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Neural Network Modeling to Stratify Peritoneal Membrane Transporter in Predialytic Patients

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The artificial neural network (ANN) model is an artificial construct composed of individual nonlinear processing elements arranged in highly interconnected layers based on the paradigm of biological neural networks (1). Every processing element is interconnected through a set of weighted signals similar to the synaptic connections involved in memory, learning, and predicting responses with the least bias.

High peritoneal membrane transport status is associated with higher morbidity and mortality in peritoneal dialysis (PD) patients. Determining peritoneal membrane transport status can result in a better prognosis (2). Therefore, we constructed an ANN model for predialytic stratification of uremic patients on the basis of peritoneal membrane transport status.

We analyzed the predialytic data from a 5-year PD database of 111 uremic patients. Continuous or nominal variables included demographic characteristics, associated diseases, and blood and urinary biochemistries as 41 input variables. All these data were collected at hospitalization before applying PD tube implantation. The associated diseases were stable and controlled under relevant drugs. The blood biochemistries were measured at 6 AM after 8-hour fasting and urinary biochemistries were gathered for 24 hours. A dichotomous variable, constructed to indicate whether patients values were high and they were high average transporters (group H) or low and low average transporters (group L) on the basis of peritoneal equilibration test results (3) established within one month after initiation of PD, was included in the ANN model.

STATISTICA 7.0 (StatSoft, Inc., Tulsa, OK, USA) was used to construct the model and the multilayer perceptron network with a back-propagation algorithm was selected. The automatic network designer decided an appropriate architecture, using a combination of heuristic strategies and an optimization approach (4). To solve the statistical problem of a finite number of patients in this study and to avoid the possible bias introduced by relying on any one particular division into training and test sets, the leave-one-out cross-validation was employed. This procedure involves removing one case from the training data, training on the basis of the remaining data, and then using the left-out case in a test.

Data were expressed as mean ± standard error (SE). To assess the quality of the classification model, discrimination and calibration were calculated simultaneously. The discriminatory power of the ANN model was analyzed using the area under the receiver operating characteristic curve (AUC). An AUC of 1.0 implied perfect discrimination, 0.5, random chance, and $\geq$0.7, diagnostically useful. The sensitivity and specificity at a cut-off value corresponding to the highest accuracy (minimal false -negative and false-positive results) were also computed. Calibration (goodness-of-fit) was assessed by the Hosmer-Lemeshow statistic (H-statistic). A lower H-statistic value and a higher p value are associated with better fit. A good fit was defined as $p>0.05$.

The numbers of patients in group H and group L were 56 (50.5%) and 55 (49.5%), respectively. The model identified hypertension, cardiovascular disease, serum potassium, 24-hour urinary creatinine, and serum urea nitrogen, as the most important input variables in order of descending importance in predicting the output (Table 1). After the analytical process, the ANN model pruned 8 variables including body mass index, hepatic cirrhosis, hepatitis C carrier, blood biochemistries (leukocyte count, aspartate aminotransferase, alanine aminotransferase, protein), and 24-hour creatinine clearance. For appraising the performance, the AUC of the model was 0.812±0.041 with 95% confidence interval (CI) between 0.727 and 0.880 ($p<0.0001$). The best sensitivity and specificity were 71.4% (95% CI, 57.8%-82.7%) and 85.5 (95% CI, 73.3%-93.5%). The H-statistic was 8.127 ($p=0.421$).

The ANN model has the advantage of recognizing relationships between input and output variables that may not be apparent in clinical medicine (5). Using the ANN model, we clearly demonstrated the usefulness of the model to stratify predialytic patients into H and L groups was shown by its significant discrimination (AUC=0.812>0.7) and best-fitted calibration (p value of H-statistic=0.421>0.05). The evaluation of peritoneal membrane transport status, if predictable prior to dialysis, will help clinicians offer their uremic patients better therapeutic options.

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Table 1. Input Variables Used to Build the ANN Model.

Variables	Mean ± SE or ratio	Rank
Demographic characteristics		
Age (years)	49.3 ± 1.5	25
Gender (male/female)	50/61	23
Height (cm)	161.2 ± 0.7	26
Weight (kg)	55.9 ± 1.0	28
Associated diseases		
Hypertension (%)	72.1	1
Diabetes (%)	26.1	29
Cardiovascular disease (%)	16.2	2
Cerebrovascular disease (%)	10.8	33
Hepatitis B carrier (%)	9.0	11
Systemic lupus erythematosus (%)	3.6	17
Blood biochemistries		
Erythrocyte count (/μl)	2729459.5 ± 63208.7	6
Hemoglobin (g/dl)	8.0 ± 0.2	27
Hematocrit (%)	23.8 ± 0.5	30
Mean corpuscular volume (μm^3)	87.8 ± 0.6	14
Platelet count (/μl)	195360.4 ± 7638.6	12
Urea nitrogen (mg/dl)	125.2 ± 4.6	5
Creatinine (mg/dl)	12.5 ± 0.6	20
Glucose (mg/dl)	126.7 ± 4.6	32
Sodium (mmol/L)	136.00 ± 0.5	7
Potassium (mmol/L)	4.6 ± 0.1	3
Chloride (mmol/L)	101.9 ± 0.6	19
Cholesterol (mg/dl)	178.5 ± 4.9	21
Triglyceride (mg/dl)	142.1 ± 9.3	8
Uric acid (mg/dl)	8.1 ± 0.2	22
Calcium (mg/dl)	8.2 ± 0.1	13
Inorganic phosphorus (mg/dl)	6.0 ± 0.2	15
Calcium-phosphorus product	48.4 ± 1.6	10
Alkaline phosphatase (IU/L)	159.0 ± 7.1	16
Bilirubin (mg/dl)	0.7 ± 0.1	24
Albumin (g/dl)	3.7 ± 0.1	31
24-hour urinary biochemistries		
Volume (ml)	1257.9 ± 64.6	18
Protein (g)	3.3 ± 0.3	9
Creatinine (g)	0.6 ± 0.1	4

In conclusion, the ANN model appears to be a promising tool for stratifying predialytic patients on the basis of peritoneal membrane transport status and helping clinicians make decisions about which dialysis modality is suitable.

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