

Impaired Dynamic Cerebral Autoregulation in Cerebral Venous Thrombosis

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Abstract

Background: Cerebral autoregulation is crucial in traumatic brain injury, which might be used for determination the optimal intracranial pressure. Cerebral venous thrombosis is a cerebral vascular disease with the feature of high intracranial pressure, but the autoregulatory mechanism of which remains unknow. We aimed to investigate the capacity of cerebral autoregulation in patients with cerebral venous thrombosis.

Methods: Twenty-three patients with cerebral venous thrombosis and 16 controls were enrolled. Cerebral autoregulation was assessed by transfer function analysis (rate of recovery / phase / gain) from spontaneous oscillations of cerebral blood flow velocity and arterial blood pressure.

Results: A total of 76 middle cerebral arteries (MCAs) were investigated including 44 MCAs from CVT patients and 32 normal ones. Phase shift and rate of recovery estimated from CVT patients was significantly different from controls (37.63 ± 33.94 vs. 54.49 ± 26.44 , $p = 0.23$; 29.74 ± 59.55 vs. 37.95 ± 22.55 , $p = 0.01$, respectively). The bilateral impairment of cebral autoregulation was demonstrated, even in the hemispheres without severe sinus stenosis and brain parenchymal lesion.

Conclusion: Our findings for the first time indicated that patients with cerebral venous thrombosis were more likely to have impaired cerebral autoregulation and suggest that cautious blood pressure control is required in such patients to prevent hyper or hypo-perfusion.

Background

Cerebral venous sinus thrombosis (CVT) is a relative rare cerebrovascular disease, usually affecting young idividuls [1]. CVT has highly variable clinical presentations, including headache, visual impairment, focal neurological deficits, seizure and encephalopathy, thus the diagnosis and management might be difficult. Although the clinical presentations is various, the pathogenesis of CVT is partly due to the elevated intracranial pressure,results of venous blood drainage obstruction and decreased cerebrospinal fluid absorption [2].

Many studies showed that the intracranial hypertension may thus impaired the mechanism of cerebral autoregulation in patients with subarachnoid hemorrhage and traumatic brain injury [3–7]. And one meta-analysis revealed that the patients with intracranial hypertension had increased risk of impaired autoregulation, through analyzing 16 relevant studies [8]. While autoregulation is a key mechanism to maintain the cerebral blood flow relatively constant in spite of variations in blood pressures. Impaired cerebral autoregulation may lead to passive changes of cerebral blood flow in response to the fluctuations of blood pressure, and increase the risk of brain hyperperfusion or hypoperfusion [9].

While it remains unknown whether CVT may impair the mechanism of cerebral autoregulation, we therefore applied this study to investigate the autoregulation in patients with CVT.

Methods

Patients and controls

Twenty-three patients (12 male, 11 female; age 34 ± 16 years [mean \pm SD]) with cerebral venous thrombosis were consecutively recruited from December 2018 to May 2019. Sixteen age-matched healthy individuals (9 male, 7 female; age 40 ± 11 years) were recruited as controls. All control subjects received transcranial doppler (TCD) examination to exclude carotid artery or intracranial stenosis [10].

The study was approved by the Beijing Tiantan Hospital Research Ethics Committee and each participant gave written informed consent.

Autoregulation Measurements

Cerebral blood flow velocity (CBFV) was measured in bilateral middle cerebral artery (MCA) via TCD (DWL, Germany). Continuous beat-to-beat arterial blood pressure (ABP) was recorded by a servo-controlled finger plethysmograph (ADInstruments, Australia). After the baseline value stable, the data of CBFV and ABP were recorded in a sample rate of 100 Hz for at least 5 minutes with the participants breathed spontaneously in supine position.

Transfer Function Analysis

Cerebral autoregulation was evaluated using transfer function analysis [11, 12]. In frequency domain, autoregulatory parameters (phase shift, gain, and coherence function) were calculated within 0.06–0.12 Hz. While in the time domain, the step response was estimated to show the recovery of CBFV after the ABP changes in step-wise. And the rate of recovery (RoRc) of CBFV (the first 3 seconds of the step response) was calculated for quantification the speed of the recovery [13].

Statistical Analysis

In statistical analysis, SPSS 25.0 (SPSS Inc, USA) was used. Student's t-test were performed to compare the continuous variables across groups, and Pearson χ^2 was used to compare categorical variables between groups. A p value less than 0.05 was considered statistically significant.

Results

Among all the 23 patients recruited, headache (91.3%) was the most frequent symptom, then focal neurological deficits (43.5%), seizures (39.1%), visual impairment (26.1%), and consciousness disturbances (17.4%).

All participants received bilateral MCAs examination except for 2 patients with one inadequate temporal window. Thus, a total of 76 MCAs was investigated including 44 MCAs from CVT patients and 32 from controls.

In the time domain, the averaged step response from the controls reached the baseline level within 3 seconds, while it took longer time (about 6 seconds) for patients with CVT. Which indicated if ABP dropped in a step-wise manner, the CBFV of CVT patients recovered more slowly (Fig. 1). And the RoRc of CVT patients was significantly lower than controls (29.74 ± 59.55 vs. 37.95 ± 22.55 , $p = 0.01$, Table 1).

