Autonomic dysfunction as measured by Ewing battery test to predict poor outcome after acute ischaemic stroke

L Xiong, G Tian, HW Leung, XY Chen, WH Lin, TWH Leung, YO Soo, DYW Siu, LKS Wong

KEY MESSAGES

1. The severity of autonomic dysfunction as measured by Ewing battery test predicts poor functional outcome after acute ischaemic stroke.
2. Severe autonomic dysfunction may be related to worse dynamic cerebral autoregulation in affected side in patients with anterior circulation infarct.
3. Relatively severe autonomic dysfunction is associated with lower variation of blood pressure in patients following acute ischaemic stroke.

Hong Kong Med J 2019;25(Suppl 5):S9-11
HMRF project number: 01120566

L Xiong, G Tian, HW Leung, XY Chen, WH Lin, TWH Leung, YO Soo, DYW Siu, LKS Wong

Department of Medicine & Therapeutics, The Chinese University of Hong Kong

* Principal applicant and corresponding author: ks-wong@cuhk.edu.hk

Introduction

Central autonomic dysfunction is commonly seen in patients with ischaemic stroke. Certain measures of autonomic function in ischaemic stroke are associated with an adverse prognosis. For example, decreased heart rate variability is an independent predictor of 1-year mortality in patients with first-ever acute ischaemic stroke.[1] Decreased heart rate variability also correlates with the severity of neurological deficits and disability 6 months after acute ischaemic stroke.[2] In addition, reduced baroreflex sensitivity in the acute phase of stroke is an independent predictor for all-cause mortality over a median 4-year follow-up.[3] Thus, early diagnosis of autonomic dysfunction has prognostic and therapeutic implications in acute stroke. This study aimed to investigate whether the severity of autonomic dysfunction as measured by Ewing battery test can predict poor outcome after acute ischaemic stroke.

Methods

In this hospital-based prospective cohort study, consecutive ischaemic stroke patients within 7 days of symptom onset were recruited from acute stroke unit in Prince of Wales Hospital. Inclusion criteria were: age ≥18 years, cerebral ischaemic stroke detected on computed tomography or magnetic resonance imaging, National Institutes of Health Stroke Scale score of 4 to 10, presence of good temporal window, and written informed consent given. Exclusion criteria were: dementia, any clinically relevant arrhythmia on admission (including atrial fibrillation), any major concurrent illness (including chronic obstructive pulmonary disease, renal failure, and malignancies), fever, hypoxia, alterations in consciousness, and any relevant haemodynamic compromise on admission.

Autonomic function tests were performed by an experienced senior technician according to the Ewing battery test[4] with a Task Force Monitor system (CNSystems Medizintechnik AG Graz, Austria) to measure non-invasive continuous heart rate and blood pressure.

Parasympathetic tests

Valsalva manoeuvre

The participant was asked to exhale for 15 s while maintaining an expiratory pressure of 40 mm Hg. The manoeuvre was performed at least three times to maximise participant compliance and ensure reproducibility. The Valsalva ratio was an index of heart rate changes that occur during a Valsalva manoeuvre. The Valsalva ratio was taken as the maximum R-R interval in the 15 s following expiration divided by the minimum R-R interval.

Deep breathing

Respiratory sinus arrhythmia was assessed by taking six deep breaths per minute with slow inhalation and exhalation (5 s each) at a frequency of 0.1 Hz. Participants were given adequate rehearsal. The timed breathing was performed with the aid of verbal coaching and a time indicator. The response was taken as the mean of the differences between the maximum and minimum instantaneous heart rate for each cycle. A minimum of three breaths was required for inclusion.

The 30:15 ratio

This was performed by rising from the supine to a standing position. The 30:15 ratio was the R-R interval at the 30th beat divides by the R-R interval at the 15th beat immediately after standing.

Sympathetic tests

Orthostasis

Change in systolic blood pressure was calculated as the difference between the nadir systolic blood pressure immediately after standing and the mean systolic blood pressure for the 20 beats immediately prior to standing.

Sustained handgrip

The participant was asked to hold the handgrip with maximal grip and then hold 30% of the maximal grip for 5 minutes. Change in diastolic blood pressure was calculated as the difference between the maximal diastolic blood pressure before releasing the handgrip and the mean diastolic blood pressure for the 20 beats immediately prior to handgrip.

Ewing classification of autonomic failure

Results for each autonomic test were classified as normal, borderline, and abnormal. Patients were classified as normal (all tests normal or one borderline), early (one of the three heart rate tests abnormal or two borderlines), definite (two or more heart rate tests abnormal), severe (two or more heart rate tests abnormal plus one or both blood pressure tests abnormal or both blood pressure tests borderline), and atypical (any other combination). The severity of autonomic dysfunction was dichotomised into severe (definite, severe or atypical) or minor (normal or early).

Data analysis

Demographic data (age, sex, and risk factors such as hypertension, diabetes, hyperlipidaemia, ischaemic heart disease, and smoking) of each patient were collected. At 3 months after stroke onset, the proportion of patients with poor outcome (defined as modified Rankin Scale score of 3 to 6) was calculated. Group differences were examined using the Chi squared test.

