Autonomic dysfunction as measured by Ewing's battery test to predict poor outcome after acute ischemic stroke

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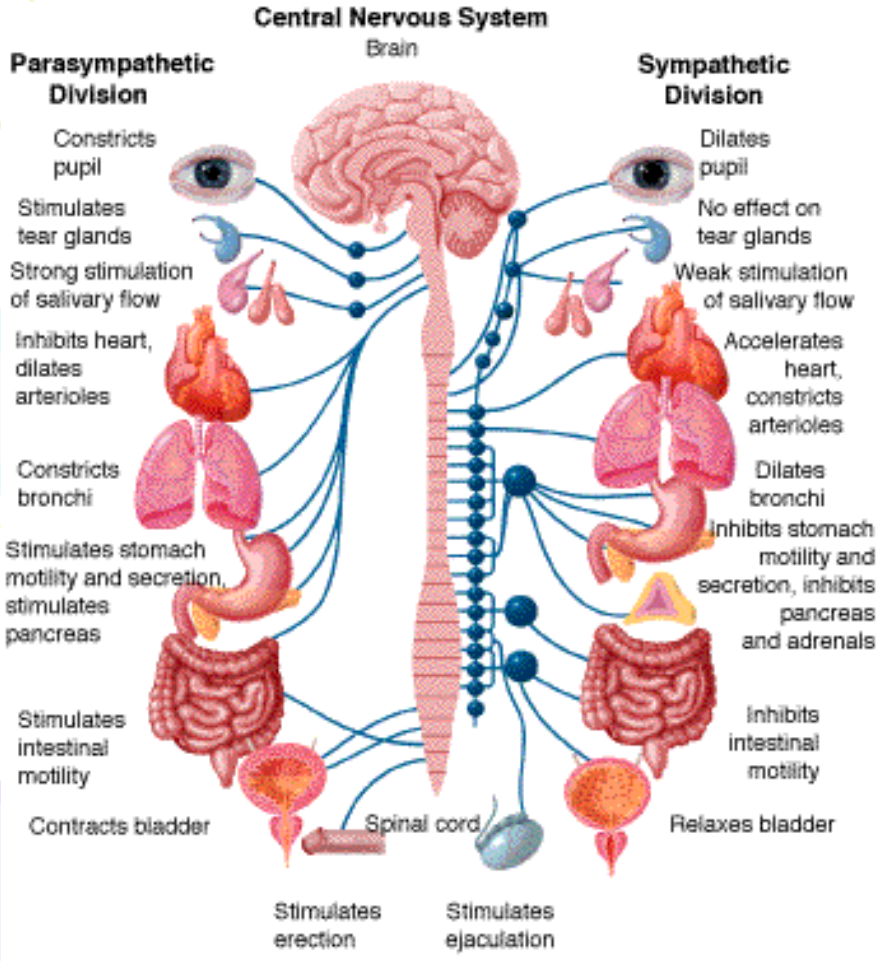
Background



- Acute ischemic stroke can alter autonomic nervous function.

  (Makikallio AM, et al. Neurology.2004;62:1822-1826)

- Autonomic dysfunction might be an important prognostic factor to mortality and morbidity after acute stroke.

Work Done by Us

- Explore whether autonomic function is impaired in different phases and different subtype after ischemic stroke patients