Table 1
Results of rate of recovery, magnitude, phase shift and coherence in controls and CVT patients.

	Controls (n = 32)	CVT patients (n = 44)
RoRc (%/s)	37.95 ± 22.55	$29.74 \pm 59.55^*$
Gain (ampl.)	0.62 ± 0.33	0.54 ± 0.35
Phase (degree)	54.49 ± 26.44	$37.63 \pm 33.94^*$
Coherence	0.44 ± 0.17	0.39 ± 0.20
* $p < 0.05$, compared with normal controls.		

As to the transfer function analysis, in the frequency domain, the phase shift at 0.06–0.12 Hz was pronounced reduced compared with controls (37.63 ± 33.94 vs. 54.49 ± 26.44 , $p = 0.23$, Fig. 1, Table 1). The gain of CVT patients was lower than controls, but there was no statistic difference (0.54 ± 0.35 vs. 0.62 ± 0.33 , $p = 0.08$, Table 1).

And among all the CVT patients included, 14 patients (60.1%) had brain parenchymal lesions, including cerebral ischemia (39.1%), intracranial hemorrhage (43.5%) and subarachnoid hemorrhage (4.3%). Thus, there were 21 hemispheres with focal lesions (except 2 with inadequate window) and 23 hemispheres without. The phase shift and RoRc estimated from CVT patients without lesions were significantly lower than which from controls (29.54 ± 37.20 vs. 54.49 ± 26.44 , $p = 0.01$; 27.36 ± 60.73 vs. 37.95 ± 22.55 , $p = 0.006$, respectively). And there was no statistic difference of phase shift and RoRc between hemispheres with and without lesions (41.19 ± 28.53 vs. 29.54 ± 37.20 , $p = 0.07$; 22.14 ± 58.05 vs. 27.36 ± 60.73 , $p = 0.53$, respectively).

Magnetic resonance venogram demonstrated the most frequent location of CVT was lateral sinus (74.0%), then sagittal sinus (65.2%), sigmoid sinus (52.2%), straight sinus (34.8%), jugular veins (17.4%) and the cerebral deep venous system (8.7%). There were 8 patients with unilateral sinus affected and 15 patients with bilateral sinus affected. All the autoregulatory parameters above did not show statistic differences between the 36 affected hemispheres (except 2 with inadequate window) and the 8 non-

affected hemispheres (phase: 37.79 ± 34.28 vs. 23.00 ± 28.36 , $p = 0.21$). Even in 8 hemispheres without severe sinus stenosis and brain parenchymal lesion, the autoregulatory parameters – phase and RoRc were significantly lower than controls (23.00 ± 28.36 vs. 54.49 ± 26.44 , $p = 0.06$; 9.94 ± 34.18 vs. 54.49 ± 26.44 , $p = 0.009$, respectively).

Discussion

In this study, the phase shift and RoRc of transfer function analysis showed pronounced reduction in patients with CVT, which indicated that the cerebral autoregulation was impaired in CVT.

In CVT patients, the venous blood drainage obstruction and decreased cerebrospinal fluid absorption may result in elevated intracranial pressure, and then venous cerebral infarction and hemorrhage, which cause damage to cerebral arterioles and capillaries [2]. While the cerebral arterioles and capillaries were just the effector of cerebral autoregulation, through the complex myogenic, metabolic and neurogenic mechanisms [9]. And this might be the reason of cerebral autoregulation impairment in CVT patients.

In our study, 44.7% hemispheres detected with brain parenchymal lesions, including cerebral ischemia, hemorrhage and subarachnoid hemorrhage, all of which has been confirmed may impair the autoregulation capacity [14–16]. However, according our results, the cerebral autoregulation deteriorate even in the hemispheres without lesions, and there were no differences between hemispheres with and without lesions. Furthermore, the bilateral impairment of autoregulation was demonstrated, even in the hemispheres without severe sinus stenosis and brain parenchymal lesion. Which might further verify the impairment of cerebral autoregulation in patients with CVT.

According to the present study, the autoregulatory capacity was pronounced impaired in patients with CVT. Therefore, the blood pressure for CVT patients should be managed carefully, as cerebral hemodynamics might become 'vulnerable' to the fluctuation of ABP. The elevations in ABP might result in hyper-perfusion, that may in turn elevate intracranial pressure, which conversely worsen the autoregulatory capacity and create a vicious circle. While the drop of ABP might induces hypo-perfusion and cerebral ischemia. Therefore, the assessment of cerebral hemodynamics in patients with CVT should be considered, especially for the guidance of hypertensive therapy. Many studies revealed that the impaired cerebral autoregulation is an independent impactor of unfavorable neurologic outcomes in patients with stroke, subarachnoid hemorrhage, traumatic brain injury, and carotid or intracranial stenosis [14–17]. And latest studies showed that traumatic brain injury patients, the optimal cerebral perfusion pressure could be determined through assessing cerebral autoregulation, and this could be used to adjust cerebral perfusion pressure for favorable outcome [18]. In the future we hope new models for determination the optimal blood pressure by analyzing autoregulation, for better blood pressure management in CVT patients.

