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Differences in laser-Doppler indices between skin-surface measurement sites in subjects with diabetes

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ABSTRACT

This study performed laser-Doppler flowmetry (LDF) measurements with the aim of identifying differences in diabetes-induced microcirculatory-blood-flow (MBF) responses between the following skin surface measurement sites: an acupoint around the wrist, an acupoint around the ankle, and a nearby nonacupoint around the ankle. The 67 study subjects were assigned to diabetic, prediabetic, and healthy groups according to the results of oral glucose tolerance tests. Beat-to-beat and spectral analyses were applied to the LDF waveform to obtain the foot delay time (FDT), the flow rise time (FRT), and the relative energy contributions (RECs) in five frequency bands. FRT and FDT were significantly shorter and the RECs of the endothelial-, neural-, and myogenic-related frequency bands were significantly smaller in the diabetic group than in the control group at the acupoint around the ankle, but there were no such prominent differences at the other sites. The acupoint around the ankle was better than the nearby nonacupoint and the acupoint around the wrist for distinguishing the age-matched diabetic, prediabetic, and healthy subjects. These findings imply that when monitoring diabetes-induced MBF responses, the measurement locations should be chosen carefully in order to minimize interference effects and to improve the ability to distinguish subjects with different conditions.

1. Introduction

Diabetes can damage the physiological functions of organs and terminal extremity in various ways. Changes in the blood flow condition and the vessel properties have been noted in diabetics (Azadzoi and Saenz de Tejada, 1992; Sun et al., 2012; Suzuki et al., 2001; Turner et al., 2008; Urbancic-Rovan et al., 2004), and even in prediabetic subjects (Hu et al., 2017). Monitoring the local perfusion of the microcirculatory blood flow (MBF) can aid the early detection of diabetes-induced microcirculatory damage.

Various techniques have been used to monitor the skin-surface MBF perfusion. Among optical methods, laser-Doppler flowmetry (LDF) is a well-suited technique for noninvasive investigations of MBF responses. LDF signal analysis can provide information on pathophysiological microcirculatory phenomena in diabetes, such as skin vasomotion changes (Sun et al., 2012), progression of autonomic neuropathy (Urbancic-Rovan et al., 2004), and endothelial function (Turner et al., 2008). We previously applied time-domain waveform analysis (for evaluating the beat-to-beat perfusion condition of MBF through the opening of the precapillary sphincter (arteriolar openings [AO])) and frequency-domain spectral analysis (for monitoring the induced changes in the microcirculatory regulatory activities) to LDF signals, with significant differences found between diabetic, prediabetic, and healthy subjects (Hsiu et al., 2014a, 2014b).

When performing skin-surface LDF measurements, precisely defining the location at which the probe is placed can improve the reliability of obtained index values. This is because there are many factors influenced by the measurement site that can interfere with LDF signals and thus result in inaccurate calculated indices. For example, LDF signals can differ between when the probe is placed on a lower or upper extremity. Furthermore, acupoints are specific points on the body on which some treatment method in complementary medicine (such as acupuncture or acupressure) is applied. The vascular beds are noted to be more abundant underneath the skin surface of acupoints than at other sites (Hwang, 1992; Zilberschtein et al., 2004), and the MBF characteristics at acupoints are different from those at nearby nonacupoints (Hsiu et al., 2007, 2009).

The present study measured skin-surface LDF signals at three different sites in diabetic, prediabetic, and healthy human subjects (as distinguished using the oral glucose tolerance test [OGTT]), with the

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aim of verifying whether LDF indices are affected differently by diabetes- or prediabetes-induced effects. LDF indices were calculated in time-domain and frequency-domain analyses. MBF responses were compared between acupoints around the wrist and around the ankle, and between at an acupoint and a nearby nonacupoint around the ankle. The present findings may be helpful for understanding how the measurement location may influence MBF responses, and thus for improving the reliability of monitoring diabetes-induced impairments in the MBF perfusion function.

2. Methods

2.1. Patients

Patient recruitment was coordinated by Division of Endocrinology and Metabolism of the Tri-service General Hospital. After receiving approval from the Review Board of Tri-service General Hospital, written informed consent was obtained from study participants or their legal designates.

