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Rapid Assessment of Blood Pressure Variability and Outcome after Successful Thrombectomy

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Abstract

Background and Purpose: High blood pressure (BP) variability after endovascular stroke therapy (EVT) is associated with poor outcome. Conventional BP variability measures require long recordings, limiting their utility as a risk assessment tool to guide clinical decision making. Here, we performed rapid assessment of BP variability by spectral analysis and evaluated its association with early clinical improvement and long-term functional outcomes.

Methods: We conducted a prospective study of 146 patients with anterior circulation ischemic stroke who underwent successful EVT. Spectral analysis of 5-minute recordings of beat-to-beat BP was used to quantify BP variability. Outcomes included initial clinical response and modified Rankin scale at 90 days.

Results: Increased BP variability at high frequencies was independently associated with poor functional outcome at 90 days (adjusted odds ratio [aOR]=1.85, 95% CI 1.07 – 3.25, p=0.03; low/high frequency ratio aOR= 0.67, 0.46 – 0.92, p=0.02) and reduced likelihood of an early

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Supplemental Materials:
Online Additional methodological details & Figure I – IV & Tables I – V

neurological recovery (aOR=0.62, 0.44 – 0.91, p=0.01 and aOR=1.37, 1.03 – 1.87, p=0.04, respectively).

Conclusions: High-frequency BP oscillations after successful reperfusion may be harmful and associate with a decreased likelihood of neurological recovery and favorable functional outcomes. Rapid assessment of BP variability throughout the post-reperfusion period is feasible and may allow for a more personalized BP management.

Introduction

There is an increased risk of hemorrhagic transformation (HT) and worse outcome in patients with increased blood pressure (BP) during the first hours after EVT.[1, 2] Because of impaired cerebral autoregulation with resulting susceptibility to cerebral hypo- or hyperperfusion,[3] avoiding large BP swings after revascularization may be as important as treating high BP levels. Conventional measures of BP variability usually require 24 hours of BP monitoring, limiting their usefulness for clinical decisions making. This study aimed to assess BP variability from 5-minute beat-to-beat recordings using spectral analysis and evaluate its ability to predict early neurological recovery and long-term functional outcome.

Materials and Methods

Data availability

Data and statistical syntax is available for research purposes and can be obtained by a reasonable request to the corresponding author.

Study design and outcomes

We conducted a prospective study of adult patients with anterior circulation large-vessel occlusion (LVO) stroke who underwent successful EVT (modified Thrombolysis in Cerebral Infarction score [mTICI] 2b-3).[4] Standard demographic/clinical variables were recorded. CT scans were centrally reviewed by an experienced neuroradiologist (SP) for lesions affecting the central autonomic network (Supplemental Figure I).[5] The study received approval from the ethics committee at both institutions. Written informed consent was obtained from all participants or legally authorized representatives.

Functional outcome was assessed using the modified Rankin scale (mRS) score at 90 days. Additional outcomes at 24 hours included midline shift, HT and early neurological recovery, the reduction in NIHSS score of at least 4 points or NIHSS<2.

BP variability

Five-minute beat-to-beat BP recordings were obtained <24 hours from last-seen-well time using non-invasive finger photoplethysmography (Finometer MIDI, FMS, Netherlands). Details in Supplemental Data. Spectral analysis was performed using the Welch method.[6] Power spectra were decomposed in very-low (VLF;<0.04 Hz), low (LF;0.04–0.15 Hz) and high (HF;0.15–0.40 Hz) frequency bands. Increased power implies more variability. Additionally, BP was assessed hourly (brachial cuff) to calculate mean and standard deviation (SD) over 24-hours.

Statistical Analysis

For details see Supplementary Data.

Results

Between September 2017 and January 2019, 146 patients were enrolled (Table I; Supplemental Figure II). Overall, unfavorable functional outcome was associated with higher systolic BP at admission and during the first 24 hours after EVT (Supplemental Table III). We found no association between BP variability measured as SD and any of the endpoints.

Normalized HF power was significantly lower in patients demonstrating faster neurological recovery and in those who were independent at 90 days (Table 1). Adjusting to baseline severity, higher normalized HF power (adjusted OR [aOR]=1.85, 95%CI 1.07 – 3.25, p=0.03) and LH/HF ratio (aOR=0.67, 0.46 – 0.92, p=0.02) were independently associated with poor functional outcome. Higher normalized HF power and lower LH/HF ratio also reduced the likelihood of neurological recovery (aOR=0.62, 0.44–0.91, p=0.01; aOR=1.37, 1.03 – 1.87, p=0.04); Supplemental Table III). Figure 1 shows representative cases.