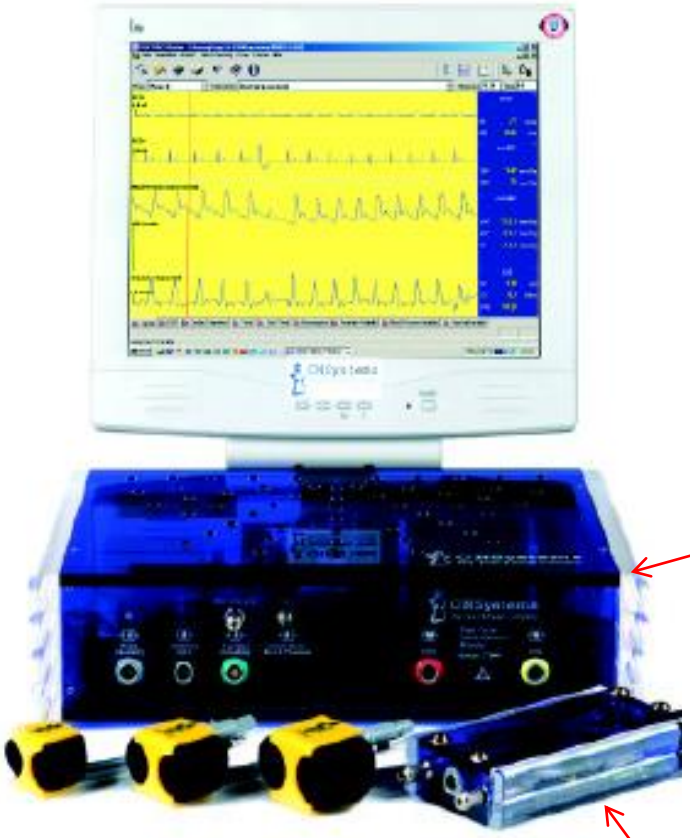
- To investigate the impact of autonomic dysfunction by Ewing's classification on functional outcome after acute ischemic stroke.

Methods

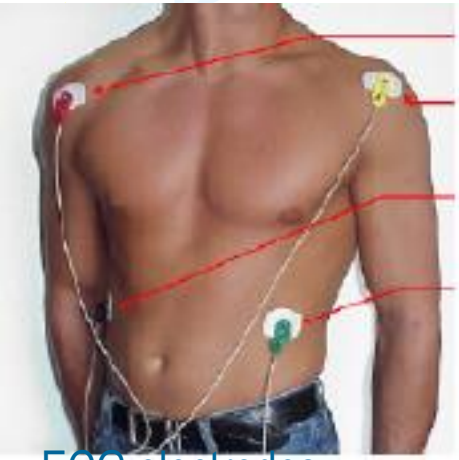
Ewing's battery Autonomic Function Test using the Task Force monitor 3040i

Pulse oximetry

Computer

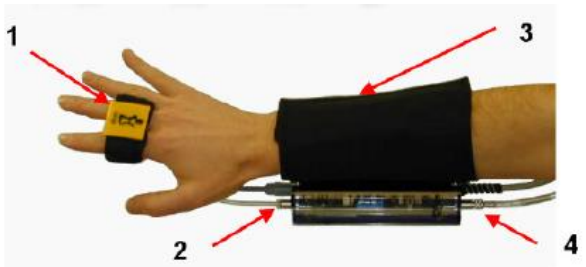


Blood pressure cuff



ECG electrodes

Sampling machine

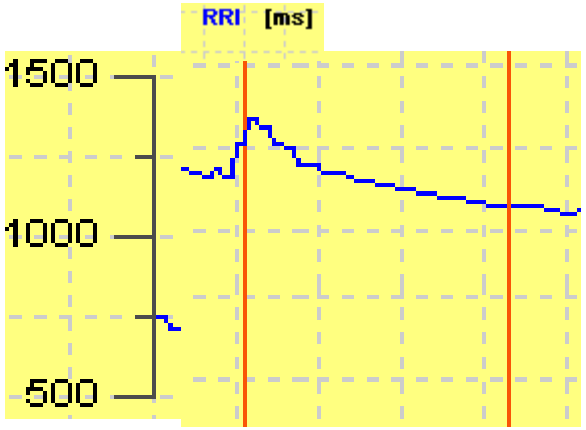


Finger probe

Ewing's battery Autonomic function test

- Parasympathetic tests
  - Valsalva manoeuvre

    Patient blows into mouthpiece (~40mmHg) for 15s. Calculate the ratio of longest and shortest R-R interval Valsalva动作15秒，RRI的比值



