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Neural Network Analysis Speeds Disease Risk Predictions

Innovative clinical models transform cardiovascular assessment algorithm

Ninad Patil, M.D., M.S. and Timothy J. Smith, R.Ph., Ph.D.

The selection and dosing of drugs is an important component of many care plans designed by clinicians in a wide variety of healthcare settings. At the University of the Pacific's Thomas J. Long School of Pharmacy and Health Sciences, research is aimed at the evaluation of factors that influence both selection and dosing of drugs based upon pathophysiological and pharmacological principles. Recently, research physician Ninad Patil and research pharmacist and pharmacologist Timothy Smith teamed up at the Long School to look at developing neural networks to assist in the evaluation of both the impact of pathological processes and their implications for drug therapy.

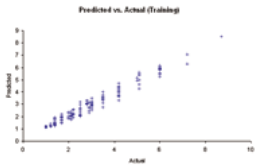

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Figure 1: Relationship between predicted (neural network) and actual (nomogram-derived) values as the result of training

Clinicians often rely upon tabular or graphical data algorithms for evaluating patient laboratory values and decisions for implementation of care plans. For case-by-case *single* patient evaluations, most of these are convenient and relatively easy to use. In order for a clinician to compare and contrast values among a *group* of patients, however, these evaluations become much more cumbersome. Nevertheless, these types of chart and graphical presentations are generally flexible enough for bedside use as well as clinical office applications.

Another one of the significant limitations of tabular and graphical data algorithms is that, as a print media, they are relatively fixed at the time of publication and cannot adapt to new factors that could significantly change the endpoints clinicians obtain from tables and charts. To overcome this limitation, a highly adaptable system for modification of these algorithms is necessary. In many cases, computerized neural network analysis may provide this adaptability.

Cardiovascular risk assessment

In monitoring the risk of cardiovascular disease, total cholesterol, high-density lipoprotein and C-reactive protein have been used as indices,[1-3] and several approaches to data analysis have been applied to assist clinicians in evaluating disease risk associated with these parameters. Among these are algorithms that stratify risk associated with the total cholesterol/HDL ratio versus C-reactive protein in graphical format.[4,5] This type of presentation algorithm is quite useful for estimating risk associated with these factors and reveals trends easily, yet is relatively inflexible to modification with other factors that an individual clinician may wish to investigate.

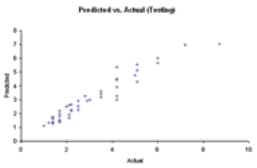

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Figure 2: Relationship between predicted (neural network) and actual (nomogram-derived) values as the result of testing

As a highly adaptive regression technique that can be easily modified and is suitable for predictive analysis, computerized neural network analysis has been previously used to transform nomograms and to evaluate dosing of HMG CoA-reductase inhibitors.[6,7] The adaptation of cardiovascular disease risk assessment to neural network analysis would be advantageous in view of the ability of HMG CoA-reductase inhibitors to reduce both cholesterol and C-reactive protein.[8,9]

Materials and methods

Patil and Smith obtained data for generating a computerized neural network from a nomogram previously published by Sarah de Ferranti from the Department of Cardiology at Children's Hospital in Boston and Harvard Medical School, and by Nader Rifai from the Department of Laboratory Medicine at Children's Hospital and Harvard Medical School's Department of Pathology.4 From this nomogram, 240 data sets were derived. In each data set, values for hs-CRP and total cholesterol/HDL ratio were entered as independent variables into Microsoft Excel. The dependent variable for risk associated with these factors completes one set.

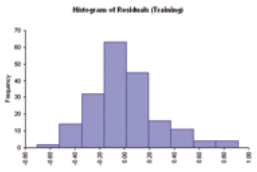

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Figure 3: Distribution of residuals after training the neural network

Palisade's NeuralTools Pro 1.0, which works through an Excel interface, was used for generation of the neural network. Training and test sets, to build and test a network, were derived from the above 240 data sets. Examples of these data sets are shown in Table 1.

To generate the neural network algorithm, training and test sets, hs-CRP, total cholesterol/HDL ratio and risk estimate from the nomogram graphic can be entered directly into Excel. NeuralTools Pro, as well as other neural network software programs, will automatically select training and test sets from all data sets entered and generate the neural network. With successful generation of a neural network, risk of cardiovascular disease can be estimated from new patients simply by entering the patients' hs-CRP and total cholesterol/HDL value(s) into Excel and allowing the neural network to generate the values for risk estimates back into Excel.

Results and discussion

A successful computerized neural network was derived from the data sets. Correlation coefficients for relative risk (neural network versus nomogram) for both training and test sets were R2=0.97 and R2=0.93, respectively (see Figures 1 and 2). In no case did a neural network predicted risk value vary from the algorithm value by 30 percent. In training, the residuals (the difference between neural network predicted versus actual nomogram values) should be relatively balanced between negative and positive values with increased frequency of low value residuals relative to high values (Figure 3).

With this computerized neural network, a patient's relative risk can be rapidly estimated through entering a cholesterol/HDL ratio and C-reactive protein value. Additional factors (independent variables) and the associated relative risk may be added as new evidence necessitates, expanding the utility of the network through retraining. This may be of considerable importance in assessing the impact of HMG CoA reductase inhibitors and related agents in a wide variety of regimens, since these drugs impact both cholesterol/HDL ratio and C-reactive protein titer independently.8,9 Consequently, the computerized neural network may be a suitable tool for reviewing therapeutic interventions and incorporating other risk factors in an assessment.

CRP	TC:HDLC	Rel.Risk
0.1	2	1
0.3	3.6	1.4
0.6	5.2	2.8
0.9	5.2	3.5
1.2	5.2	4.2
1.9	6.5	6
3	6.5	7.2

Table 1: Examples of data input fields for neural network analysis.

For example, a clinician could quickly evaluate the change to cardiovascular disease risk resulting from a change in a care plan, whether that would be a dietary, exercise, co-morbid disease index or a drug-related change. As data accumulate, these changes could eventually be used as additional independent variables for retraining the network and enhancing the utility of this approach. Additionally, while Excel is useful for batch operations (in this case, data from groups of patients), the availability of handheld devices that can run Excel and compatible programs are becoming widely available and will undoubtedly encourage the use of such programs by clinicians in a wide variety of clinical environments.

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