

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

Jin Ook Chung, Dong Hyeok Cho, Dong Jin Chung, Min Young Chung

Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea

We appreciate the interest and comments on our study, "Association between diabetic polyneuropathy and cardiovascular complications in type 2 diabetic patients," which was published in *Diabetes & Metabolism Journal* 2011;35:390-6.

Diabetic polyneuropathy is one of the complications of chronic diabetes related to long-standing hyperglycemia and is a common cause of morbidity in diabetic patients. Diabetic polyneuropathy develops under the conditions of chronic hyperglycemia, associated with metabolic derangements and cardiovascular risk factors [1]. Recently, the close relationships between diabetic polyneuropathy and micro- or macroangiopathy have been reported [2-4]. Results from a population-based study of type 2 diabetic patients in Sweden showed that peripheral sensory neuropathy, assessed by 10 g monofilament and vibration perception threshold was associated with retinopathy and overt nephropathy [2]. In the EURODIAB Prospective Complications Study, the risk factors for cardiovascular disease including hypertension, total cholesterol, smoking, and previous cardiovascular disease increased the incidence of abnormal vibration perception threshold in type 1 diabetes mellitus [5]. Several studies have reported associations between diabetic polyneuropathy and cardiovascular mortality [6-8]. In our study, we investigated the association between diabetic polyneuropathy assessed by electrophysiological testing and chronic complications in type 2 diabetic patients. In our study,

the prevalence of diabetic retinopathy, nephropathy or autonomic neuropathy was higher in patients with diabetic polyneuropathy. Diabetic polyneuropathy was associated with a high prevalence of risk factors for macrovascular complications, such as poor metabolic control, dyslipidemia, and hypertension. In multivariate analysis, diabetic polyneuropathy was independently associated with cardiovascular disease (odds ratio, 1.801; 95% confidence interval [CI], 1.009 to 3.214).

Diabetic sensorimotor polyneuropathy is a form of axonal neuropathy associated with diabetes. Among several methods for evaluating peripheral neuropathy, nerve electrophysiological tests have emerged as important tools for tracing the onset and progression of peripheral neuropathy. Recently, the Toronto Diabetic Neuropathy Expert Group proposed the use of nerve conduction testing as an early and reliable indicator of the development of polyneuropathy for epidemiologic surveys or controlled clinical trials [9]. The diagnostic sensitivity of nerve conduction studies can be improved by additional parameters such as F-wave. However, as noted by Dr. Ko et al., our study has some limitations. Although nerve electrophysiological studies are highly reproducible, sensitive and objective methods of investigating diabetic polyneuropathy and have a key role in excluding the other causes of neuropathy, they have limitations in the assessment of small-fiber dysfunction [10]. Also, there are the discomforts of the procedures and

Corresponding author: Min Young Chung
Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonnam National University Medical School, 8 Hak-dong, Dong-gu, Gwangju 501-757, Korea
E-mail: mychung@chonnam.ac.kr

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limits on the availability for routine diagnostic evaluation in clinical practice [11]. Despite these limitations, the results of our study indicate the close relationship between electrophysiologically diagnosed polyneuropathy and cardiovascular disease in type 2 diabetic patients. Further studies are necessary to determine a causal relationship or possible mechanisms between diabetic polyneuropathy and cardiovascular adverse events.

REFERENCES

1. Valensi P, Giroux C, Seeboth-Ghalayini B, Attali JR. Diabetic peripheral neuropathy: effects of age, duration of diabetes, glycemic control, and vascular factors. *J Diabetes Complications* 1997;11:27-34.
2. Karvestedt L, Martensson E, Grill V, Eloffsson S, von Wendt G, Hamsten A, Brismar K. Peripheral sensory neuropathy associates with micro- or macroangiopathy: results from a population-based study of type 2 diabetic patients in Sweden. *Diabetes Care* 2009;32:317-22.
3. Cohen JA, Jeffers BW, Faldut D, Marcoux M, Schrier RW. Risks for sensorimotor peripheral neuropathy and autonomic neuropathy in non-insulin-dependent diabetes mellitus (NIDDM). *Muscle Nerve* 1998;21:72-80.
4. Yokoyama H, Yokota Y, Tada J, Kanno S. Diabetic neuropathy is closely associated with arterial stiffening and thickness in type 2 diabetes. *Diabet Med* 2007;24:1329-35.
5. Elliott J, Tesfaye S, Chaturvedi N, Gandhi RA, Stevens LK, Emery C, Fuller JH; EURODIAB Prospective Complications Study Group. Large-fiber dysfunction in diabetic peripheral neuropathy is predicted by cardiovascular risk factors. *Diabetes Care* 2009;32:1896-900.
6. Pop-Busui R, Evans GW, Gerstein HC, Fonseca V, Fleg JL, Hoogwerf BJ, Genuth S, Grimm RH, Corson MA, Prineas R; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of cardiac autonomic dysfunction on mortality risk in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Diabetes Care* 2010;33:1578-84.
7. Coppini DV, Bowtell PA, Weng C, Young PJ, Sonksen PH. Showing neuropathy is related to increased mortality in diabetic patients: a survival analysis using an accelerated failure time model. *J Clin Epidemiol* 2000;53:519-23.
8. Young LH, Wackers FJ, Chyun DA, Davey JA, Barrett EJ, Taillefer R, Heller GV, Iskandrian AE, Wittlin SD, Filipchuk N, Ratner RE, Inzucchi SE; DIAD Investigators. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. *JAMA* 2009;301:1547-55.
9. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, Lauria G, Malik RA, Spallone V, Vinik A, Bernardi L, Valensi P; Toronto Diabetic Neuropathy Expert Group. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care* 2010;33:2285-93.
10. Claus D, Mustafa C, Vogel W, Herz M, Neundorfer B. Assessment of diabetic neuropathy: definition of norm and discrimination of abnormal nerve function. *Muscle Nerve* 1993;16:757-68.
11. American Diabetes Association. Standards of medical care in diabetes--2011. *Diabetes Care* 2011;34 Suppl 1:S11-61.