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Characteristics of beat-to-beat photoplethysmography waveform indexes in subjects with metabolic syndrome

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ABSTRACT

Metabolic syndrome (MetS) increases the risk of the subsequent development of cardiovascular disease. This study aimed to determine if the harmonic indexes of finger photoplethysmography (PPG) waveforms can be used to discriminate different arterial pulse transmission conditions between MetS and healthy subjects. Three-minute PPG signals were obtained in 65 subjects, who were assigned to 3 age-matched groups (MS, with no less than three MetS factors; pre-MS, with one or two MetS factors; Control: with no MetS factor). FDT (foot delay time) and amplitude proportions (C_n) and their standard deviations (SD_n) and coefficients of variations (CV_n) were calculated for harmonics 1 to 10 of the PPG waveform. FDT was smaller in MS than in Control. C_1 and C_2 values were significantly smaller, whereas C_4–C_9 values were significantly or appeared to be larger in MS than in pre-MS. Most of the SD_n and CV_n values were largest in MS. This study is the first to demonstrate that harmonic-analysis indexes of the beat-to-beat PPG waveform can provide information about MetS-induced changes in the arterial pulse transmission and cardiovascular regulatory activities. The present findings may therefore be useful in developing a noninvasive and easy-to-perform technique that could improve the early detection of cardiovascular diseases.

Introduction

Metabolic syndrome (MetS) comprises a cluster of vascular risk factors—including abdominal obesity, glucose intolerance, dyslipidemias, and hypertension—that may increase the risk of the subsequent development of cardiovascular disease and diabetes mellitus (Nitzan et al., 1999). For example, MetS accelerates arterial deterioration and is associated with a higher risk of cardiovascular events (Scuteri et al., 2014). The pathogenesis underlying the association between MetS and cardiovascular disease has been widely studied but is still incompletely understood.

The association between MetS and increased arterial stiffness is well known from previous studies. The pathophysiology underlying the increased arterial stiffness in MetS is not completely clear, but several mechanisms have been postulated (Scuteri et al., 2014), including hyperinsulinemia, elevated blood glucose, endothelial dysfunction, and low-grade inflammation. Increased aortic pulse pressure (Gorelick et al., 2011), increased systemic vascular resistance, and decreased left ventricular stroke index (Scuteri et al., 2014) have also been reported to be associated with MetS.

Photoplethysmography (PPG) is an optical measurement technique used to monitor blood volume changes in microvascular beds of peripheral tissues, and also to monitor arterial pressure and compliance. Changes in the blood-pressure (BP) pulse can be correlated with changes in the vessel volume and thus the PPG signal. Many indexes associated with PPG signals have been developed to aid noninvasive monitoring of the cardiovascular system. For example, changes in the pulse width of the PPG waveform were found to be correlated with changes in peripheral vascular resistance (Awad et al., 2007), and the pulse transit time calculated from a dual PPG measurement can be used to evaluate the BP (Awad et al., 2001) or the pulse wave velocity (Tsai et al., 2005). Frequency-domain analysis in lower-frequency bands has also been applied to the PPG signal, for example to study autonomic nervous control of the peripheral circulation (Nitzan et al., 1999) and to characterize the hypovolemic response (Middleton et al., 2008).

Among various frequency-domain analysis methods, harmonic analysis is particularly appropriate for several types of cardiovascular signal, including BP and PPG waveforms (Sherebrin and Sherebrin, 1990; Wei and Chow, 1985), due to the heartbeat being quasiperiodic. We previously used noninvasive PPG measurements and harmonic-component analysis to demonstrate that an appropriate contact pressure could improve the reconstruction of the BP waveform from the PPG waveform (Hsiu et al., 2011), and also that applying mild cold stimulation to the skin surface (which can change wave transmission and arterial

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stiffness) can significantly change several harmonic-analysis indexes of PPG waveforms (Hsiu et al., 2012).

In the present study we aimed to determine if the harmonic indexes of the finger PPG waveforms can be used to discriminate between MetS and healthy control subjects; measurement was also performed on the pre-MS group to study if there can be some possible differences in the vascular properties induced by cardiovascular disease in early stage. The information obtained might be pertinent to developing a new non-invasive index for detecting the MetS-induced changes in the arterial pulse transmission condition.

Materials and methods

Experimental procedure

Measurement was performed on 65 volunteers; details of subjects are listed in Tables 1–3. The study population was recruited at the Health Management Center of Tri-Service General Hospital during June 2012 to December 2013. The adults aged 40–64 years who came for a health check-up were eligible. The exclusion criteria were: (1) patients with diabetes, or hypertension, and on medications, (2) pregnant women, (3) patients with severe illnesses: i.e. cirrhosis of liver, renal failure, heart failure, cancer, or cerebral vascular diseases, (4) patients with severe mental illnesses, (5) patients with severe endocrine diseases, i.e. hyper- or hypothyroidism, (6) patients with skin ulceration or wounds that could interfere PPG detection, and (7) patients on medications that could affect vascular endothelial function. The eligible participants were invited by study assistants and jointed in this study voluntarily. All participants were informed and signed the consents. According to the criteria listed in Table 1, the subjects were assigned into three age-matched groups: MS, with no less than three MetS factors; pre-MS, with one or two MetS factors; Control: with no MetS factor.

