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# Detecting occult coronary artery disease followed by early coronary artery bypass surgery in patients with diabetic retinopathy: Report from a diabetic retinocoronary clinic

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**Objectives:** We hypothesized that a large number of patients with diabetic retinopathy who could benefit greatly from early coronary artery bypass grafting would not be identified.

**Methods:** Patients with diabetic retinopathy receiving ophthalmologic care as outpatients in our hospital in whom coronary artery disease was not previously suspected were referred randomly to the diabetic retinocoronary clinic and were asked to participate in diagnostic tests, including an exercise treadmill test and exercise thallium scintigraphy or coronary computed tomography. Patients who had type 1 diabetes mellitus, required hemodialysis, or both were excluded from this study. A definitive diagnosis of coronary artery disease was confirmed by means of coronary angiography.

**Results:** Of 214 patients with diabetic retinopathy, 55 (25.7%) were confirmed as having significant stenotic coronary artery disease. Patients with angiographically confirmed coronary disease were older than those with negative results on diagnostic tests (62.2 ± 9.8 vs 57.9 ± 10.3 years, $P = .01$). Fifteen had 1-vessel disease, 17 had 2-vessel disease, 14 had 3-vessel disease, 1 had left main trunk plus 1-vessel disease, 2 had left main trunk plus 2-vessel disease, and 5 had left main trunk plus 3-vessel disease. Eight patients had left main trunk disease, and 18 patients with non–left main trunk disease had proximal left anterior descending coronary artery (LAD) disease. Forty-two patients showed indications of coronary revascularization (coronary artery bypass grafting in 17 and percutaneous coronary intervention in 25). During the entire follow-up (287.6 ± 183.2 days) of 39 patients undergoing coronary revascularization, all were alive without myocardial infarction, but 8 experienced vitreous hemorrhage.

**Conclusions:** Approximately 25% of patients with diabetic retinopathy receiving ophthalmologic care as outpatients have a significant stenotic coronary artery disease. Of the total diabetic population, a large number of patients with diabetic retinopathy who show strong indications for early coronary artery bypass grafting might well go unrecognized. (J Thorac Cardiovasc Surg 2010;139:92-7)

Coronary artery disease (CAD) is the leading cause of death in diabetic patients, accounting for 75% of deaths.[1] The risk of CAD events varies widely from patient to patient and even within a diabetic patient as the disease progresses. Diabetic retinopathy (DR) is an early sign of microvascular complication of diabetes, its severity being directly related to the duration of the diabetes and to the amount of increase in blood glucose concentration.[2] Evidence demonstrates that the severity of DR is associated with a graded increased risk of myocardial infarction and death from CAD.[3-11] We reviewed the literature regarding the association between DR and CAD and hypothesized that a large number of patients with DR and CAD who could benefit greatly from early coronary artery bypass grafting (CABG) would not be identified until the occurrence of a catastrophic event, such as overt heart failure or sudden death.[12] In this regard we opened a novel clinic named the diabetic retinocoronary clinic for the purpose of identification and treatment of occult CAD in patients with DR, and this article reports our experience in this clinic.

## MATERIALS AND METHODS

### Study Patients

The concept of a diabetic retinocoronary clinic was approved by the University of Tokyo Institutional Board for Outpatients in December 2006, and the clinic was opened in April 2007. Patients with DR receiving ophthalmologic care as outpatients in our hospital in whom CAD had not previously been suspected were referred randomly to the clinic by ophthalmologists or endocrinologists. Patients who had type 1 diabetes mellitus, required hemodialysis, or both were excluded from this study. All patients provided informed consent

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**Abbreviations and Acronyms**

CABG = coronary artery bypass grafting
CAD = coronary artery disease
CT = computed tomography
DES = drug-eluting stent
DR = diabetic retinopathy
ECG = electrocardiography
ETT = exercise treadmill test
LAD = left anterior descending coronary artery
LMT = left main trunk
NPDR = nonproliferative diabetic retinopathy
PCI = percutaneous coronary intervention
PDR = proliferative diabetic retinopathy

and were asked to participate in a screening that included a cardiovascular history and a physical examination, risk factor assessment, resting electrocardiography (ECG), and an exercise treadmill test (ETT). The positivity of the ETT was determined by using conventional criteria (≥1 mm of horizontal or downsloping ST-segment depressions at 80 ms after the end of the QRS complex [from the J points]). The results of the ETT were classified as negative, positive (if ST-segment depression exceeded 2 mm), or nondiagnostic.[13] If patients had limitations that precluded the ETT, such as limitation of physical activity associated with severely impaired vision, peripheral arterial disease, or an abnormal resting ECG result or if the results of ETT were nondiagnostic, they were approached for exercise thallium scintigraphy or coronary computed tomography (CT). Patients with positive ETT results, abnormal scintigraphic results, or CT results indicating CAD were approached for coronary angiography. A significant stenotic CAD was confirmed by means of coronary angiography. The findings reported in this study were documented for all patients as of November 15, 2008.

