence of the stone in kidneys, ureters, and bladder. 1: Stone presence; 0: Stone absence.

ureter, age, and sex) were used as inputs in a subset of patients, giving excellent outcomes in the training of the network, but poor outcomes in the evaluation (Table 4). When all 12 parameters were used though, the outcomes were improved in both the training and the evaluation of the neural network (Table 5).

A data set of 12 variables was finally applied to construct the ANN (Fig. 1). The performance of the ANN (predictive/real values) at the end of the training state reached 98.72%. The four basic ratios (sensitivity, specificity, positive predictive value, and negative predictive value) were calculated for both training and evaluation data sets (Table 6).

The ANN showed high accuracy in predicting complications (81.43%) in evaluation set with high positive predictive value (83.82%), indicating that prediction of complications with the use of a neural network is very likely and extremely promising. The input given the greatest weight by the ANN was the stone location. BMI was in fourth position in terms of significance. Stone size was given negative weight by the ANN, which may be due to the total number of patients in our training set or the linearity of size measurements used as inputs that did not enable the program to locate stones with small size differences.

Table 5 Artificial neural network with 12 inputs.

Variable	Training set (334 patients), %	Evaluation set (84 patients), %
Performance	99.10	75.00
Specificity	99.40	71.18
Sensitivity	98.80	84.00
Positive predictive value	98.80	91.30
Negative predictive value	99.39	55.26

Table 6 Final artificial neural network.

Variable	Training set (549 patients), %	Evaluation set (167 patients), %
Performance	98.72	81.43
Specificity	98.88	74.02
Sensitivity	98.56	87.77
Positive predictive value	98.52	83.82
Negative predictive value	98.92	79.79

4. Discussion

Computational intelligence methods are gaining appreciation more and more nowadays in the medical field. With a variety of paradigms, comprising expert systems, ANNs, fuzzy systems, *etc.*, these approaches are oriented in solving medical problems resistant to conventional computing methods. ANNs in particular, typically examine a relationship between the variables of a data set, which is not clearly understood. With specific variables as inputs and outputs, the network is trained choosing cases from a data set, while others are held to be used for testing the trained network. The trained network's effectiveness then is evaluated by giving it input values from the withheld cases of the data set, which are then compared with the corresponding actual values from the testing cases. A good performance of the ANN indicates that the neural network is indiscriminate the pattern in the training cases, to identify it in cases it has never seen before [10].

Numerous studies nowadays compared the different statistical and neural computing methods, while others merged neural computing into statistical processes [11—14]. In most of them, trained neural models have shown superiority as a predicting approach compared to statistical estimation tools. While the latter usually offer concise descriptive outcomes, neural networks make fewer mistakes, uncovering relationships in data sets which conventional statistics fail to identify at all. It is suggested that the backpropagation training method for ANNs is equivalent to maximum likelihood estimation, making eventually the multilayered feed-forward neural network a powerful modeling instrument. Furthermore, a two-layer feed-forward neural network with an adequate amount of hidden nodes can estimate any continuous function accurately. ANNs are back-propagated neural networks, which typically employ training methods (phases) to minimize errors [15].

Table 4 Artificial neural network with seven inputs.

Variable	Training set (334 patients), %	Evaluation set (84 patients), %
Performance	92.81	59.52
Specificity	93.41	55.93
Sensitivity	92.21	68.00
Positive predictive value	92.30	80.48
Negative predictive value	93.33	39.53

In the latter body of evidence, ANNs for the analysis of medical data are increasing attention in the literature. Indeed, the nature of medical conditions and the complexity in differential diagnosis are critical motivators of this concern. Numerous studies have adopted this method in almost every medical field. In 1991, Baxt [16] created a neural network for diagnosing myocardial infarction. Medical history, clinical condition, comorbidities, and imaging of patients who visited the emergencies were used as inputs. The diagnostic accuracy was markedly improved. In another study, ANNs were used in the diagnosis of coronary artery disease, reaching 91.2% of accuracy [17], while age, cholesterol, and arterial hypertension have been used as data in ANNs to diagnose coronary artery disease [18]. Neural models have also been employed in other heart diseases, such as heart valve defects and arrhythmias with 95% and 99.2%—99.8% of accuracy, respectively [19,20]. In 1993, McGonigal et al. [21] constructed a neural network model to estimate survival in patients with penetrating trauma, improving sensitivity over the well-known survival prediction tools [22].

