Editorial

eISSN 2005-8330
https://doi.org/10.3348/kjr.2023.0779
Korean J Radiol 2023;24(11):1057-1058

Korean Journal of Radiology
KJR

Pushing Boundaries: Cardiac Computed Tomography Reveals Myocardial Microvascular Dysfunction in Patients With Diabetes

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See the corresponding article "Microvascular Myocardial Ischemia in Patients With Diabetes Without Obstructive Coronary Stenosis and Its Association With Angina" by Yu et al., in volume 24(11) on page 1081 to 1092, https://doi.org/10.3348/kjr.2023.0297.

Keywords: Computed tompgraphy; Coronary microvascular disease; Myocardial microvascular dysfunction; Myocardial perfusion

Despite advances in medical therapy for type 2 diabetes mellitus and lifestyle modifications, patients with diabetes remain prone to diffuse obstructive coronary artery disease (CAD) and multivessel disease, putting them at a high risk of major cardiac adverse events (MACEs). The prognosis of patients with diabetes is poorer than that of nondiabetic patients with a similar extent of CAD, and exploration of the underlying causes is underway.

The PROSPECT II (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) trial followed diabetic and non-diabetic patients with a history of acute myocardial infarction for 3.7 years, revealed that the risk of MACE in diabetic patients was 1.94 times higher than that in non-diabetic patients. However, studies using intravascular ultrasound and near-infrared spectroscopy have found no significant differences in coronary plaque characteristics between patients with and without diabetes, suggesting that the poor prognosis of patients with diabetes cannot be explained by differences in coronary plaque characteristics [1].

Coronary microvascular disease (CMD), an early feature of diabetes that precedes macrovascular disease, is widely accepted as an important component of diabetic cardiomyopathy. In patients with diabetes, oxidative stress and the formation of advanced glycation end products due to hyperglycemia lead to vascular endothelial damage, vascular inflammation, vessel wall thickening, and reduced capillary density. CMD, indicated by a decreased coronary flow reserve (CFR), is a strong independent predictor of cardiac mortality in both diabetic and non-diabetic patients, offering valuable risk stratification. Diabetes patients without CAD and with reduced CFR face event rates are similar to non-diabetes patients with known prior CAD (history of revascularization or myocardial infarction), while diabetes patients without CAD and with preserved CFR have rates similar to non-diabetes patients without CAD [2].

However, microvascular dysfunction (MVD) in patients with diabetes and the underlying pathological mechanisms remain insufficiently understood owing to the limited methods for assessing patients' microcirculation. The non-invasive diagnosis of MVD relies on CFR evaluation via positron emission tomography or magnetic resonance imaging, although the availability of these tests is generally restricted. Furthermore, assessing the extent of epicardial CAD requires separate evaluation using coronary computed tomography (CT) or invasive coronary angiography.

Received: August 18, 2023 **Accepted:** August 20, 2023
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In the current issue of *Korean Journal of Radiology* (*KJR*), the study titled "Microvascular myocardial ischemia in patients with diabetes without obstructive coronary stenosis and its association with angina" by Yu et al. [3] attempts to assess myocardial MVD and fibrosis in diabetic patients without coronary stenosis using coronary CT, myocardial CT perfusion, and CT delayed enhancement. The authors enrolled 113 diabetic patients without obstructive CAD and compared them with non-diabetic patients without obstructive CAD, revealing a significant decrease in global myocardial blood flow (MBF) and a noteworthy increase in global extracellular volume (ECV) in diabetic patients. Additionally, there was a markedly higher frequency of segments with reduced MBF below 100 mL/min/100 mL that could be attributed to MVD, as well as a significantly higher frequency of segments with an ECV of > 30%.

Comprehensive cardiac CT can evaluate epicardial CAD, stress myocardial perfusion, and myocardial fibrosis in a single examination lasting approximately 40 min. The investigators deserve praise for successfully demonstrating the utility of comprehensive cardiac CT scans in detecting myocardial MVD in patients with diabetes. However, it must be acknowledged that several hurdles remain before comprehensive cardiac CT can be established as a method for testing impaired microcirculation. First, this study demonstrated decreased stress MBF rather than decreased CFR, which is currently required by the guidelines for noninvasive diagnosis of MVD. Because decreased CFR can also result from an increase in resting MBF, careful consideration must be given to whether stress MBF alone is sufficient to diagnose MVD. Second, it is important to note that MVD has been identified as a diffuse change, namely, a decrease in the global CFR. Although this study reported the number of segments with MVD, it remains unclear whether this implies regional MVD or whether it stems from physiological heterogeneity. Finally, although MVD is expected to be highly prevalent in patients with obstructive CAD, whether it is possible to diagnose the presence or exent of MVD in such cases remains uncertain.

Currently, there is insufficient evidence to support the use of CT for the diagnosis of MVD. However, cardiac CT undeniably presents an appealing modality for addressing the growing interest in ischemia with nonobstructive coronary arteries (INOCA) in recent years. Based on the findings of this study, cardiac CT has taken a significant step forward in the evaluation of coronary microcirculation.

Conflicts of Interest

Kakuya Kitagawa, the editor board member of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. The author has no potential conflicts of interest to disclose.

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Funding Statement

None

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https://doi.org/10.3348/kjr.2023.0779