Normal >=1.21

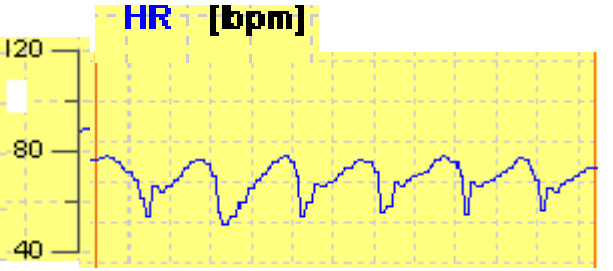
Borderline 1.11-1.2

Abnormal <=1.10

- Deep breathing

  Patient sits on a chair, breathing 6 breaths/min. Calculate maximum HR-minimum HR

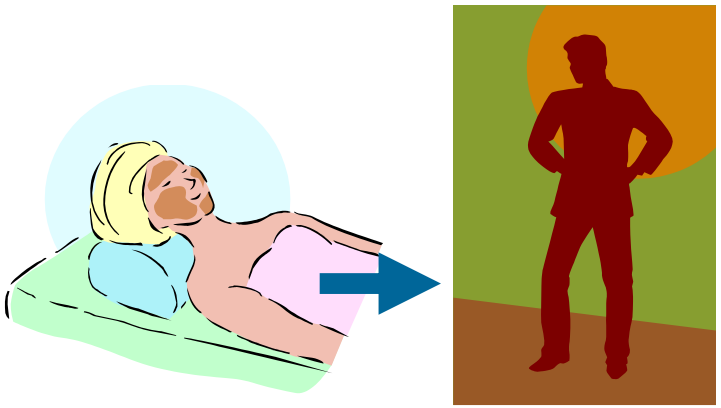
  Normal >15 bpm
  Borderline 11-14 bpm
  Abnormal <= 10 bpm



- Heart rate response to standing

- Monitor the HR while the patient is supine, then ask the patient to stand up,Record the HR at the 15th beat and the 30th beat
- Calculate 30:15 ratio (RR interval)

Normal >=1.04
Borderline 1.01-1.03
Abnormal <=1.00

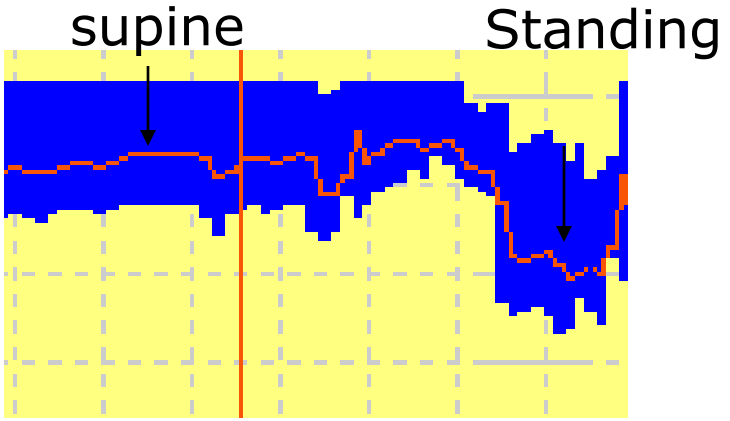


Supine & then standing

- Sympathetic tests
  - SBP response to standing

    SBP measured during supine position & then after standing for 3 mins, Calculate the difference in SBP