Another field with widespread use of ANNs is oncology. They were initially adopted for breast and ovarian cancer in 1994, raising an argument on the suitability of certain data as inputs for ANN analysis, such as demographic, radiological, oncological, and biochemical data [23]. In radiology, ANNs aim at developing automated decision supporting systems, with extended application in various fields [24].

In urology, ANNs have been applied mostly in oncological diseases, such as prostate cancer (PCa). Snow et al. [25] constructed a neural model for PCa using prostate biopsy results and patient outcomes after prostatectomy. They revealed 87% and 90% of accuracy in predicting biopsy results and tumour recurrence, respectively [25]. Finne et al. [26] compared a neural network based on the percentage of the free prostate-specific antigen (%fPSA) to conventional statistical analysis (logistic regression), showing that the precision in predicting PCa in 656 patients who had undergone biopsy was higher in the ANN group than that in the logistic regression group ($p<0.001$). Accordingly, Babaian et al. [27] constructed an ANN to detect PCa in 151 biopsied men. The study showed higher specificity at 92% sensitivity than the %fPSA biomarker (62% *vs.* 11%). Interestingly, they found that 64% of all biopsies (71 of 114 men without cancer) could have been avoided using their neural network model [27]. Another ANN assessed cancer risk in regard to the outcome of prostate biopsies in 928 patients employing serum prostate-specific antigen, %fPSA, age, prostate volume, and digital rectal examination as inputs. At 90% of sensitivity, the neural model performed better than serum prostate-specific antigen alone [28]. Additionally, ANN was superior when evaluated in a multicentre study with 1188 patients [29]. In final, several studies addressing neural networks exist in the literature in different medical fields, such as oncology, radiology, and cardiology [30], but they can also be found in interesting conditions, *i.e.*, auditory brainstem response [31], sleep classification in infants [32], glaucoma [33], and even interhospital transport mode [34].

Our study is the first attempt in the literature to construct a neural network predicting urinary lithiasis treatment. The initial concept was to feed the network with as many data (inputs) considered statistically significant with the conventional statistical methods, as possible. It is of note that when univariate and multivariate analyses were used, the significance of their results did not have a positive effect on the network. The outcome in the evaluation arm of the ANN was rather disappointing (59.52% performance). When all 12 parameters were used as inputs though, the performance of the network in the evaluation arm improved dramatically (75%), indicating that the algorithm used for the ANN delivers better with a greater number of inputs. Eventually, the performance of our ANN reached 81.43% in our study population.

Study limitations are the relatively small sample of patients and the lack of knowing the stone composition prior to ESWL. The latter gives strength to our ANN, since it can be used as a prediction method to all stones regardless of the unknown stone composition. Furthermore, an ANN can be strengthen by numerous inputs, such as stone to skin distance (SSD), patient's performance status, and ureteral impaction. Our concept was to build a predictive model exploiting the most commonly parameters used in the daily practice before the ESWL session. SSD and ureteral wall thickness measurements depend much on the radiologist's and the radiologist technician's experience and are generally not routinely performed before ESWL. Furthermore, since CT imaging is not routinely performed when planning a lithotripsy, SSD and stone hardness were not included in our ANN. Additionally, the high radiation dosage and the economical costs of CT make it sometimes redundant, especially when the stone size and location are obvious from ultrasound and a kidney-ureter-bladder X-ray film. Still, we agree that SSD and stone hardness based on CT imaging could improve ESWL prediction and a different setup of a neural network with these two values included could be more accurate in the future.

5. Conclusion

The use of a neural network appears to be a powerful modeling tool for the diagnosis and treatment of several medical conditions. Our ANN achieved high score in predicting the outcome and the side effects of the ESWL treatment for urinary stones. In fact, the accuracy of the network may further be improved by using larger sets of data, different architecture in designing the model, or using different set of input variables, making ANN a quite promising instrument for effective, precise, and swift medical diagnosis.

Author contributions

Study design: Anastasios Karatzas.
Data acquisition: Georgios Chasiotis, Georgios Perifanos.
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Critical revision of the manuscript: Anastasios Karatzas.

Conflicts of interest

The authors declare no conflict of interest.

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