Association between Heart Rate Variability and Secondary Brain Injury in Patients with Large Hemispheric Infarct

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Introduction

- Large hemispheric infarct (LHI) patients (acute anterior circulation ischemic stroke with an admission NIHSS score of ≥ 15) are at risk for secondary brain injury (SBI) characterized by early neurological decline (END) and malignant cerebral edema (MCE).
- We hypothesized that admission characteristics and time- and frequency-domains of heart rate variability (HRV) can predict both END and MCE.

Methods

- LHI patients were selected from consecutive NCCU admissions between January 2016 and December 2019
- END was defined as delta NIHSS ≥ 4 at 24 hours from admission.
- MCE was defined as clinical and/or radiographic herniation or need for craniectomy within 48 hours of injury.
- Continuous ECG was collected over the first 3 hours of admission to calculate time- and frequency-domain HRV features.
- Multivariable logistic regression was performed to determine factors independently associated with END, MCE, and poor outcome at 90 days (mRS ≥ 4).

Results

Table 1. Baseline Characteristics of LHI Patients

Characteristic	N = 452
Women	233 (52)
Age, years	66 (15)
Race	
White non-Hispanic	230 (52)
African American	172 (39)
White Hispanic	15 (3)
Asian	9 (2)
Other	16 (4)
Unknown	2 (1)
Past Medical History	
Hypertension	372 (82)
Congestive heart failure	66 (15)
Coronary artery disease	88 (20)
Diabetes mellitus	173 (38)
NIHSS score	21 (4)
Stroke Syndrome	
Right MCA	152 (34)
Left MCA	212 (48)
Right ICA	17 (4)
Left ICA	21 (5)
Other	9 (2)
t-PA administered	196 (44)
IA thrombectomy	254 (56)
TICI ≥ 2B	207 (81)
Glucose, *mg/dL*	145 (61)

Categorical data shown as n (%), continuous data as mean (SD).

Table 2. Independent Predictors of Early Neurological Decline

Predictor	Odds Ratio	95% CI	P value
NIHSS	0.83	0.71, 0.99	0.045
CAD	0.32	0.11, 0.95	0.04
LF:HF Ratio	1.15	1.04, 1.26	0.003

Model adjusted for intervention with mechanical thrombectomy, mean ECG-NN interval. ORs adjusted for following: NIHSS for every 2-point increase in scale, LF:HF Ratio for every 20-point increase in ratio.

Table 3. Independent Predictors of Malignant Cerebral Edema

Predictor	Odds Ratio	95% CI	P value
Admission Glucose (mg/dL)	1.01	1.00, 1.01	0.045
Age (years)	0.97	0.95, 0.99	0.001
R to R interval (sec)	1.01	1.00, 1.02	0.036
tPA administration	1.96	1.11, 3.47	0.021

Model adjusted for admission scan midline shift, intervention with mechanical thrombectomy, history of diabetes, history of renal disease, race, syndrome, NIHSS on admission, and ECG Shannon score. ORs adjusted for the following: admission glucose for every 20 mg/dL increase, age for every 5-year increase, R to R interval for every 60-second increase.

Results

Table 4. Factors Associated with Poor Outcome at 90 Days

Risk Factor	Odds Ratio	95% CI	P value
Admission NIHSS	1.35	1.12, 1.63	0.001
IA thrombectomy	0.48	0.24, 0.97	0.04
Admission Glucose (mg/dL)	1.27	1.06, 1.53	0.01
Age (years)	1.35	1.19, 1.53	< 0.001
Early neurological decline	8.66	1.71, 43.88	0.01
Malignant cerebral edema	4.33	1.40, 13.36	0.01

Model adjusted for mean ECG-NN interval, race, syndrome, admission scan midline shift, sex, tPA administration, history of diabetes, history of renal disease, delayed presentation, mean low to high frequency ratio. ORs adjusted for the following: NIHSS for every 2-point increase in scale, admission glucose for every 20 mg/dL increase, age for every 5-year increase

Discussion

- Frequency and time - domain features of HRV in the first 3 hours after admission and baseline clinical factors are associated with SBI after LHI.
- SBI in the first 48 hours significantly contributes to poor outcome at 90 days in LHI patients.
- Further analyses exploring the relationship between HRV and SBI after LHI are warranted.