Early Detection of Vasovagal Syncope in Tilt-up Test with Hemodynamic and Autonomic Study

Chun-An Cheng[1,2], Hsin Chu[2], Hung-Wen Chiu[1]

[1]Graduate Institute of Biomedical Informatics, Taipei Medical University,
[2]Neurology department, Tri-service General Hospital, Taipei, Taiwan

Abstract

The diagnosis of vasovagal syncope (VVS) is according to history, tilt table test and blood pressure change with postural stress. We collected 30 patients below 55 years-old, received tilt table test without pharmacological challenge from 2005 to 2010. Due to this disorder is the heterogeneity, multiple factor. The pathophysological pathway was not fully understood. We used logistic regression and neural network to evaluate variables during baseline and first 3 minutes tilt table test to early detect vasovagal syncope with tilt table test. We found using parameters of baseline heart rate, body mass index and mean blood pressure, cardiac index, left ventricular work index during 3minutes of tilt up test for neural network model, the model revealed good train and test performance (accuracy:95.5%) with good sensitivity and specificity.

1. Introduction

Syncope is the most common reason for a transient loss of consciousness. Repeat syncope can affect daily living and life quality. The pathophysiology of vasovagal syncope is still a potential field for discovery. Hemodynamic and autonomic tests have been considered an important influence on vasovagal syncope in young group [1]. A tilt table test was first applied to syncope assessment and it produces abnormal results in 10 to 30 % of asymptomatic patients. Accordingly, using vasodilator agents with higher false positive rate is not usually recommended [2]. Patients susceptible to VVS can often be identified by means of tilt up test with a fall in blood pressure accompanied by slowing of the heart rate [3]. The predictions about vasovagal syncope conducted by previous research are controversial. Therefore, this study establishes an early prediction model with the application of hemodynamic and autonomic nervous system tests to patients in the tilt-up test, using a computer-based decision-making tool to develop an early prediction model.

2. Patients and methods

We retrospectively enrolled subjects who were referred to the Tri-Service General Hospital to evaluate the cause of syncope or pre-syncope from 2005 to 2010. The patients more than 55 years-old and without impedance cardiographic data were excluded. VVS subjects (mean age 27.2±11.63 years; 5 females, 25 males) and control subjects (mean age 24.7±8.6 years, 4 females, 26 males) were enrolled. All subjects were unremarkable after cardiological and neurological evaluation.

A passive head up tilt-table test was performed between 2:00 and 5:00 pm in a quiet and temperature controlled room (24–25 ◦C) with dimmed lighting. The patients were placed in a supine position on a motorized tilt table, with footboard, knee, and abdominal straps to prevent falling. The upright tilt test protocol began with a 10 minute supine rest period, followed by a second phase in which patients sat upright at 70° for up to 45 minutes or until the onset of symptoms (mean syncopal time around 17.27 minutes of HUT). During the test, patients underwent continuous electrocardiographic monitoring: beat-to-beat blood pressure was monitored noninvasively (Task Force Monitor, CNSystems, Graz, Austria). The upright tilt test was considered positive on the reproduction of syncopal (loss of consciousness and postural tone) or near-syncopal (pallor, nausea, dizziness, lightheadedness, sensation of imminent syncope) symptoms associated with hypotension (drop in systolic blood pressure >60% from baseline values or an absolute value <80 mmHg) alone, or combined with bradycardia (drop in heart rate >30% from baseline value or an absolute value <40 bpm) or asystole.

2.1. Statistical methods

Data are presented as mean ± standard deviation (SD). The between-group comparisons were made by means of a Student’s t test for continuous variables, and the Chi-square test to compare categorical variables. The tests were considered statistically significant at $p<0.05$.The statistical methods performed with SPSS 18.