Normal <=10mmHg
Borderline 11-29mmHg
Abnormal >=30mmHg



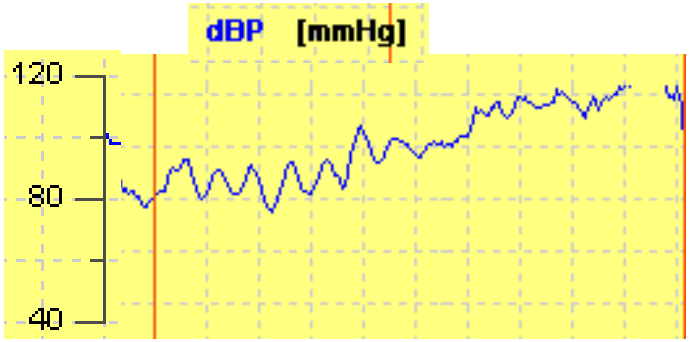
- DBP response to sustained handgrip

  - Perform isometric muscle exercise with handgrip dynamometer with grip maintained at 30% of max for 5min.
  - Calculate difference between diastolic BP at the starting and stopping point.

Normal >=16mmHg

Borderline 11-15mmHg

Abnormal <=10mmHg



Ewing's classification

Results

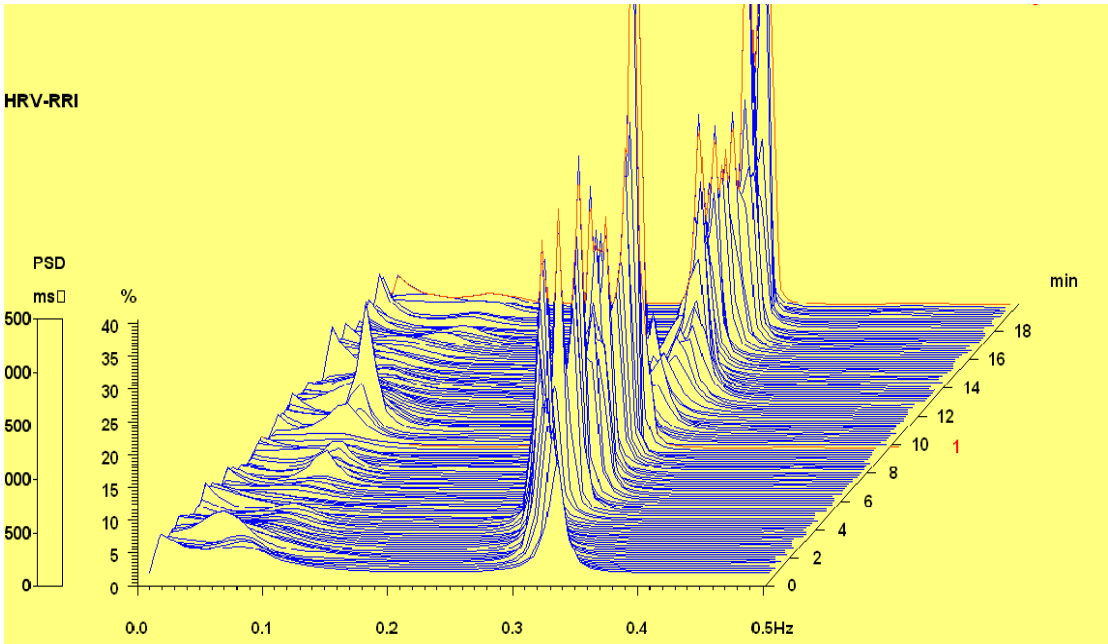
	Normal	Borderline	Abnormal
Valsalva Ratio	>/= 1.21	1.11–1.20	< / =1.10
Max – Min HR Deep breathing	>/=15bpm	11-14 bpm	</ =10bpm
30:15 ratio	>/ =1.04	1.01–1.03	</ =1.00
BP to standing	</=10mmHg	11-29mmHg	>/=30mmHg
Increase diastolic BP to hand grip	>/=16mmHg	11–15mmHg	</=10mmHg

Classification Ewing's

Category 1	Normal	All 5 normal or only 1 borderline
Category 2	Early involvement	1 of 3 HR tests abnormal or 2 borderline
Category 3	Definite involvement	2 or more HR tests abnormal
Category 4	Severe involvement	At in category 3 plus 1 or both BP tests abnormal, or both borderline
Category 5	Atypical	Other combination

