

# Diabetic Retinopathy and Endothelial Dysfunction in Patients with Type 2 Diabetes Mellitus (*Diabetes Metab J* 2013;37:262-9)

Seok Man Son

Department of Internal Medicine, Pusan National University School of Medicine, Yangsan, Korea

The mechanisms underlying the association of type 2 diabetes mellitus (T2DM) with vascular dysfunction are complex. Classical cardiovascular risk factors (hypertension, dyslipidemia, and smoking) may play a role, while diabetes-related parameters such as hyperglycemia, insulin resistance obesity, as well as other associated emerging risk factors such as inflammation, may also contribute to the impairment of vascular function indices in T2DM.

In the article entitled "Diabetic retinopathy and endothelial dysfunction in patients with type 2 diabetes mellitus," Yun et al. [1] reported that endothelial dysfunction as an independent predictor of increased diabetic retinopathy (DR) prevalence in patients with T2DM. This study is of great interest in that the authors examined the relationship between macrovascular endothelial dysfunction and retinopathy in type 2 diabetic subjects. Although the authors emphasized that diabetic subjects with retinopathy showed more severely impaired flow-mediated dilatation than diabetic subjects without retinopathy, they also found that patients who had DR demonstrated longer duration of diabetes, poorer glucose control and increased use of medications. This was an observational study that could not reveal causal relationships.

The pathogenesis of DR is insufficiently understood and potentially involves inflammation and endothelial dysfunction. Tomic et al. [2] investigated the relationship between inflammatory markers, other markers of endothelial dysfunction and

anthropometric parameters and their association with DR in patients with T2DM, divided into three groups: no DR, mild/moderate nonproliferative DR (NPDR) and severe NPDR/proliferative DR. They found that C-reactive protein (CRP) was correlated with fibrinogen, hemoglobin A1c (HbA1c), low density lipoprotein cholesterol, body mass index, waist circumference, and waist hip ratio. Logistic regression analysis showed that diabetes duration and HbA1c median were the main predictors of retinopathy. The study demonstrated that the association between obesity, inflammation and other risk factors plays an important role in the endothelial impairment involved in the pathogenesis of DR. Increased levels of systemic inflammatory markers have been found in persons with diabetes [3,4]; however, few studies have examined the role of systemic inflammation in DR in persons with diabetes mellitus [4]. In two case-control studies, diabetic subjects with macular edema (ME) [5] or proliferative DR (PDR) [6] had higher levels of vascular endothelial growth factors and cytokines in their vitreous than those without ME or PDR. In a cross-sectional study of normotensive persons with type 1 diabetes mellitus, serum CRP and fibrinogen levels were positively associated with the severity and progression of DR [4]. However, no prospective or population-based data have demonstrated the relationship between elevated concentrations of these molecules and the progression of DR or incidence of ME, or whether these associations remain significant while controlling for

Corresponding author: Seok Man Son  
Department of Internal Medicine, Pusan National University School of Medicine, and Diabetes Center and Endocrine Clinic, Pusan National University Yangsan Hospital, 20 Geumo-ro, Yangsan 626-787, Korea  
E-mail: sonsm@pusan.ac.kr

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HbA1c level, blood pressure, and signs of diabetic nephropathy in T2DM.

Endothelial dysfunction may result in increased vascular permeability, alteration of blood flow, oxidative stress, angiogenesis and DR [7,8]. Endothelial dysfunction is characterized by elevated levels of soluble vascular cell adhesion molecule (sVCAM-1) and soluble intercellular adhesion molecule (sICAM-1). In addition, homocysteine (Hcy) levels, which have been found to be elevated in persons with type 1 diabetes mellitus, have been shown to damage endothelial cells via generation of hydrogen peroxide [9]. Leukocyte adherence to the retinal endothelium may be a cause of capillary occlusion and an important factor in the pathogenesis of DR [10]. Adherence of leukocytes to the capillary and arteriolar endothelium occurs as a result of a process involving the expression of adhesion molecules (e.g., selectins and sICAM-1) and sVCAM-1 [10]. More studies are needed to investigate associations between selected markers of inflammation that have been commonly associated with systemic disease (high-sensitivity CRP, interleukin-6, and tumor necrosis factor) and with endothelial dysfunction (sVCAM-1, sICAM-1, and Hcy) with diabetic retinal outcomes.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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