Biomedical Signal Processing and Control 31 (2017) 102–107

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

Technical note

Nonlinear analyses applied in cerebral autoregulation and blood flow changes in patients with acute intracerebral hemorrhage

Yun-Kai Lee [a,1], Sung-Chun Tang [b,1], Jiann-Shing Jeng [b], Jiann-Shing Shieh [a,c,*]

[a] Department of Mechanical Engineering, and Innovation Center for Big Data and Digital Convergence, Yuan Ze University, Taoyuan, Taiwan
[b] Stroke Center and Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan
[c] Center for Dynamical Biomarkers and Translational Medicine, National Central University, Taoyuan, Taiwan

ARTICLE INFO

Article history:
Received 13 May 2016
Received in revised form 12 July 2016
Accepted 21 July 2016

Keywords:
Intracerebral hemorrhage
Cerebral autoregulation
Blood pressure
Cerebral blood flow velocity
Sample entropy

ABSTRACT

Cerebral autoregulation (CA) is an important mechanism for maintaining constant cerebral blood flow during changes in blood pressure. Although previous studies have shown that CA may be impaired in patients with intracerebral hemorrhage (ICH), the variability of cerebral blood flow (CBF) in response to changes in CA has not been investigated. In the present study, we recruited twelve patients presenting with acute subcortical ICH and seven non-stroke controls. The status of CA was determined by assessing Pearson's moving correlation coefficient between arterial blood pressure and cerebral blood flow velocity (CBFV) of the middle cerebral artery (MCA). The variability of CBFV was calculated using nonlinear sample entropy analyses. The results indicated that ICH patients significantly showed poorer CA than controls, particularly localized to the MCA ipsilateral to the ICH (controls 0.17 ± 0.13 versus ICH side 0.41 ± 0.27 and non-ICH side 0.34 ± 0.26, $p = 0.044$ and 0.120, respectively). Moreover, the variability of CBFV in the hemisphere ipsilateral to the ICH was significantly increased in ICH patients when compared to controls (1.145 ± 0.26 versus 1.66 ± 0.193 and 1.595 ± 0.43, $p < 0.001$ and 0.024). Taken together, our data suggest that acute ICH may impair CA and increase CBF variability within the MCA ispilateral to the hematoma.

1. Introduction

Cerebral autoregulation (CA) is an important mechanism for maintaining constant cerebral blood flow (CBF) in the brain during changes in systemic blood pressure. Previous studies have shown that several pathological conditions such as traumatic brain injury (TBI), chronic ischemic stroke, diabetes, etc., may affect CA [1–12]. Several recent studies analyzed dynamic CA following acute intracerebral hemorrhage (ICH) using transfer function analysis (TFA), and showed that the impairment in CA was correlated with hematoma volume, neurological severity, and outcome [13,14]. However, the associated changes in CBF in response to alterations in CA have not been previously evaluated. Furthermore, many previous reports have used linear analytic methods for the analysis of many different physiological signals such as electrocardiogram, intracranial pressure, blood pressure (BP) and cerebral blood flow velocity (CBFV) although they are nonlinear and non-stationary.

In the present study, we sought to comprehensively investigate the effect of acute regional brain hematoma on CA, and evaluate the variability of CBF alterations bilaterally in the middle cerebral artery (MCA) following ICH, using a series of linear and nonlinear algorithms, including Pearson's moving correlation coefficient between BP and CBFV and sample entropy (SampEn) analysis of the mean component of CBFV in the MCA.

2. Materials and methods

2.1. Study design

This prospective case-control study was conducted at the stroke intensive care unit (sICU) of the National Taiwan University Hospital (NTUH), with the approval of the Research Ethics Committee of NTUH. Written informed consent was obtained either directly from the patient or from the next of kin of patients exhibiting decreased consciousness.

2.2. Subjects

The arterial BP and CBFV from bilateral MCAs of twelve ICH patients were recorded within 3 days after the initial occurrence

* Corresponding author at: Department of Mechanical Engineering, Yuan Ze University, Taoyuan, Taiwan.
E-mail address: jsshieh@saturn.yzu.edu.tw (J.-S. Shieh).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.bspc.2016.07.009
1746-8094/