Considering the prognostic performance of BP parameters (Figure 2), we found that normalized HF power was the best predictor of early neurological recovery (AUC=0.63, 0.61 – 0.68, p=0.02) and functional outcome (AUC=0.65, 0.63 – 0.67, p<0.01) (Supplemental Figure III); optimal cuff-off at 0.45. HF>0.45 was significantly associated with a shift towards worse mRS classes (aOR=2.71, 1.44 – 5.14, p<0.01, Figure 2). Sensitivity analyses showed no bias due to atrial fibrillation, hypertension, or time of recanalization (Supplemental Figure IV).

Normalized HF power was associated with the development of significant cerebral edema (aOR=5.87, 1.01 – 44, p=0.04, Supplemental Table IV). Infarct volume or location did not relate to BP parameters (Supplemental Table V).

Discussion

In 146 consecutive patients with anterior circulation LVO stroke, increased high-frequency BP variability after successful EVT was associated with the development of significant cerebral edema, a lower probability of early neurological recovery and increased risk of unfavorable functional outcome

Our results suggest that the harmful effects of BP variability may, in part, be related to cerebral edema and possibly dysfunction of blood-barrier that follows successful EVT.[7] Our results consistent with previous studies that showed increased variations of hourly BP measurements after stroke are associated with an increased risk of cerebral edema and HT.[8–10] On the other hand, severe edema can cause BP changes by itself. However, unlike traditional methods, our approach can detect harmful patterns of BP variability within minutes, and thus can provide a real-time measure to guide BP management in individual patients.[11–13]

Autonomic dysfunction is common in stroke,[14] despite strong conceptual reasons, we found no association between HF BP variability and injury to the structures of the central autonomic network or infarct volume.

Limitations concerns a modest sample size, restriction to successful EVT, and lack of MRI protocol to evaluate blood-barrier dysfunction.[15] Spectral BPV should be studied also in unsuccessful recanalization and different collateral grades to broaden the extension of our results. Vasoactive drugs can be confounding factors for BP parameters, despite multivariate adjustment, as infection and other respiratory parameters. Finger plethysmography presents several challenges in the acute stroke settings (Supplementary Data).

Summary

Rapid bedside assessment of BP variability is feasible and carries prognostic significance. Further research is needed to test novel treatment strategies to minimize potentially harmful BP fluctuations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Conflict(s)-of-Interest/Disclosure(s):

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Non-standard Abbreviations and Acronyms

BP	Blood Pressure
LVO	Large vessel occlusion
EVT	Endovascular treatment
VLF	Very-low frequency
LF	Low frequency
HF	High frequency