Measurement of heart rate variability

- ECG was recorded for 5mins at rest
- Power spectral analysis (Fast Fourier transformation) performed to obtain spectral bands in the very low(<0.04Hz).low(0.04-0.15Hz) and high(0.15-0.40Hz) frequency bands and also total spectral power(<0.40Hz)
- Sympathovagal balance examined by LF/HF



Inclusion criteria

- Age ≥ 18 years old
- CT or MRI showed cerebral ischemic infarct not including insular infarct
- ECG showed sinus rhythm
- Absence of any major concurrent illness

Autonomic function test (AFT)

- Parasympathetic tests
- Sympathetic tests

Ewing's classification

- Normal
- Early
- Definite
- Severe
- Atypical

Commonly Dichotomize

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Research

Comprehensive assessment for autonomic dysfunction in different phases after ischemic stroke

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Objective

- To determine whether autonomic function was impaired during different phases in ischemic stroke by Ewing's battery of autonomic function tests as well as power spectral analysis of heart rate variability.

Results

Table 1 Baseline characteristics of all participants

Characteristics	Control *n* = 37 No. (%)	Stroke in acute phase *n* = 34 No. (%)	Stroke in chronic phase *n* = 60 No. (%)	*P*

Table 5 Parasympathetic clinical autonomic function tests

Diagnosis	Control	Stroke in acute phase	Stroke in chronic phase	*P*
Mean Valsalva ratio	1·21 (1·17–1·25)	1·13 (1·07–1·16) 0·002 (0·002)	1·14 (1·06–1·21) 0·005 (0·005)	0·003
Mean change in heart rate during deep breathing	13·29 (11·12–15·47)	7·85 (4·00–12·00) <0·001 (0·009)	8·52 (5·25–11·00) <0·001 (0·019)	<0·001
Mean heart rate response to standing	1·04 (1·02–1·06)	1·02 (0·99–1·05) 0·102 (0·100)	1·01 (0·99–1·03) 0·003 (0·003)	0·013

Data expressed as mean (95% confidence interval).
Columns 3–4 show the *P* values for that patient group in comparison with the control group in univariate analysis of variance and in multivariate analysis in parentheses.

*$P < 0.05$ compared with controls.
Smoker and drinker include ex- and current smokers and drinkers.
COPD, chronic obstructive pulmonary disease; LAD, large artery disease; NA, not applicable; SVD, small vessel disease; SD, standard; NIHSS, National Institutes of Health stroke scale.

Conclusion

- The comprehensive assessment indicates that autonomic dysfunction occurs in acute phase of ischemic stroke and may persist up to six months after stroke.

- Parasympathetic dysfunction rather than sympathetic dysfunction is predominant after ischemic stroke.

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ACTA NEUROLOGICA SCANDINAVICA

Autonomic dysfunction in ischemic stroke with carotid stenosis

Xiong L, Leung HW, Chen XY, Han JH, Leung WH, Soo OY, Lau YL, Wong KS. Autonomic dysfunction in ischemic stroke with carotid stenosis.
Acta Neurol Scand: 2012: 126: 122–128.