Conclusion

Our study suggests that the impairment of autoregulation in patients with CVT. Whether autoregulation may be of potential clinical value in the management CVT patients need further investigation.

Abbreviations

CVT: Cerebral venous sinus thrombosis; TCD: Transcranial doppler; CBFV: Cerebral blood flow velocity; MCA: middle cerebral artery; RoRc: rate of recovery.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

XG, YW, XZ and YW designed the study. JC, XG and KD gathered the data. JL and JC conducted the data analysis. JC and XG drafted the manuscript.

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None.

Availability of data and materials

The datasets are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Beijing Tiantan Hospital Research Ethics Committee and each participant gave written informed consent.

Consent for publication

Written informed consent was obtained from the patient for the publication.

Competing interests

The authors declare that they have no competing interests.

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Figures

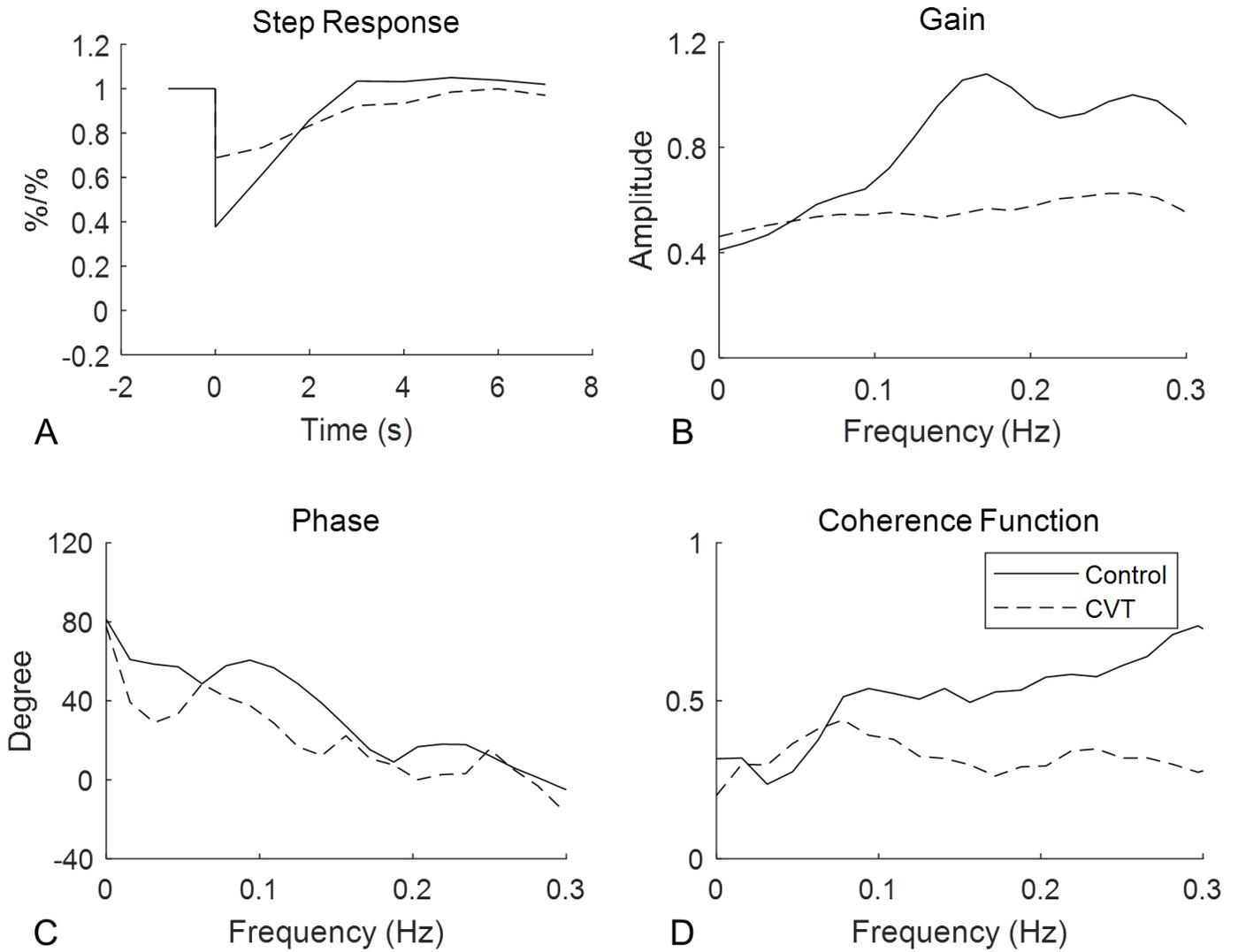


Figure 1

Transfer function analysis of cerebral autoregulation in controls and CVT patients. The figures are the averaged step response, gain, phase, and coherence function, respectively for the controls and patients with cerebral venous sinus thrombosis derived from the transfer function.