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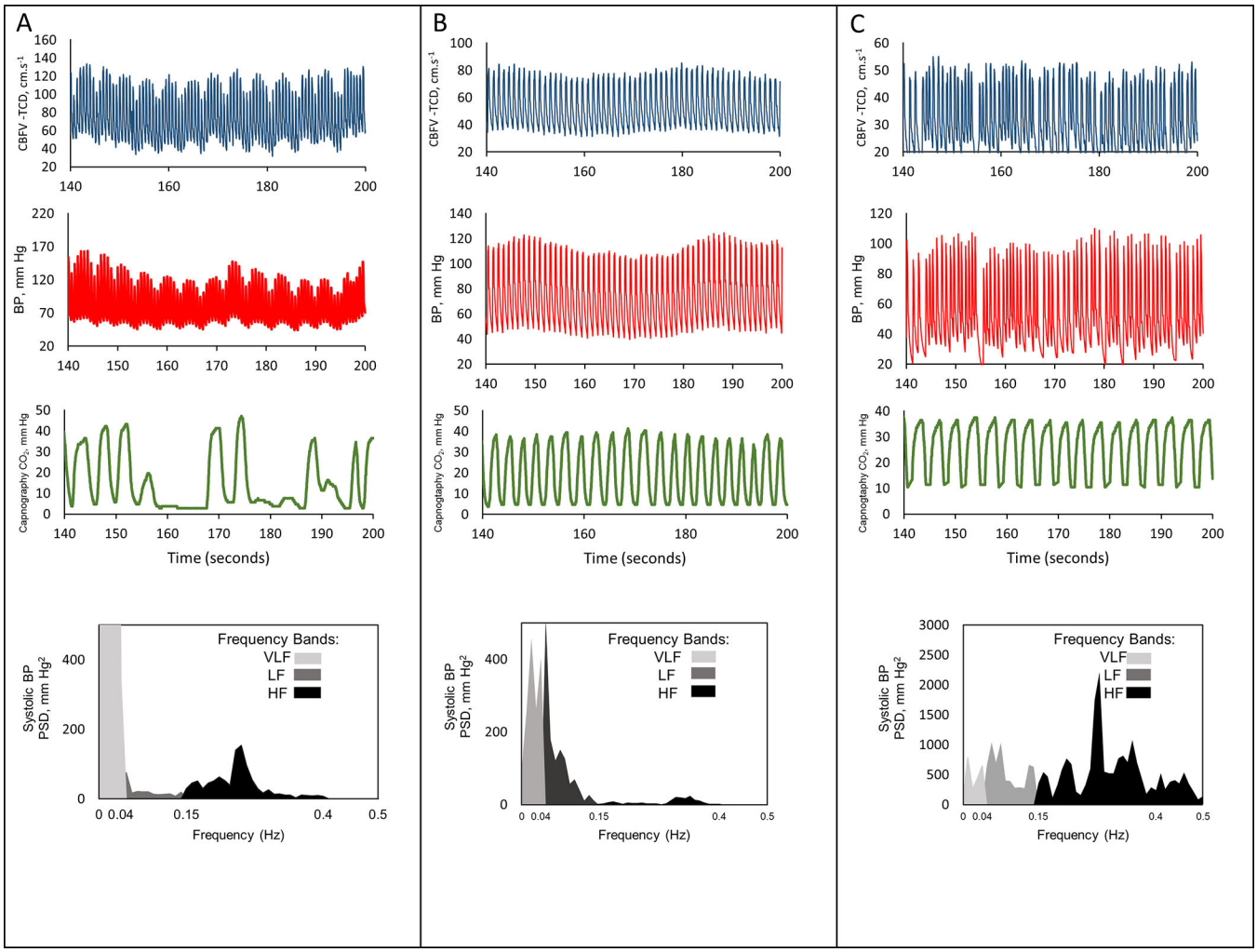

Figure 1.

Representative cases (A, B and C) of very short-term variability. Red, blue and green lines represent continuous blood pressure (BP; Finometer), cerebral blood flow velocity (CBFV; transcranial Doppler) and expiratory carbon dioxide (CO_2; capnography). At bottom, spectral density of systolic BP in very-low (VLF/light grey), low (LF/dark grey) and high (HF/ black) bands. A–poor prognosis; BP variability peak~0.3 Hz (HF range). B–good prognosis; increased LF over HF power. C–poor prognosis; atrial fibrillation, still shows a peak within HF band.