Experiments were performed on subjects with suspected glucose intolerance (as detected by doctors in the Division of Endocrinology and Metabolism of the Tri-service General Hospital). A 75-g OGTT (150-cm^3 50% warm glucose water) was performed in all subjects after they had fasted for at least 10 h. The subjects were assigned into the following three groups to compare the MBF characteristics among different stages:

- Group A (diabetes; $n = 26$): fasting glucose $\geq$ 126 mg/dl, or 2-h postload glucose $\geq$ 200 mg/dl, or A1C (glycated hemoglobin) $\geq$ 6.5%.
- Group B (prediabetes; $n = 22$): fasting glucose between 100 and 125 mg/dl, or 2-h postload glucose between 140 and 199 mg/dl, or A1C between 5.7% and 6.4%.
- Group C (healthy glucose tolerance; $n = 19$): fasting glucose < 100 mg/dl with a 2-h postload plasma glucose of < 140 mg/dl and A1C < 5.7%.

2.2. Measurements

Details of experimental procedure were described previously (Hsiu et al., 2014a, 2014b). Each assessment involved a 20-min recording prior to the OGTT. ECG and LDF signals were obtained simultaneously and noninvasively. Subjects were asked to sit on a chair, lean the back to the chair back, put both arms on the chair armrests, keep both feet on the ground, and to relax and breathe naturally throughout the measurement period so as to avoid motion artifacts. The measuring sites of the LDF probe were as follows (Fig. 1; typical waveforms shown in Fig. 2):

- Left Tai-Tsih (K3; Site 1): an acupoint located on the kidney meridian around the ankle.
- One nonacupoint located 2.5 cm above left Tai-Tsih (Site 2) as a comparison.
- Left Hoku (Li4; Site 3): an acupoint located on another meridian (the large-intestine meridian) on the hand.

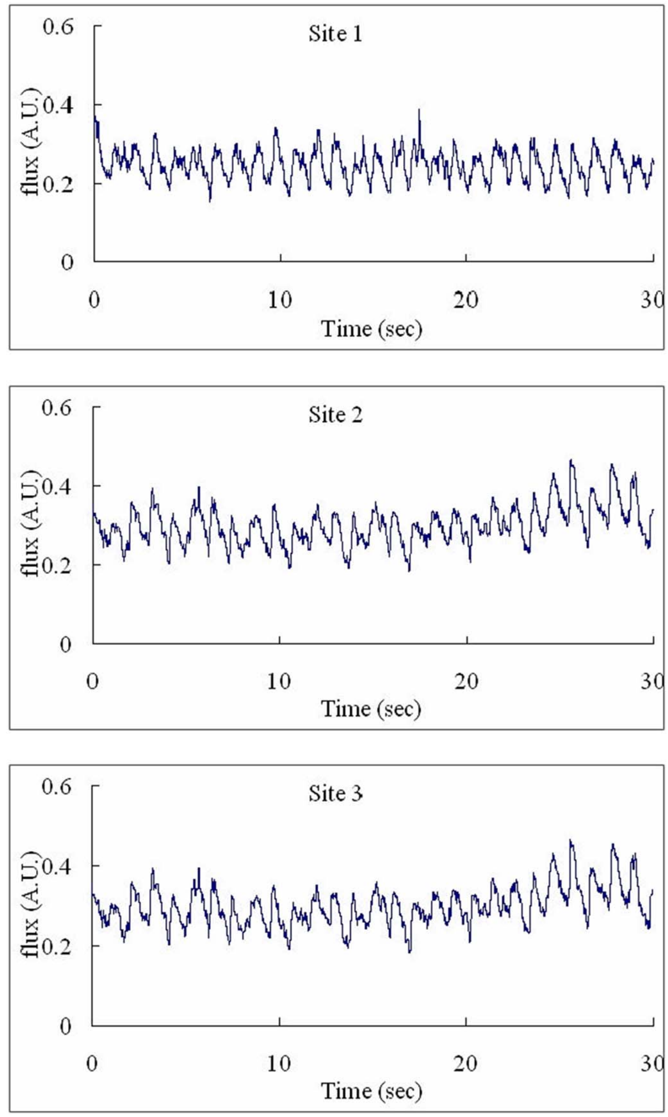

Fig. 2. Typical time-domain LDF waveforms.
(a) Site 1; (b) Site 2; (c) Site 3.

2.3. Data analysis

Time-domain waveform analysis (for evaluating the beat-to-beat perfusion condition of MBF through arteriolar openings [AO]) and frequency-domain spectral analysis (for monitoring the induced

Fig. 1. The LDF measurement sites.
Tai-Tsih acupoint (Site 1); nearby nonacupoint (Site 2); Hoku acupoint (Site 3). The locations of the LDF measurement sites were circled.