Influence of HbA1c on short-term blood pressure variability in type 2 diabetic patients with diabetic nephropathy*

Fang LIU†§, Min WU§, Yan-huan FENG, Hui ZHONG, You-qun HUANG, Ya-ping LIANG, Yong-shu DIAO, Li ZANG, Ling LI, Jing ZANG, Hong-yu QIU, Song-min HUANG, Ping FU†‡

(Division of Nephrology, West China Hospital of Sichuan University, Chengdu 610041, China)

†E-mail: liufangfh@163.com; fupinghx@163.com

Received Jan. 27, 2013; Revision accepted May 3, 2013; Crosschecked Oct. 3, 2013

Abstract: The aim of this study was to understand the characteristics of blood pressure (BP) variability in subjects with diabetic nephropathy (DN), and identify the probable predictors affecting BP variability. Fifty-one chronic kidney disease (CKD)-hypertensive patients without diabetes (NDN group) and sixty type 2 diabetic patients with overt DN (DN group) were enrolled in this study. The values of short-term BP variability were obtained from 24 h ambulatory BP monitoring (ABPM). Variance analysis or nonparametric analysis revealed that 24-h systolic BP variability and night-time systolic BP variability of the DN group were significantly higher than those of the NDN group [(12.23±3.66) vs. (10.74±3.83) mmHg, \( P < 0.05 \); (11.23±4.82) vs. (9.48±3.69) mmHg, \( P < 0.05 \)]. Then the patients of the DN group were divided into two groups according to glycated hemoglobin (HbA1c) level: Group A (HbA1c < 7%) and Group B (HbA1c \( \geq \) 7%), and the \( t \)-test showed that patients in Group B had larger 24-h diastolic, daytime diastolic, and nighttime systolic/diastolic BP variability compared with Group A. In the DN group, partial correlation analysis revealed that HbA1c exhibited a strong association with 24-h diastolic, daytime diastolic, nighttime systolic and diastolic BP variability (\( P < 0.001 \), \( P < 0.001 \), \( P < 0.05 \), and \( P < 0.001 \), respectively). Taken together, larger short-term BP variability was detected in hypertensive type 2 diabetic patients with overt nephropathy and renal insufficiency. It may imply that the optimal BP variability level could benefit from a better glycaemic control.

Key words: Short-term blood pressure variability, Diabetic nephropathy, Glycated hemoglobin (HbA1c), Hypertension, Glycaemic control
doi:10.1631/jzus.B1300030

1 Introduction

Hypertension is one of the most common co-morbidity symptoms in patients with diabetes, and it exists in up to 80% of diabetic patients with overt nephropathy. A significant number of patients have hypertension or rising blood pressure (BP) even in the earlier stages of diabetic nephropathy (DN) and it contributes to subsequent cardiovascular morbidity and mortality. Cardiovascular disease (CVD) is the main cause of death in patients with chronic kidney disease (CKD), in particular, DN (Adler et al., 2003), and hypertension is a major risk factor for CVD in CKD (Adler et al., 2000). However, it has been clarified that office BP or clinic BP measurements were the least predictive indicator of CVD either in diabetic or non-diabetic patients (Kamoi et al., 2002), and BP variability has been recently considered as consistently predicting the risk of future cardiovascular events independent of mean BP (Kikuya et al., 2000; Verdecchia et al., 2007). Eguchi et al. (2009) observed that neither an abnormal dipping pattern of the circadian rhythm of BP nor the morning BP surge was a predictor of CVD events, whereas the nighttime BP variability appeared to be a strong predictor, independent of ambulatory blood pressure level and other traditional risk factors in type 2 diabetic mellitus.
Previous studies have shown that BP variability is a complex phenomenon that includes both short-term and long-term changes (Mancia and Parati, 2000). This phenomenon of BP fluctuation has been shown to depend on sympathetic vascular modulation and changes in arterial distensibility (Parati et al., 1996; Pickering, 1998). Increasing evidence has shown that sympathetic overactivity, impaired baroreflex sensitivity, and arterial stiffness in diabetes may give rise to higher BP fluctuation, severe target organ damage (Parati et al., 1987; Mancia et al., 2001), and the subsequent higher frequency of CVD events (Kikuya et al., 2000).

However, studies on BP variability in DN patients are lacking and factors that affect BP variability in DN patients are also seldom studied and clearly elucidated. More evidence on BP variability is needed to lead to a more precise controlling of CVD in DN patients. In this study, data from the recordings of 24-h ambulatory BP monitoring (ABPM) performed in hospitalized DN and NDN patients were obtained to clarify the characteristics of BP variability and analyze the factors that might influence short-term BP variability in patients with DN.

2 Subjects and methods

2.1 Subjects

Sixty Chinese hospitalized hypertensive patients (38 men and 22 women aged (59±13) years) with type 2 diabetes mellitus with overt nephropathy (DN group) and fifty-one hypertensive patients (30 men and 21 women aged (53±16) years) with non-diabetic CKD, whom were diagnosed with primary glomerulonephritis (NDN group), were enrolled in our study. Inclusion criteria were an age ≥18 years, mild-to-moderate hypertension (clinic systolic BP ≥130 mmHg and/or diastolic BP ≥80 mmHg or receiving antihypertensive agents), and estimated glomerular filtration rate (eGFR) ≥15 ml/(min·1.73 m²). Renal function was assessed with eGFR using the abbreviated MDRD (modification of diet in renal disease study) equation. Exclusion criteria included patients who were receiving dialysis or renal transplantation, and patients with clinically significant heart disease, stroke, renal artery stenosis, hepatic dysfunction, pheochromocytoma, hyperthyroidism, and hyperaldosteronism. For hypertensive patients on admission, BP was treated and optimized according to the guidelines with antihypertensive drugs [calcium channel blockers (CCBs), α-blockers, β-blockers, and angiotensin II type 1 receptor blockers (ARBs)] to try to attain normotensive BP values. Additionally, the use of antihypertensive agents and erythropoietin was recorded. The main demographic and clinical characteristics of the population enrolled in this study are detailed in Table 1. The study was approved by the ethics committee of West China Hospital of Sichuan University. According to the level of glycated hemoglobin (HbA1c), the DN group was divided in two subgroups: Group A (HbA1c<7%) and Group B (HbA1c≥7%).

2.2 ABPM and short-term BP variability

ABPM was performed every 30 min with a fully automatic device (Spacelab-90217, USA). BP was measured using a cuff with the oscillometric method. Short-term BP variability (24-h BP variability, daytime and nighttime BP variability) was defined as the within-subject SD of all systolic and diastolic readings at 30-min intervals during the daytime and nighttime measurement periods, respectively. The patients were instructed to fill out individual diaries to record the time of sleeping, rising and other daytime activities. Therefore, the terms of ‘daytime’ and ‘nighttime’ used in this study reflected the average period during which the patients were awake/upright and asleep/supine, respectively. In each individual, the daytime and nighttime values were determined based on the individual diaries. The patients with a >20% incidence of missing values or missing values for more than two consecutive hours had received repeated ABPM. The following readings were omitted because of technical artifacts: systolic BP >240 or <70 mmHg, diastolic BP >150 or <40 mmHg, and pulse pressure >150 or <20 mmHg compared with the immediately preceding or successive values. Circadian rhythm of BP was calculated by the following equation: circadian rhythm of BP=(daytime average systolic BP−nighttime average systolic BP)/(daytime average systolic BP)×100%. Circadian rhythm of BP with nocturnal BP decline of 10%–20% was considered a normal dipping pattern, while circadian rhythm of BP with nocturnal BP decline of <10% was considered an abnormal non-dipper pattern.