Prospective Assessment of a Symptomatic Cerebral Vasospasm Predictive Neural Network Model

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■ INTRODUCTION: **The author introduced a symptomatic cerebral vasospasm (SCV) prediction model built with freeware based on a 91-patient dataset. In a prospective test group of 22 patients at the same hospital, this model outperformed logistic regression models in vasospasm prediction on the basis of the same datasets. One of the model's limitations was a question of reproducibility in other centers. In this report, the author describes his experience with the prospective use of the model at a different hospital with a different population setting.**

■ METHODS: **Patient data of 25 consecutive cases of aneurysm rupture were prospectively assessed by the model to predict SCV. The prediction was then compared with actual outcome. For the purpose of this report, SCV is defined as a delayed focal decline in neurological examination correlated with an area of radiographic vasospasm. This serves as the primary end point of the predictive model. Each case prediction is reported, along with strength of prediction, which is built into the model. The model's positive predictive value, negative predictive value, and sensitivity and specificity are reported.**

■ RESULTS: **Thirty patients are included in the analysis. Seven patients (23%) were diagnosed with SCV. The model predicted 10 patients would have SCV (positive predictive value 70%). The model predicted 20 patients would not have SCV (negative predictive value 100%). The sensitivity of the model was 100%, and the specificity of the model was 87%.**

■ DISCUSSION: **The present analysis displays the predictive value of a neural network to model symptomatic cerebral vasospasm.**

INTRODUCTION

Symptomatic cerebral vasospasm (SCV) after cerebral aneurysm rupture is a common complication encountered by neurologic surgeons.[1] With unclear or incompletely understood pathophysiology, the luminal diameter of cerebral vessels in affected patients is constricted, limiting brain flow in a manner to cause cerebral ischemia. In severe cases, SCV onset may cause additional morbidity or mortality due to ischemic stroke to patients after aneurysm rupture.[1]

Symptomatic cerebral vasospasm represents an ideal clinical scenario to incorporate use of predictive modeling in medicine. Its presence is commonplace, occurring in roughly one third of cases in a predictable time frame of 3–14 days after aneurysm rupture.[1] Although pathophysiology is incompletely understood, several risk factors are clear, principal among them the extent of hemorrhage by location and size. Furthermore, its identification typically results in successful interventional treatment strategies (namely angioplasty) that are commonly employed and safe,[2] albeit not rigorously tested. Given that cerebral vasospasm is a commonly encountered complication of aneurysm rupture with known risk factors for its development with safe treatment options, the ability to predict its onset would be of clinical value in treatment of this patient population, potentially identifying patients for prophylactic treatment.

With improved connectivity, capability, and portability of computing devices, mathematic modeling provides an ideal

Key words
- Artificial neural network
- Cerebral aneurysm
- Mathematic modeling
- Subarachnoid hemorrhage
- Vasospasm

Abbreviations and Acronyms
ANN: Artifical neural network
NPV: Negative predictive value
PPV: Positive predictive value
SCV: Symptomatic cerebral vasospasm
TCD: Transcranial Doppler

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solution to the neurosurgical clinician wanting reliable prediction tools. Neural network modeling provides a contemporary fulfillment of this ideal, allowing the clinician to take advantage of stronger computing power for practical clinical modeling. Where linear regression modeling is exclusive of data inputs, neural network modeling is inclusive, effectively approximating nonlinear relationships between input data points (risk factors) and output data points (in this case, symptomatic vasospasm). As such, a powerful and accurate artificial neural network (ANN) prediction model may be designed to provide more relevant or reliable modeling solutions to the nonlinear world of medicine compared with regression models.[3-5]

To this end, the author introduced a proof-of-concept ANN prediction model of symptomatic cerebral vasospasm (SCV).[6] The model was designed with freeware neural network software and based on a 91-patient training set. Although the model was designed for proof of concept only, the author has found the model to be surprisingly accurate and thus useful with respect to prediction.

The ANN SCV prediction model tested in the present report was created with a single-center dataset from a hospital based in northern New England. It was designed to compare models with existing regression models,[7,8] so it has simplistic and easily observed or measured inputs. In a prospective test group of 22 patients with aneurysm rupture at the same hospital, this model accurately predicted symptomatic vasospasm in all but 1 false-positive case. One of the limitations of the model was a question of reproducibility in other centers. In the present report, the author describes experience with prospective use of the same predictive model in a quite different population setting in southern Arizona. The purpose of this study is to test the efficacy of the model to predict symptomatic vasospasm after cerebral aneurysm rupture.

