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Arterial stiffness is associated with diabetic retinopathy in type 2 diabetes

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Abstract

The purpose of this study was to investigate the association between arterial stiffness and diabetic retinopathy. The subjects comprised 1004 patients with type 2 diabetes. Pulse-wave velocity (PWV) was used as a marker of arterial stiffness. Clinical characteristics, including PWV and diabetic retinopathy (DR), were investigated in a cross-sectional study. PWV, duration of diabetes, systolic blood pressure and hemoglobin A1c level were all significantly higher in patients with diabetic retinopathy than in individuals without this disorder. The association between brachial-ankle PWV and diabetic retinopathy remained significant after statistical adjustment, with increasing odds ratios (ORs) from the second quartile (OR, 2.09; 95% confidence interval (CI), 1.21–3.61), to the third (OR, 2.80; 95% CI, 1.61–4.86) and fourth (OR, 4.64; 95% CI, 2.54–8.52) quartiles. Diabetic retinopathy was, therefore, associated with arterial stiffness in patients with type 2 diabetes. Our findings also suggested that PWV might be a marker of vascular injury caused by chronic hyperglycemia.

Keywords: Arterial stiffness; Diabetic retinopathy; Pulse-wave velocity

1. Introduction

Pulse-wave velocity (PWV) measures the velocity of a pulse wave over a given distance between two sites in the arterial system, and can be used to estimate arterial stiffness [1,2]. A previous study showed that the PWV of patients with diabetes was higher than that of healthy subjects [3]. One difference between diabetic and non-diabetic subjects is the occurrence of a chronic hyperglycemic state in the former. It can be assumed that a chronic hyperglycemic state causes the progression of arterial stiffness. Chronic hyperglycemic states also give rise to diabetic microangiopathies, including diabetic retinopathy (DR); however, the association between arterial stiffness and diabetic retinopathy has not been established. In the present

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study, the association between PWV as a marker of arterial stiffness and the presence of diabetic retinopathy was investigated in patients with type 2 diabetes.

2. Materials and methods

Type 2 diabetics who randomly underwent measurements of brachial-ankle PWV (baPWV) between April 2000 and November 2002, at the outpatients department of the Juntendo University Hospital (Tokyo, Japan), were enrolled into this study. Informed consent was obtained from all subjects. Clinical data were collected cross-sectionally from medical records. Type 2 diabetes was indicated by a fasting plasma glucose concentration >7.0 mmol/L without treatment, a plasma glucose concentration ≥11.0 mmol/L measured 2 h after a 75 g oral glucose load, or by treatment with a glucose-lowering drug. The patients selected for the study had no history of ketoacidosis, ischemic heart disease, peripheral artery disease or ischemic stroke. Patients with an ankle-brachial pressure index (ABI) <0.9 were excluded from the analysis. Diagnoses of diabetic retinopathy were made by ophthalmologists based on the presence of one or more of the following clinical features in the fundus: hemorrhages, hard or soft exudates, venous beading, intra-retinal microvascular abnormalities, cotton-wool spots, pre-retinal new vessels, fibrous proliferation and scars of photocoagulation. In addition, participants were divided into the following three groups using the Davis classification: no diabetic retinopathy (NDR); simple retinopathy (SDR); and either pre-proliferative or proliferative diabetic retinopathy (prePDR or worse). Diabetic nephropathy was defined as a casual urinary albumin/creatinine ratio >30 mg/g Cr.

Total cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride and hemoglobin A1c (HbA1c) levels were also determined using standard laboratory techniques.

2.1. Measurements of PWV

BaPWV was used as a marker of arterial stiffness. There was a good correlation between aortic PWV and baPWV [4]. Measurements of baPWV, ABI and blood pressure (BP) were carried out using an automatic waveform analyzer (BP-203RPE; Colin Medical Technology Corporation, Komaki, Japan); this device records PWV, BP, electrocardiograms and heart sounds simultaneously. Measurements were taken with patients lying in a supine position after 5 min of rest. Occlusion and monitoring cuffs were placed snugly around both sites on the upper and lower extremities of patients. Pressure waveforms of the brachial and tibial arteries were then recorded simultaneously using an oscillometric method. Electrocardiogram monitoring was performed using electrodes placed on both wrists. Any arrhythmia recorded was evaluated. Heart sounds (S1 and S2) were detected using a microphone placed on the left edge of the sternum at the fourth inter-costal space. The pressure waveforms obtained at two different sites were simultaneously recorded to determine the time interval between the initial rise in the brachial and tibial pressure waveforms (T). The path lengths from the suprasternal notch to the elbow (La), and from the suprasternal notch to the femur to the ankle (Lb) were calculated based on the height of the patient and were derived from statistical studies. BaPWV was calculated using the formula: baPWV = (Lb–La)/T. Measurements of the right and left baPWV were taken for an average of 10 s; the mean of the two values was used for analysis. ABI was calculated using the formula: ABI = ankle systolic BP/brachial systolic BP. The reproducibility of the baPWV measurements was high. In healthy subjects, the inter-observer coefficient of variation (CV; $n = 15$) was 2.4% and the intra-observer CV ($n = 17$) was 5.8% [4]. Previous studies reported associations between baPWV and blood pressure, age and nephropathy [5,6].

2.2. Statistical analysis

In order to assess the association between baPWV and diabetic retinopathy, we performed three statistical analyses.

First, subjects were divided into two groups: those with and those without diabetic retinopathy. Clinical characteristics, including baPWV, were analyzed within the two groups. Continuous variables were presented as the mean ± standard deviation (S.D.). Continuous variables were compared using the Student's t-test and categorical data were compared