Objectives – Impaired autonomic function is common in acute ischemic stroke. Previous limited studies have suggested that atherosclerosis may affect the distensibility of the carotid sinus and then impair the cardiovascular autonomic function. This study sought to investigate cardiovascular autonomic function in patients with ischemic stroke with carotid stenosis. *Methods* – Eighty-five patients with ischemic stroke (58 ones without carotid stenosis and 27 ones with carotid stenosis, average 6 months after stroke onset) and 37 elderly controls were recruited. All performed Ewing's battery autonomic function tests. *Results* – From Ewing's battery of autonomic function tests, atypical, definite, or severe autonomic dysfunction was identified in 69.0% patients without carotid stenosis and 88.9% with carotid stenosis, with significant difference between the two groups, and the prevalence of autonomic dysfunction in both groups was higher than that in controls (21.6%). Patients with carotid stenosis showed impairment of all parasympathetic tests (all $P < 0.05$) and one of the sympathetic tests [Mean fall in systolic blood pressure (BP) on standing: $P = 0.051$], and those without carotid stenosis only showed impairment in two parasympathetic tests (Valsalva ratio: $P = 0.014$; heart rate response to deep breathing: $P < 0.001$) in comparison with controls. Patients with carotid stenosis had significantly more impairment than those without carotid stenosis in some autonomic parameters (Valsalva ratio: $P < 0.05$; mean fall in systolic BP on standing: $P < 0.05$). *Conclusions* – Cardiovascular autonomic function is impaired in patients with ischemic stroke, but patients with carotid stenosis show more severely impaired parasympathetic and sympathetic functions.

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Key words: autonomic dysfunction; ischemic stroke; carotid stenosis

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Autonomic dysfunction in different subtypes of post-acute ischemic stroke

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Abstract: Objectives Central autonomic impairment is frequent in ischemic stroke at acute or chronic stages. The mechanism by which these symptoms occur in patients with ischemic stroke has not been elucidated. This study sought to investigate cardiovascular autonomic function in patients with different subtypes of post-acute ischemic stroke.

Methods 77 ischemic stroke patients [50 patients with large-artery atherosclerosis (LAA) and 27 patients with small-vessel occlusion (SVO), average 6 months after stroke onset] and 37 elderly controls were recruited. All performed Ewing's battery autonomic function tests and and power spectral analysis of heart rate variability (HRV).

Results Stroke patients with both LAA and SVO had significantly lower low frequency power spectral density than controls. The prevalence of autonomic dysfunction in both groups (82.0% patients with LAA and 63.0% with SVO) was higher than that in controls (21.6%). Patients with LAA showed impairment of all parasympathetic tests (all $P<0.05$) and one of the sympathetic tests (Mean fall in systolic blood pressure on standing: $P=0.058$) and those with SVO only showed impairment in two parasympathetic tests (heart rate response to deep breathing: $P=0.010$; heart rate response to standing: $P=0.004$) in comparison with controls. Patients with LAA had significantly more impairment than those with SVO in some autonomic parameters (Valsalva ratio: $P=0.039$; mean fall in systolic blood pressure on standing: $P=0.015$).

Conclusions Irrespective of the subtype of the ischemia, post-acute stroke patients showed a parasympathetic cardiac deficit. Additionally, parasympathetic and sympathetic cardiovascular modulations were more severely impaired in patients with LAA.

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Preliminary findings of the effects of autonomic dysfunction on functional outcome after acute ischemic stroke

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Table 1
Baseline characteristics of acute stroke patients according to Ewing classification.