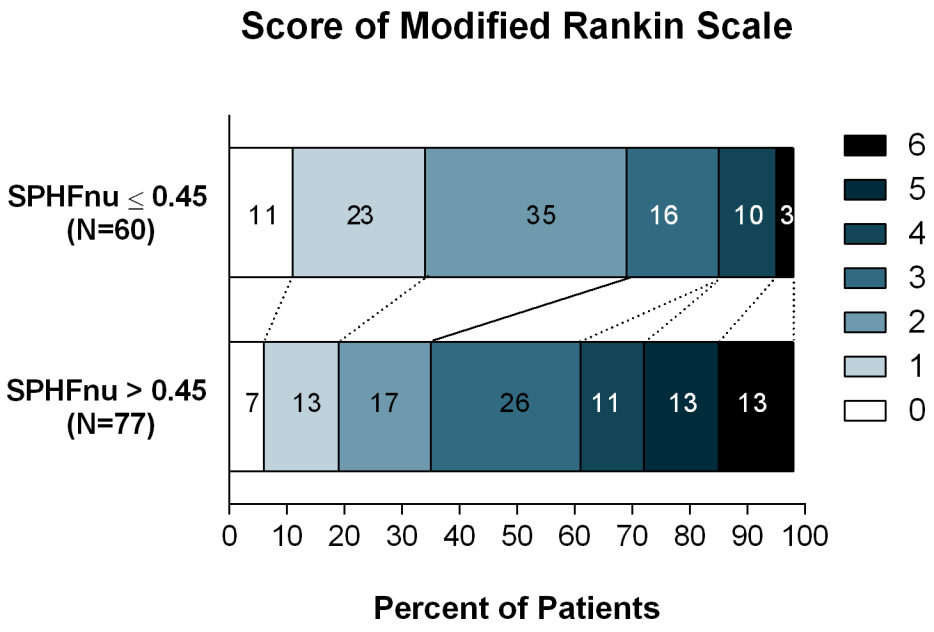

Figure 2.

Distribution of scores on the modified Rankin scale at 90 days among patients with high versus low very-short-term BP variability (normalized units, SPHFnu)

Table 1

BP parameters among subgroups of clinical outcome

	All (n=146)	Independent mRS 0–2 (n=63)	Dependent mRS 3–6 (n=58)	P value*	Early neurological recovery Yes (n=61)	Early neurological recovery No (n=60)	P*
Admission							
Systolic BP, mm Hg – mean (SD)	141 (24)	136 (26)	146 (21)	0.02	140 (24)	143 (24)	0.53
Diastolic BP, mm Hg – mean (SD)	77 (19)	76 (24)	79 (15)	0.33	77 (21)	77 (18)	0.34
24-hour monitoring							
Averaged Systolic BP, mm Hg – mean (SD)	125 (16)	121 (17)	130 (15)	<0.01	124 (15)	126 (17)	0.41
SD of Systolic BP, mm Hg – median (IQR)	13 (10 – 16)	13 (10 – 15)	14 (11 – 16)	0.12	13 (10 – 15)	14 (10 – 17)	0.10
Averaged Diastolic BP, mm Hg – mean (SD)	68 (11)	68 (12)	68 (10)	0.75	69 (11)	68 (11)	0.61
SD of Diastolic BP, mm Hg – median (IQR)	9 (7 – 12)	9 (7 – 12)	10 (8 – 12)	0.10	9 (7 – 11)	10 (8 – 13)	0.08
Very Short-term systolic BP variability (5 min)							
Total spectral power, mm Hg^2 – median (IQR)	45.3 (21.3 – 78.3)	45.5 (20.3 – 74.1)	43.2 (21.6 – 81.3)	0.75	45.3 (21.0 – 76.7)	43.2 (21.1 – 78.4)	0.86
VLF power, mm Hg^2 – median (IQR)	20.6 (10.2 – 41.5)	21.2 (10.5 – 42.0)	20.2 (9.28 – 39.4)	0.69	19.1 (10.5 – 43.1)	21.7 (9.2 – 39.8)	0.92
LF power, mm Hg^2 – median (IQR)	7.1 (3.5 – 17.4)	7.8 (3.6 – 20.0)	7.1 (3.3 – 14.9)	0.41	7.0 (3.6 – 19.2)	7.4 (3.2 – 14.3)	0.59
HF power, mm Hg^2 – median (IQR)	5.7 (2.5 – 17.8)	4.5 (2.1 – 14.6)	7.0 (2.7 – 25.3)	0.07	4.5 (1.9 – 15.1)	7.1 (2.8 – 20.8)	0.12
LF spectral power, nu – mean (SD)	0.52 (0.25)	0.59 (0.23)	0.46 (0.25)	<0.01	0.57 (0.25)	0.48 (0.24)	0.02
HF spectral power, nu – mean (SD)	0.48 (0.25)	0.41 (0.23)	0.54 (0.25)	<0.01	0.43 (0.25)	0.52 (0.24)	0.02
LF/HF ratio – median (IQR)	1.09 (0.46 – 2.7)	1.71 (0.64 – 3.94)	0.71 (0.38 – 1.93)	<0.01	1.58 (0.58 – 3.78)	0.83 (0.42 – 1.99)	0.02

Abbreviations: Blood pressure (BP); High, Low and Very-Low Frequency (HF;LF;VLF); interquartile range (IQR); normalized units (nu); standard deviation (SD)

*Differences between subgroups from chi-square/Fisher's exact or Student's t/Mann-Whitney tests.