The subjects were lightly clothed, supine, and were allowed to stabilize for at least 10 min before recording commenced. The subjects were enquired about their psychological condition to prevent the interference effect. The environmental temperature was within 23–25 °C during the entire measuring period. The study was reviewed and approved by the institutional review board of Tri-Service General Hospital (TSGHIRB 2-101-05-045). All subjects gave their informed consent before experiments commenced, were asked to not take any medication for 3 days before experiments, and did not consume food at least 1 h before each experiment. All subjects were non-smokers, and did not take coffee or drinks containing alcohol at least 1 day before experiments (Hsiu et al., 2011, 2012).

Details of the measurement procedure were described in our previous works (Hsiu et al., 2011, 2012). ECG and PPG signals were measured noninvasively (typical waveforms of the three groups are shown in Fig. 1). ECG signals were measured by surface electrodes, and acquired by a preamplifier (lead II, RA-LL; 6600-series, Gould, USA). The PPG signal from a 940-nm-wavelength infrared LED (QED233, Fairchild Optoelectronic) penetrating the finger tissue was acquired by a photodiode (L-SB1R9PD1D1, Para, Japan). When performing PPG measurements, subjects were instructed to put the right middle finger into a self-made measurement cavity that had a black inner wall to reduce interference from light leakage. A hand-shaped mold was placed under the palm to improve the positioning reproducibility of the hand and finger. A contact pressure was applied around the first knuckle of the finger using a 3-mm-thick sponge as a force cushion. The vertically applied pressure was precalibrated and monitored by a force gage (1000 gw, OHBA SIKI, Japan) to be around 60 mm Hg to improve the PPG measurement stability and to reduce user discomfort. The signals were connected to a self-made current-to-voltage converter circuit, and then connected to an analog-to-digital converter card (PCI-9111DG, Adlink Technology, Taiwan) operating at a sampling rate of 1024 Hz.

For each experiment, we recorded a 3-minute data sequence. Before the PPG measurement, we measured fundamental physiological parameters of the subject, including HR, systolic BP (SBP), and diastolic BP (DBP) using a sphygmomanometer (MediGuard 150i, Rossmax).

One thermistor was attached around the wrist to monitor the skin-surface temperature. The resistance of the thermistor was transformed into voltages (by a custom-made circuit) that were also sampled every minute by the analog-to-digital converter card. The acceptable range for the temperature stability during the baseline period was a temperature variation of less than 1.0 °C. The average values of monitored temperature were 29.2 ± 2.0 °C, 28.8 ± 2.1 °C, and 28.2 ± 2.1 °C, respectively for MS, pre-MS, and Control.

Table 1
Number of subjects fulfilled the criteria of metabolic syndrome.

Factor criteria	Number of subjects		
	MS (n = 17)	Pre-MS (n = 32)	Control (n = 16)
Waist circumference: ≥90 cm (male); ≥80 cm (female)	11	18	0
Blood pressure: ≥140/90 mm Hg	10	13	0
High-density lipoprotein cholesterol ≤0.9 mmol/l (male), ≤1.0 mmol/l (female)	13	8	0
Fasting plasma glucose: ≥100 mg/dl	7	2	0
Triglycerides: ≥100 mg/dl	11	3	0

Table 2
Number of subjects who have chronic conditions.

Chronic condition	Number of subjects		
	MS (n = 17)	Pre-MS (n = 32)	Control (n = 16)
Diabetes	0	0	0
Cardiovascular disease	0	1	1
Hyperlipidemia	4	1	1
Hypertension	0	0	0
Liver disease	0	7	2
Peptic ulcer disease	0	2	0
Renal disease	0	0	0
Polycystic ovary syndrome	0	2	1

Signal analysis

Procedure of PPG index calculation is shown in Fig. 2. The PPG signals were first passed through a digital 11th-order high-pass Chebyshev filter with a lower cut-off frequency of 0.01 Hz to eliminate the baseline drift. To determine their beat-to-beat waveforms, the two neighboring minima of the signal helped to identify the cut points to define each pulse.

In time-domain analysis, the foot delay time (FDT) for each pulse was defined as the average time difference between the ECG R-peak and the foot point (the onset lowest point) of the PPG pulses during each 3-min measurement period.

In frequency-domain analysis, each individual PPG pulse (between foot points) can be represented by the following finite series (Chen et al., 2011; Nichols and O'Rourke, 1998):

$$x(t) = \frac{A_0}{2} + \left\{ \sum_{n=1}^{k/2} A_n \cos n\omega t_s + \sum_{n=1}^{k/2} B_n \sin n\omega t_s \right\}. \quad (1)$$

The Fourier coefficients (A_n and B_n) of the BPW pulse can be calculated by

$$A_n = \frac{2}{k} \sum_{s=0}^{k} x_s \cos n\, \omega\, t_s \left(\text{for } n = 0, 1, \ldots, \frac{k}{2} \right)$$
$$B_n = \frac{2}{k} \sum_{s=0}^{k} x_s \sin n\, \omega\, t_s \left(\text{for } n = 0, 1, \ldots, \frac{k}{2} \right) \quad (2)$$

where ω is the angular frequency and t_s is the sampling time interval.