Results

Of 150 patients (mean age, 66.4±9.9 years; 70.7% men) recruited, 36 (24.0%) were classified as minor autonomic dysfunction and 114 (76.0%) as severe autonomic dysfunction. The two groups were comparable in terms of baseline characteristics and current drugs use (all P>0.05) [Table]. At month 3, more patients in the severe autonomic dysfunction group had poor functional outcome (32.5% vs 13.9%, P=0.031) [Table]. Crude odds ratio (OR)

TABLE. Baseline characteristics and functional outcome at 3 months in patients with acute stroke patients classified according to Ewing battery test*

	Total cohort (n=150)	Minor autonomic dysfunction (n=36)	Severe autonomic dysfunction (n=114)	P value
Baseline characteristic				
Sex, men:women	106:44	29:7	77:37	0.135
Age, y	66.4±9.9	63.6±11.2	67.2±9.3	0.058
Hypertension	93 (62.0)	21 (58.3)	72 (63.2)	0.315
Diabetes mellitus	51 (35.4)	12 (33.3)	39 (36.1)	0.763
Previous stroke	34 (22.7)	8 (22.2)	26 (22.8)	0.986
Ischaemic heart disease	15 (10.0)	5 (13.9)	10 (8.8)	0.279
Hyperlipidaemia	65 (43.3)	14 (38.9)	51 (44.7)	0.783
Current smoker	64 (42.7)	22 (61.1)	42 (36.8)	0.066
Current drinker	34 (22.7)	13 (36.1)	21 (18.4)	0.098
National Institutes of Health Stroke Scale score on admission	5.7±1.8	5.4±1.7	5.8±1.8	0.246
BI on admission	69.8±9.6	70.2±8.3	68.5±10.2	0.825
Systolic blood pressure	165.5±31.2	167.2±31.6	164.9±31.3	0.749
Diastolic blood pressure	88.9±18.4	94.2±20.4	87.3±17.6	0.097
Functional outcome at 3 months				
Modified Rankin Scale score of >2	42 (28.0)	5 (13.9)	37 (32.5)	0.031

* Data are presented as mean ± standard deviation or No. (%) of patients

of the association between severity of autonomic dysfunction and 3-month unfavourable functional outcome after acute ischaemic stroke was 2.979 (95% confidence interval [CI]=1.071-8.284, P=0.036). After adjusting for confounding factors (diabetes mellitus and ischaemic heart disease), the severity of autonomic dysfunction remained significantly associated with unfavourable outcome (OR=3.171, 95% CI=1.116-9.009, P=0.030).

Discussion

In accordance with previous studies, we found that autonomic dysfunction occurs in acute ischaemic stroke. About 76.0% acute ischaemic stroke patients were diagnosed as having severe autonomic dysfunction. Patients with atypical, definite, or severe autonomic dysfunction were more likely to have a poor modified Rankin Scale score at 3 months. Thus, severe autonomic dysfunction is related to poor outcome in patients with acute ischaemic stroke.

Autonomic imbalance predicts poor outcome after stroke. Decreased heart rate variability correlates with the severity of neurological deficits and disability at 6 months after acute ischaemic stroke.[2] Lower 24-hour standard deviation of all normal-to-normal R-R interval values on admission may predict an unfavourable rehabilitation outcome and dependency in post-stroke patients, despite hospital-based rehabilitation.[5] In general, lower normal-to-normal R-R interval values are due to a shift in autonomic balance toward sympathetic dominance, not only as an effect of impaired parasympathetic function but also as a result of increased sympathetic activity. In the current study, autonomic function was assessed by the Ewing battery test rather than heart rate variability analysis, because the Ewing battery test has been extensively evaluated and represents a simple and accurate approach for quantification of cardiovascular autonomic function, even when performed by physicians without a specific cardiovascular expertise. Furthermore, the severity of autonomic dysfunction can be determined according to the Ewing battery test, which may be more accurate than other assessment methods. Therefore, autonomic monitoring using this method may be useful in predicting long-term outcome after acute ischaemic stroke.

Conclusion

Severe autonomic dysfunction is related to an unfavourable functional outcome in patients with acute ischaemic stroke. Findings of our study may have important implications for the risk of adverse cardiovascular events and mortality rates in stroke survivors.

Acknowledgements

This study was supported by the Health and Medical Research Fund, Food and Health Bureau, Hong Kong SAR Government (#01120566). We thank The Chinese University of Hong Kong (Focused Investment Scheme B) and the Institute of Innovative Medicine, The Chinese University of Hong Kong.

References

1. Colivicchi F, Bassi A, Santini M, Caltagirone C. Cardiac autonomic derangement and arrhythmias in right-sided stroke with insular involvement. Stroke 2004;35:2094-8.
2. Korpelainen JT, Sotaniemi KA, Huikuri HV, Myllya VV. Abnormal heart rate variability as a manifestation of autonomic dysfunction in hemispheric brain infarction. Stroke 1996;27:2059-63.
3. Robinson TG, Dawson SL, Eames PJ, Panerai RB, Potter JF. Cardiac baroreceptor sensitivity predicts long-term outcome after acute ischemic stroke. Stroke 2003;34:705-12.
4. Ewing DJ, Borsey DQ, Bellavere F, Clarke BF. Cardiac autonomic neuropathy in diabetes: comparison of measures of R-R interval variation. Diabetologia 1981;21:18-24.
5. Bassi A, Colivicchi F, Santini M, Caltagirone C. Cardiac autonomic dysfunction and functional outcome after ischaemic stroke. Eur J Neurol 2007;14:917-22.