2.2. Artificial neural networks

The primary functions of neural networks include categorization, prediction, control, and function fitting. The disadvantage of the model was the black box that may yield the good results but unexplainable. First, the variables of baseline and 3 minutes tilt up used logistic regression with forward stepwise to find the potential input parameters. In this study, we used Statistica 7 (StatSoft Co.) to build the artificial neural networks (ANN) model. The input parameters with category or continuous format were set as input nodes. Two output nodes were used to signify the occurrence conditions (negative or positive). 80 % and 20 % of population data were randomly divided as train and test groups, respectively. Multiple layer perceptron (MLP) ANN model with supervised learning algorithm were trained using train group data. Statistica software would generate different MLPs with different number of hidden layer nodes for the training. We chose the best MLP from these MLPs as our model for detection of vasovagal syncope. To evaluate the performance of this model, receiver operating characteristic (ROC) curves and area under ROC were calculated.

3. Results

The statistical results of the two patient groups are displayed in Table 1 and Table 2 .The results indicated that body mass index, and mean blood pressure of the positive group while in the supine and early 3 minutes postural position were lower than that of the negative group. The logistic regression analysis found lower baseline heart rate, body mass index and mean blood pressure, cardiac index during 3minutes of HUT and higher left ventricular work index during 3minutes of HUT induced VVS more easily. While the output threshold was selected as 0.439, a total sensitivity of 90 %, a specificity of 86.7 %, and an accuracy of 88.3 % were obtained with logistic regression model.

In ANN model analysis, five parameters (baseline heart rate, body mass index and mean blood pressure, cardiac index, left ventricular work index during 3minutes of HUT) are used as input nodes. Among total collected 60 subjects, 48 and 12 subjects were randomly selected as training and testing groups, respectively. The MLP with best performance is with the following structure (Figure 1): five neurons were in the input layer, 10 neurons were in the hidden layer, and two neurons (negative/positive) were in the output layer. This model had the performance with an area under the ROC curve 0.979. When the output threshold was set as 0.5, the accuracy in the train and test groups were 93.75 % and 100 %, respectively. And, this model generated a sensitivity of 93 %, a specificity of 96 %, and an accuracy of 95.5 % for total 60 subjects (train+test groups). The performance 0f our ANN model summarized in Table 3.

Table 1. The comparison of variables at supine position in negative and positive vasovagal syncope groups.

	Negative	Positive	P
Age	24.67±8.64	27.2±11.63	0.34
Gender	26M:4F	25M:5F	0.72
BMI	23.39±2.79	21.55±2.88	0.02
HR	72.12±13.47	68.13±11.54	0.22
MBP	88.72±8.99	83.77±8.69	0.03
TPRI	2037±409.66	1913±457.03	0.28
TFC	31.88±3.86	31.25±3.64	0.52
CI	3.54±0.75	3.53±0.65	0.93
EDI	79.39±12.9	81.61±11.99	0.49
LVWI	4.3±1.3	3.88±0.74	0.13
LVET	312.47±19.38	315.4±21.93	0.59
LF/HF	1.38±0.83	1.06±0.57	0.08
BRS	22.57±11.15	22.31±11.91	0.93

Note: Data are presented as the mean value ± SD, except for gender. BMI: body mass index; HR : heart rate; MAP: mean blood pressure; TPRI : total peripheral resistance index; TFC: total chest fluid content; CI : cardiac index; EDI: end-diastolic index; LVWI : left ventricular work index; LVET: left ventricular ejection time ; LF/HF: heart rate variability low/high frequency; BRS: baroreceptor sensitivity.

Table 2. The comparison of variables at 3mins of head tilt up test in negative and positive groups.

	Negative	Positive	P
HR	80.451±3.26	84.11±11.81	0.26
MBP	103.66±17.97	88.65±12.66	<0.01
CI	2.9±0.44	3.06±0.41	0.16
TPRI	2835±630	2583±614	0.12
EDI	63.44±8.7	65.3±6.93	0.36
LVWI	4.03±1.05	4.15±1.11	0.67
LVET	275.2±22	275.5±17.1	0.95
TFC	30±3.49	29±3.35	0.26
LF/HF	3.53±1.83	4.17±3.35	0.37
BRS	10.08±7.1	9.8±3.76	0.85

Note: The abbreviations are same as Table 1.