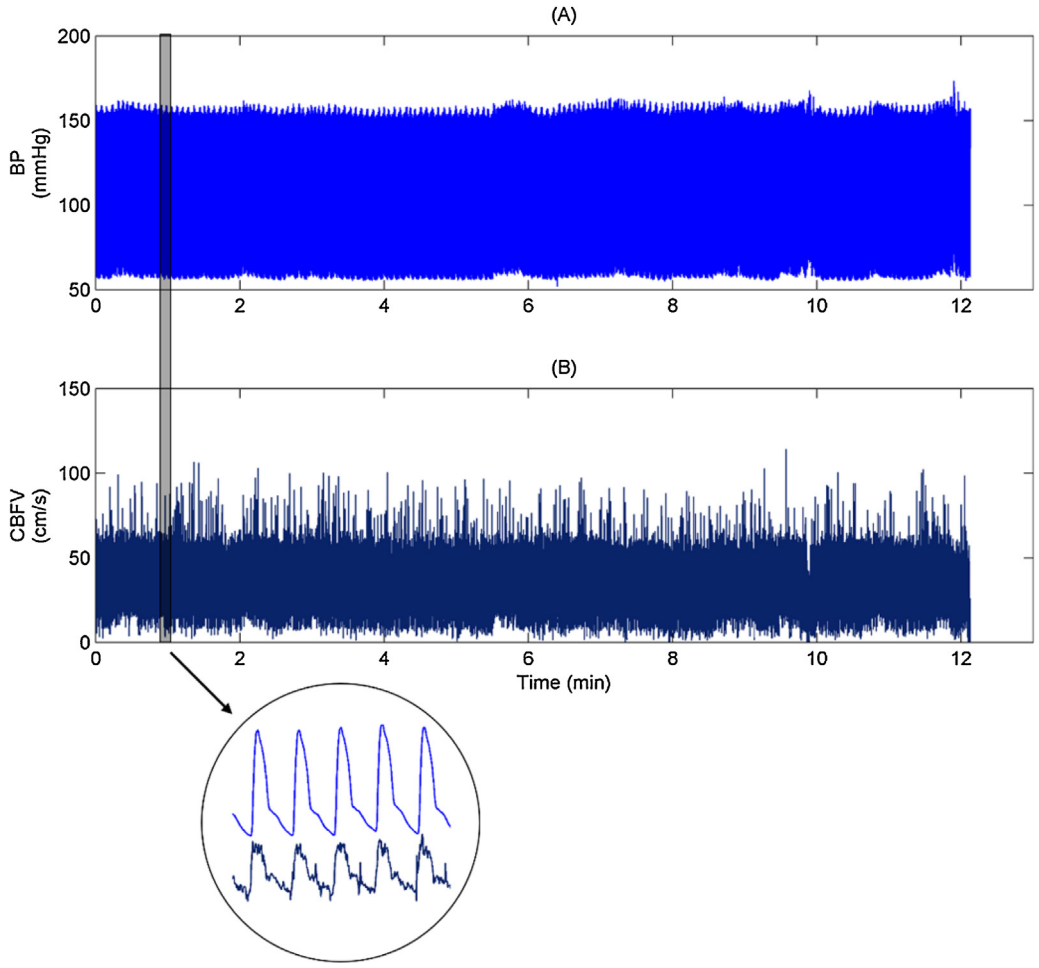

Fig. 1. The continuous measured time-domain signals of a patient with severe intracerebral hemorrhage (ICH) (A) The noninvasive arterial blood pressure (BP); (B) The cerebral blood flow velocity (CBFV).

of stroke in the sICU of the National Taiwan University Hospital. Continuous noninvasive BP and CBFV from a unilateral MCA of seven age- and sex-matched non-stroke controls were recorded for comparison. Noninvasive arterial BP was measured by an inflatable cuff around the middle phalange of the finger (Nexfin, BMEYE) [15] and the CBFV of the MCAs was obtained using transcranial Doppler ultrasound (EZ-Dop, DWL) techniques [8]. The measured time-domain BP and CBFV signals of a patient with severe ICH were shown in Fig. 1.

The clinical presentation of patients enrolled in the present study included those with hemorrhage in the putamen and thalamus. For the cases of intra-putamen hemorrhage ($n = 5$), 4 patients were diagnosed with left hemispheric hemorrhage and 1 with right hemispheric hemorrhage. For patients with thalamic hemorrhage ($n = 7$), 5 patients were diagnosed with left hemispheric hemorrhage and 2 with right hemispheric hemorrhage. The region of hemorrhage was examined by neurological evaluation and confirmed with computed tomography (CT). Hematoma volume was calculated by using the following equation:

$$\textit{Hematoma Volume}\ (ml) = ABC/2 \tag{1}$$

where A is the largest hemorrhage diameter by CT, B is the diameter perpendicular to A, and C represents the number of CT slices with hemorrhage multiplied by the slice thickness [16]. We excluded patients with underlying carotid stenosis more than 50% from the carotid duplex, based on CT angiography or MR angiography.

2.3. BP and CBFV data acquisition and correlation coefficient index analyses

Data representing continuous waveforms of BP and CBFV were obtained simultaneously over a 10–15 min study period (mean = 11.5 ± 3.9 min) during resting conditions. Arterial BP and CBFV were captured using a sampling rate of 512 Hz. The methods for obtaining Mx were identical to those previously described [1–10]. According to a previous study [11], the frequency range of CA is 0.008–0.05 Hz. In order to reduce the frequency, BP and CBFV values over time were averaged over discrete 6-s periods offline. Then, for every 10 consecutive 6-s averages of mean BP and CBFV (i.e. 60-s period, 0.016 Hz), Pearson's moving correlation coefficient between BP and CBFV was calculated and the mean values obtained were labeled as Mx. The equation of Pearson's correlation coefficient was expressed as follows:

$$r = \frac{\sum_i (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_i (x_i - \bar{x})^2}\sqrt{\sum_i (y_i - \bar{y})^2}} \tag{2}$$

where i is the data length, x and y represent the 6-s averaged arterial BP and CBFV signals, $\bar{x}$ and $\bar{y}$ are the mean of the averaged BP and CBFV signals in the present study. Since Pearson's correlation coefficient has a standardized value ranging from −1 to 1, it can be analyzed as a time-dependent variable responding to dynamic changes in the cerebral vasculature. According to previous studies [1–10], a higher correlation coefficient index indicates a greater