METHODS

The design of the model has been previously published (**Supplementary Data**).[6] In brief, the model was designed with a freeware ANN program (Tiberius 6.1.1, 2008, Tiberius Data Mining, Inc., Melbourne, Australia) using a back-propagation algorithm, with 15 binary inputs and 3 hidden layers. The inputs were defined on the basis of existing logistic regression models[7,8] to allow for comparison between the ANN and existing regression models. The inputs include easily observed demographic (gender, age); clinical (clot thickness, GCS and level of arousal, aneurysm location, transcranial Doppler [TCD] elevation); and treatment measures (ventriculostomy placement, treatment technique). The model generates a binary prediction for SCV and a strength of prediction, which may be considered as a measure of expected outcome, with values close to 1 being strongly positive for SCV and values at or below −1 being strongly negative for SCV.

By protocol, patient data for all patients admitted with ruptured aneurysm were entered into the predictive model. These data were collected prospectively at the time of patient admission. All patients admitted with aneurysm rupture from 24 August 2013—January 16, 2016 presenting within 5 days (4 patients excluded) and surviving at least 5 days after their rupture event (5 patients excluded) were included in this analysis (25 patients).

At Banner—University Medical Center Phoenix, Arizona, all aneurysm rupture patients are admitted to and treated by the neurologic surgery team led by the author. After diagnosis, patients are treated with endovascular or open neurosurgical techniques decided by the author on the basis of aneurysm morphology characteristics. External ventricular drains are placed for symptomatic hydrocephalus or at the time of craniotomy for asymptomatic patients with ventriculomegaly. Patients are admitted to a surgical intensive care unit and treated with goals of euvolemia, and once the aneurysm is secured broad blood pressure parameters (systolic blood pressure 90—200 mm Hg) are permitted. Patients are dosed with nimodipine, 60 mg every 4 hours for 21 days, unless not tolerated due to hypotension. Most patients are treated with magnesium (8 g/500 mL in normal saline at 30 mL hourly × 14 days), aspirin (325 mg), and deep-venous thrombosis prophylaxis with heparin (5000 units subcutaneously twice daily) or enoxaparin sodium (Lovenox, 40 mg subcutaneously daily). Transcranial Doppler is performed daily.

Neurologic examinations are performed at least hourly by an intensive care unit nursing team or a physician team. Delayed neurologic deficits are defined as a focal decline in the neurologic examination correlated with an area of radiographic vasospasm. Radiographic vasospasm is defined as a Lindegaard ratio >6 for patients not treated with angiographic means or angiographically confirmed diminished vessel diameter at the time of interventional treatment of SCV. For patients with delayed neurologic deficits, a computed tomography scan is performed and hypertensive therapy initiated after cerebral hemorrhage is ruled out (goal systolic blood pressure >180). If patients have no improvement in examination within 30 minutes of initiation of hypertensive therapy, pending consent patients are brought to the angiographic suite for intra-arterial treatment of vasospasm with intra-arterial vasodilators and angioplasty.

For the purpose of this report, SCV is defined as a delayed focal decline in neurologic examination correlated with an area of radiographic vasospasm. This serves as the primary end point of the predictive model and is the same end point as defined in the earlier publication.[6] Each case prediction is reported, along with strength of prediction, which is built into the model. The model's positive predictive value (PPV), negative predictive value (NPV), and sensitivity and specificity are reported.

RESULTS

Twenty-five patients were included in the analysis, and patient data are summarized in **Table 1**. Most patients were women ($n = 19$, 76%) aged younger than 65 years ($n = 15$, 60%). External ventricular drain placement ($n = 12$, 48%), TCD elevation ($n = 6$, 24%), and diffuse thin/localized clot ($n = 7$, 28%) were the strongest factors in the model on the basis of the original dataset. Six patients (24%) were diagnosed with SCV. As one would expect, the incidence of SCV was associated with additional morbidity, including death in 3 patients due in part to malignant cerebral edema from ischemic stroke as a direct result of vasospasm. No patients without SCV had ischemic stroke, and all survived to time of discharge with the exception of 2 patients, who had poor neurologic examination with support withdrawn at the request of family.

The model predicted 9 patients would have SCV (PPV 67%). The model predicted 16 patients would not have SCV (NPV 100%). The