	Total cohort (n = 34)	Minor autonomic dysfunction (n = 8)	Relatively severe autonomic dysfunction (n = 26)	p^a
Male/female	23/11	5/3	15/11	0,809
Age, years	71,7 ± 8,7	68,8 ± 7,8	72,5 ± 8,9	0,289
Hypertension (%)	28 (82,4)	4 (50,0)	18 (69,2)	0,410
DM (%)	17 (50)	2 (25,0)	15 (57,7)	0,225
Duration of DM, months	12,8 ± 2,2	14,0 ± 1,4	12,5 ± 8,5	0,815
HA1c, % Hb	7,4 ± 0,5	7,6 ± 0,1	7,4 ± 1,9	0,892
Previous stroke (%)	14 (41,2)	4 (50,0)	10 (40,0)	0,689
IHD (%)	2 (7,1)	1 (12,5)	1 (3,8)	0,421
Hyperlipidemia (%)	18 (52,9)	3 (37,5)	15 (57,7)	0,429
Current smoker (%)	9 (26,5)	4 (50,0)	5 (19,2)	0,165
Current drinker (%)	7 (20,6)	3 (37,5)	4 (15,4)	0,315
NIHSS on admission	4,4 ± 3,0	3,3 ± 3,4	4,8 ± 2,9	0,221
mRS ≤2 on admission	20 (58,8%)	6 (75,0%)	14 (53,8%)	0,422
BI on admission	68,8 ± 15,6	76,3 ± 15,3	66,5 ± 15,2	0,125
Systolic BP	173,9 ± 25,2	177,0 ± 32,4	173,0 ± 23,3	0,701
Diastolic BP	87,3 ± 15,1	93,8 ± 20,0	85,4 ± 13,1	0,173
Length of hospital stay, days	5,5 ± 0,5	4,6 ± 2,3	5,8 ± 3,1	0,336
Carotid stenosis (%)	9 (26,5%)	2 (25,0%)	7 (26,9%)	0,914
Localization of stroke				0,510
Cortical–subcortical	13	2	11	
Subcortical	8	3	5	
Cortical	13	3	10	
Stroke subtypes				0,099
LAD	15	2	13	
SVD	5	1	4	
LAD + SVD	11	3	8	
Cardioembolic	1	0	1	
Undetermined	2	2	0	

醫療衞生研究基金
Health and Medical Research Fund

HMRF 2012 Funded Project

- Autonomic Dysfunction as Measured by Ewing's Battery Test to Predict Poor Outcome after Acute Ischemic Stroke

  Ewing's battery 測試自主神經功能損傷用於預測急性缺血性腦中風不良預後

- Grant of HK$ 723,960

香港中文大學
The Chinese University of Hong Kong

Objectives

- To investigate whether the severity of autonomic dysfunction as classified by Ewing's battery test can predict poor outcome after acute ischemic stroke.

Methods

- A prospective observational study;
- Consecutive ischemic stroke patients within 7 days of symptom onset enrolled;
- Autonomic function assessed by Ewing's battery tests;
- The severity of autonomic dysfunction dichotomized into two groups: severe (definite, severe or atypical) and minor (normal or early);
- Clinical outcome evaluated 3 months after index stroke using modified Rankin scale (mRS)
  - Good outcome: mRS 0~2
  - Poor outcome: mRS 3~6

Table 1 Baseline characteristics of acute stroke patients according to Ewing classification

	Total cohort (n=150)	Minor autonomic dysfunction (n=36)	Relatively severe autonomic dysfunction (n=114)	*P**
Male/female	106/44	29/7	77/37	0.135
Age, years	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
DM (%)	51 (35.4)	12 (33.3)	39 (36.1)	0.763
Previous stroke (%)	34 (22.7)	8 (22.2)	26 (22.8)	0.986
IHD (%)	15 (10.0)	5 (13.9)	10 (8.8)	0.279
Hyperlipidemia (%)	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
NIHSS 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 BP	165.5 ± 31.2	167.2 ± 31.6	164.9 ± 31.3	0.749
Diastolic BP	88.9 ± 18.4	94.2 ± 20.4	87.3 ± 17.6	0.097

Table 2 Functional outcome at 3 months after acute stroke onset

Total cohort (n=150)	Minor autonomic dysfunction (n=36)	Relatively severe autonomic dysfunction (n=114)	P*
42 (28.0%)	5 (13.9%)	37 (32.5%)	0.031

* Comparison at 3 months between the two groups; Chi-Square test was used.

Table 3 Crude and adjusted ORs of severity of autonomic dysfunction and 3-month unfavourable Functional Outcome

	Unadjusted		Adjusted for DM and IHD	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
utonomic dysfunction	2.979 (1.071-8.284)	0.036	3.171 (1.116-9.009)	0.030

OR, odds ratios; DM, diabetes mellitus; IHD, ischemic heart disease.

Conclusion

- The severity of autonomic dysfunction as measured by Ewing's battery test predicts poor clinical functional outcome after acute ischemic stroke.

Acknowledgment

Thank You!

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