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Diabetic Polyneuropathy and Cardiovascular Complications in Type 2 Diabetic Patients (*Diabetes Metab J* 2011;35:390-6)

Sun-Hye Ko, Seung-Hyun Ko

Division of Endocrinology & Metabolism, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea

Among chronic diabetic complications, diabetic peripheral polyneuropathy (DPN) is characterized by a progressive natural course and severe symptoms. The reported prevalence of DPN varies dramatically depending on differences in diagnostic methods, patient selection, and definition of neuropathy from 8.3% for patients with newly diagnosed type 2 diabetes to up to 50% in patients who have had diabetes for 25 years [1,2]. DPN is often subclinical. Up to 50% of DPN cases may be asymptomatic, and such patients are at risk of insensate injury to their feet. DPN is an important risk factor for foot ulceration, lower limb amputation, and mortality [3,4].

Recently reported observational and epidemiologic studies have shown that the clinical significance of DPN is not confined to the prevention of diabetic foot problems. Relationships have been demonstrated between DPN and other diabetic microvascular complications. Close associations among diabetic nephropathy, retinopathy, and neuropathy have been reported by many studies, both in patients with type 1 and type 2 diabetes mellitus. The EURODIAB Prospective Complication Study showed that diabetic nephropathy and retinopathy were both associated with low nerve conduction velocity and amplitude response in type 1 diabetes [5]. According to a population-based study of type 2 diabetes performed in Sweden, peripheral sensory neuropathy was related to diabetic retinopathy, overt nephropathy, and peripheral vascular disease [6].

Among diabetic neuropathies, cardiovascular autonomic neuropathy (CAN) is widely accepted as an independent risk factor for future adverse cardiovascular outcomes such as silent myocardial ischemia, cardiac arrhythmia or sudden death [7]. CAN is common in patients with diabetes and is associated with modifiable factors including central fat distribution, hypertension, dyslipidemia, poor diabetes control, and smoking, and with other microvascular complications of diabetes [8]. However, the relationships between DPN and cardiovascular disease (CVD) outcomes in patients with type 2 diabetes have not been fully investigated.

Due to a lack of large prospective long-term epidemiologic studies of DPN and cardiovascular or cerebrovascular disease, clinical evidence of their relationships are limited. The EURODIAB Prospective Complications Study included 1,407 patients with type 1 diabetes and showed that cardiovascular risk factors such as male sex, hypertension, obesity, dyslipidemia, and smoking predict the development of large-fiber dysfunction, as measured by vibration perception threshold [9]. Previous clinical history of cardiovascular disease increased the incidence of large-fiber dysfunction with an odds ratio (OR) of 2.13. Coppini et al. [4] showed that higher vibration perception thresholds were more strongly associated with increased mortality than were other microvascular complications in diabetic patients.

Corresponding author: Seung-Hyun Ko
Division of Endocrinology & Metabolism, Department of Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, 93 Ji-dong, Paldal-gu, Suwon 442-723, Korea
E-mail: kosh@catholic.ac.kr

Owolabi et al. [10] showed that aggregate cardiovascular risk load, which was determined using the UK Prospective Diabetes Study risk engines, was more strongly correlated with and a predictor of clinically evident diabetic peripheral neuropathy than was hemoglobin A1c (HbA1c). In addition, Jarmuzewska et al. [11] demonstrated an independent association between pulse pressure and hypertension and diabetic peripheral neuropathy in patients with type 2 diabetes. In The Detection of Ischemia in Asymptomatic Diabetics (DIAD) study, which was a prospective randomized controlled trial in which participants were randomized either to be systematically screened with stress myocardial perfusion imaging or not to be screened, relationships were detected between development of CVD and symptoms of peripheral neuropathy (numbness and pain) or diminished peripheral sensation in type 2 diabetic patients [12].

Contrary to the relationship between DPN and cardiovascular risk factors or CVD in subjects with type 2 diabetes, the EURODIAB Prospective Complication Study of type 1 diabetes demonstrated a close relationship between the presence of microvascular complications and reduced peripheral nerve conduction velocity and amplitude. However, no associations between cardiovascular disease and nerve conduction study findings were observed [5].

In the present cross-sectional study, Chung et al. investigated the relationships between DPN and cardiovascular complications in Korean type 2 diabetic patients. The mean age of the participants was 62.2 years, and all patients had long-standing type 2 diabetes (mean diabetic duration, 12.2 years). The authors assessed the presence of peripheral neuropathy using sensory and motor nerve conduction studies in a large study sample (n=1,041), and the prevalence of DPN was 52.8%. Although nerve conduction studies (NCS) are considered the gold standard for assessing nerve damage and the most consistent indicator of neuropathy [13], NCS are generally not available or recommended as routine screening for the diagnosis of diabetic neuropathy. According to clinical practice guidelines, electrophysiological testing is rarely needed except when clinical features are atypical [14,15]. However, Chung et al. performed NCV in this large sample, and provided valuable information about NCV abnormalities in type 2 diabetic patients with peripheral neuropathy. Consistent with previous reports, the prevalences of diabetic retinopathy, nephropathy, or autonomic neuropathy were higher in patients with DPN, remaining significant after adjustment for age, diabetes duration, and hypertension. Importantly, diabetic polyneuropathy was more prevalent in patients with clinical history with CVD, based on NCS findings. In addition, diabetic polyneuropathy was independently associated with presence of CVD in type 2 diabetic patients (OR, 1.801).

The pathogenic mechanism or causal relationship between CVD and diabetic peripheral neuropathy was not clarified. As the authors suggested, distal symmetrical neuropathy might be associated with medial arterial calcification in diabetes mellitus patients. In addition, patients with long-standing diabetes develop not only microvascular complications, including peripheral neuropathy, but also cardiovascular autonomic neuropathy. Moreover, metabolic abnormalities related to cardiovascular risk factors might coexist and influence each other. A prospective, long-term cohort study should be conducted in the future.

Regardless of pathogenesis, like other microvascular complications, diabetic polyneuropathy may be prevented by intensive glycemic control. The recently published ACCORD study found that intensive glycemic control delayed the onset of diabetic microvascular complications, including neuropathy [16]. Most importantly, somatic and autonomic dysfunction are significant risk factors for CVD, and therefore the presence of peripheral and cardiovascular autonomic neuropathy should be actively screened at the time of diagnosis of diabetes and aggressively treated in patients with type 2 diabetes. We appreciate the efforts of Chung et al., who provide important information about diabetic polyneuropathy and cardiovascular risk factors for CVD in Korean patients with type 2 diabetes.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

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