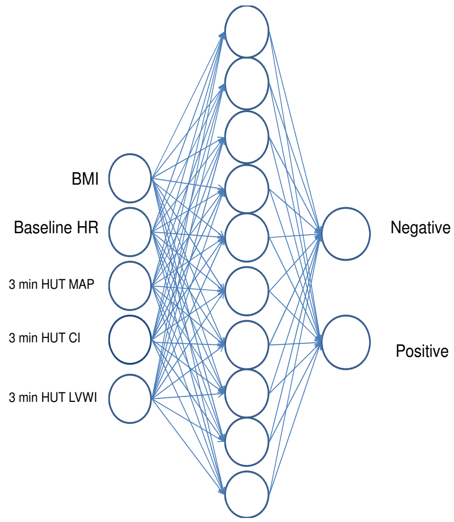

Figure 1. ANN model, MLP 5-10-2, 5 input neurons, 10 hidden neurons and 2 output neurons.

Table 3. The performance of ANN MLP 5-10-2 model.

	Sensitivity	Specificity	Accuracy
Train	92%	95%	93.7%
Test	100%	100%	100%
Total	93%	96%	95.5%

4. Discussion and conclusions

The positive group had a lower body mass index and mean blood pressure while in the supine position. Those with lower values of body composition had lower mean blood pressure on average. The previous literature investigated non-vasovagal syncope patients as those whose heartbeats ≦ 18 times in six minutes using a 60° upright tilt table, indicating a superior specificity of 100 % and a sensitivity of 88.6 %; meanwhile, a specificity of 96.4 % and a sensitivity of 87.3 % was found among other valid patient subjects [4]. Opposing opinions, the changes in heartbeat were not related to syncope prognosis, and the area under the ROC curve was 0.546 (P = 0.30) [5]. Another study measured the times of decline in systolic blood pressure (SBP) over 15 minutes of a tilt table test to predict vasovagal syncope. The results found that vasovagal syncope occurred among patients with SBP declines more than 14 times. The model group had 93 % sensitivity, 58 % specificity, 28 % positive prediction rate, and a 98 % negative prediction rate; the test group had 80 % sensitivity, 85 % specificity, 57 % positive prediction rate, and a 94 % negative prediction rate. That research suggested that SBP declines induce baroreflex, subsequently resulting in heartbeat acceleration [6].

The cardiac output and left cardiac work in elder patients represent the myocardial oxidative metabolism. However, chronic blood stasis in lower limbs increases cardiac work, resulting the cardiac output while in the supine position higher than 3.5 ml/m^3, the end diastolic volume index higher than 77 ml/m^3, and the left cardiac work higher than 4.7 ml/m^3 tends to induce vasovagal syncope [7]. With great sensitivity and poor specificity, the method is only suitable for selecting patients and easily results in false positive results. In a study, the parameters of RR intervals, SBP, low frequency (LF) of heart rate variability, and LF of systolic pressure variation was used to predict the occurrence of vasovagal syncope using a tilt table test for 3 minutes. The research results showed the sensitivity and specificity of the train group were 92 % and 96 %, respectively; and the sensitivity and specificity of the valid group were 95 % and 93 %, respectively [8].

The previous literature used artificial neural networks (ANN) to conduct data mining and discovered that the single use of hemodynamics might not have better predictions than the body composition predictions underwent a tilt table test. The sensitivity and specificity of prediction results were 76 % and 81 %, respectively, by combing hemodynamics and body composition prediction with a tilt table test [9].

This study employed ANN to establish a prediction model with high accuracy. The majority of subjected patients are young males, whose body mass index is lower than that in previous literature; therefore, this model can be applied to the young people.

The model with 5 parameters of baseline heart rate, body mass index and mean blood pressure, cardiac index, left ventricular work index during 3minutes of HUT can be employed to diagnose young patients with unexplained syncope, providing predictions in advance to prevent accidents. Because only few positive patients were collected, we suggests more positive patients must be collected to validate accuracy in the future.

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Address for correspondence

Hung-Wen Chiu
Graduate Institute of Biomedical Informatics, Taipei Medical University, 250 Wu-Hsing Street, Taipei 110, Taiwan
hwchiu@tmu.edu.tw