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Basal C-peptide Level as a Surrogate Marker of Subclinical Atherosclerosis in Type 2 Diabetes Patients (*Diabetes Metab J* 2011;35:41-9)

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Patients with type 2 diabetes mellitus (T2DM) are at high risk for coronary heart disease, cerebrovascular disease or stroke, and peripheral vascular disease. These macrovascular diseases are common causes of morbidity and mortality among people with diabetes [1,2]. Therefore, there has been considerable clinical interest in the development of novel biomarkers that may help in the detection of individuals at high risk for cardiovascular diseases [3].

In a recent issue of *Diabetes & Metabolism Journal*, Kim and colleagues presented an article regarding basal C-peptide level as a surrogate marker of subclinical atherosclerosis in type 2 diabetic patients [4]. The authors found a simple positive correlation between basal C-peptide and intima-media thickness (IMT). The multiple regression analysis also showed that basal C-peptide significantly correlated with IMT (P=0.043) but did not correlate with the ten-year coronary heart disease (CHD) risk as defined by the United Kingdom Prospective Diabetes Study (UKPDS) risk engine (P=0.226). The study concluded that basal C-peptide was related to cardiovascular predictors (IMT) of T2DM, suggesting that basal C-peptide provides a further indication of cardiovascular disease.

Although it yielded interesting results, the study by Kim et al. left some questions to be answered. The relationships between insulin or C-peptide and atherosclerosis or the risk of cardiovascular disease are controversial. The result of their study was consistent with those of previous studies that showed that levels of fasting plasma proinsulin, C-peptide, and insulin due to cross-reacting RIA were associated with common carotid artery IMT independent of several conventional risk factors for atherosclerosis [5]. However, some studies have reported that C-peptide level was associated with diabetic microvascular but not macrovascular complications in patients with T2DM [6]. Others have reported that early thickening and damage to the arterial wall in T2DM might be related to relative fasting hypoinsulinaemia [7].

These differences in results may be originated to differences in the clinical characteristics of the study subjects. In the present study, the IMT measurement was performed in hospitalized patients in only one of two involved institutes. Kim et al. did not explain how many subjects were included in IMT measurement or whether there were differences in the clinical characteristics between those who underwent IMT measurement and those who did not.

As mentioned, basal C-peptide level has a strong association with insulin resistance and is a better surrogate than insulin for estimating insulin resistance. In the present study, however, C-peptide level had a simple negative correlation with HbA1c, suggesting that glycemic control in the more insulin-resistant patients was more intensive. Selvin et al. [8] reported several important associations between A1C and known risk

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factors for cardiovascular disease and suggested that A1C is independently related to carotid IMT. Kim et al. [2] also reported that changes in the mean IMT correlated with average values of HbA1c (r=0.219, P=0.007) in Korean type 2 diabetic patients, whereas the present study reported that HbA1c, a possible risk factor of cardiovascular diseases, did not correlate with IMT. It could influence the result that C-peptide did not correlate with the ten-year CHD risk according to the UKPDS risk engine, although it correlated with IMT, a cardiovascular predictor of T2DM.

Although their study had some limitations, this study of Kim and colleagues is an important work because they not only suggested a candidate surrogate marker of atherosclerosis in T2DM patients, but also illustrated the role of insulin in the pathogenesis of atherosclerosis in T2DM. We greatly appreciate the efforts of the authors in conducting such an intriguing work.

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