EnM
ENDOCRINOLOGY AND METABOLISM

Response

Endocrinol Metab 2014;29:103-104
http://dx.doi.org/10.3803/EnM.2014.29.1.103
pISSN 2093-596X · eISSN 2093-5978

Association between Cardiac Autonomic Neuropathy, Diabetic Retinopathy and Carotid Atherosclerosis in Patients with Type 2 Diabetes (*Endocrinol Metab* 2013;28:309-19, Chan-Hee Jung et al.)

Chan-Hee Jung, Ji-Oh Mok

Division of Endocrinology and Metabolism, Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea

We would like to express our deep gratitude to the editor for giving us the opportunity to publish this article, and we are also deeply grateful to our reviewer, who read our manuscript and provided us with helpful comments and advice. Because few previous studies have been performed on the association between cardiac autonomic neuropathy (CAN) and carotid atherosclerosis, we investigated the relationship between these two conditions in patients with type 2 diabetes mellitus (T2DM).

We assessed CAN using five standard cardiovascular reflex tests, according to Ewing's protocol. We diagnosed CAN when a patient showed at least two abnormalities or CAN score of ≥2. However, there is no widely accepted single approach to the diagnosis of CAN in diabetes. Moreover, the diagnostic criteria and staging of CAN are still being debated. Therefore, the wide ranges (2.5% to 50%) of CAN prevalence reported by different authors can be attributed to the heterogeneous methodology used as well as differences in the definition of CAN [1]. Among several methods that provide indexes of both parasympathetic and sympathetic autonomic function, the assessment of heart rate variability by simple bedside tests devised by Ewing et al. has been used widely in clinical settings. Cardiovascular reflex tests are the gold standard in clinical autonomic testing and these tests have good sensitivity, specificity, reproducibility and are easily performed [2]. Several authors suggest that the presence of one abnormal cardiovascular reflex test identifies possible or early CAN and at least two abnormal tests are required for a definite or confirmed diagnosis of CAN [1]. Numerous clinical studies that have examined the association between CAN and mortality or CAN and silent myocardial ischemia used the CAN definition of an abnormal result on at least two of the five tests [3,4]. Additionally, a study that examined the relationship between CAN and coronary artery calcification in Korean patients with T2DM used the same CAN definition as we used in the present study [5]. However, as mentioned in the letter from the reviewer, we also think that a CAN score ≥2 can be too high to detect early atherosclerotic condition. On the contrary, it should be considered that a low CAN score may lead to low specificity in the detection of subclinical atherosclerosis.

In addition, the reviewer commented that the definition of 'two abnormal tests' contains many combinations of 'different two' types of abnormal CAN tests. Because each of the five CAN tests has a different meaning, each of those different combinations will also have unique clinical implications. There-

Corresponding author: Ji-Oh Mok
Division of Endocrinology and Metabolism, Department of Internal Medicine, Soonchunhyang University College of Medicine, 170 Jomaru-ro, Wonmi-gu, Bucheon 420-767, Korea
Tel: +82-32-621-5156, **Fax:** +82-32-621-5016, **E-mail:** hanna@schmc.ac.kr

fore, we agree with the reviewer's opinion. To our knowledge, however, no studies regarding the different clinical applications of the different combinations of CAN tests have been reported, even though each test or each different combination of the five tests has a different power in the sense of atherosclerotic progression, as mentioned above.

In conclusion, although the diagnosis of CAN as 'two or more' abnormal tests or a CAN score ≥2 in our study has several limitations, this diagnostic criteria has been widely used in numerous clinical studies. Additionally, we agree that further studies are needed to standardize and unify the various diagnostic criteria of CAN, as the reviewer commented.

Thank you again for your insightful and comprehensive review of our paper.

CONFLICTS OF INTEREST

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

REFERENCES

1. 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.
2. Pop-Busui R. Cardiac autonomic neuropathy in diabetes: a clinical perspective. Diabetes Care 2010;33:434-41.
3. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. Diabetes Care 2003;26:1553-79.
4. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. Circulation 2007;115:387-97.
5. Moon SS, Choi YK, Seo HA, Jeon JH, Lee JE, Jeong JY, Lee JY, Lee DH, Park WJ, Kim JG, Kim BW, Lee IK. Relationship between cardiovascular autonomic neuropathy and coronary artery calcification in patients with type 2 diabetes. Endocr J 2010;57:445-54.