### Severity of DR

The severity in the more affected eye was used, and the patients with retinopathy were grouped into 2 categories: those with nonproliferative diabetic retinopathy (NPDR; only microaneurysms or microaneurysms plus 1 or more the following: retinal hemorrhages, soft exudates, hard exudates, intraretinal microvascular abnormalities, or venous beading) and those with proliferative diabetic retinopathy (PDR; the presence of new vessels, preretinal or vitreous hemorrhages, panretinal photocoagulation scarring, and a history of vitreous surgery).[2]

### Coronary Angiography

Angiographic analysis was performed and evaluated by experienced cardiologists. The severity of CAD was determined based on stenosis of the left main trunk (LMT; defined as lesions causing lumen narrowing by ≥50%) and the number of vessels with 70% or greater stenosis. The proximal LAD was defined as the vessel between the circumflex takeoff and the first major septal or diagonal branch.

## RESULTS

Between April 2007 and October 2008, 286 consecutive patients with DR were referred to the diabetic retinocoronary clinic. Thirty-four patients refused to undergo diagnostic tests, and 38 did not have a definitive diagnosis by November 15, 2008. The remaining 214 patients were included in this study. Of them, 59 patients had NPDR, and 155 had PDR.

One hundred seventy-six (82.2%) patients were completely asymptomatic; 25 (11.7%) were revealed during history taking by cardiac surgeons and cardiologists to have chest discomfort, but their symptoms were not typical of angina pectoris. Furthermore, limited physical activity prevented a precise evaluation of angina pectoris in 11 (5.1%) patients with severely impaired vision and in 2 (0.9%) patients with peripheral arterial disease. Of the study group, normal resting ECG results were seen in 159 (74.3%), Q waves were seen in 4 (1.9%), nonspecific ST-T changes were seen in 39 (18.2%), right bundle branch block was seen in 9 (4.2%), atrial fibrillation was seen in 2 (0.9%), and second-degree atrioventricular block was seen in 1 (0.5%).

Of the 172 patients undergoing ETT, 50 (29.1%) had a positive ETT result, 106 (61.7%) had a negative ETT result, and 15 (8.7%) had nondiagnostic results. The patients who had limitations that precluded the ETT (n = 42) or had nondiagnostic results on the ETT were approached for exercise thallium scintigraphic analysis or coronary CT scanning. Thirty-three patients underwent exercise thallium scintigraphy, and 8 (24.2%) had abnormal results. Twenty-four patients underwent coronary CT, which revealed atherosclerotic CAD in 7 (29.2%).

Sixty-five patients underwent coronary angiography. Overall, of 214 study patients, 55 (25.7%) were confirmed as having significant stenotic CAD (Figure 1). The baseline characteristics of the patients with an angiographically confirmed CAD were compared with those of patients with negative results on diagnostic tests (Table 1). Patients with angiographically confirmed CAD were older (62.2 ± 9.8 vs 57.9 ± 10.3 years, $P = .01$). Twenty (46.5%) of 43 patients with Q-wave or ST-T changes on resting ECGs had CAD, whereas 35 (20.5%) of 171 patients without these abnormalities had CAD ($P = .001$). The serum creatinine level, estimated glomerular filtration rate, hemoglobin A1c level, low-density lipoprotein level, and high-density lipoprotein level were similar in the 2 groups. Neither the severity of DR nor treatment with insulin was associated with angiographically confirmed CAD.

Of the 55 patients with CAD, 8 (14.5%) had LMT disease, 18 (32.7%) patients without LMT disease had proximal LAD disease, and 29 patients had non-LMT, nonproximal LAD disease (Figure 1). One-vessel disease was seen in 15 (27.3%), 2-vessel disease was seen in 17 (30.9%), 3-vessel disease was seen in 14 (25.5%), LMT plus 1-vessel disease was seen in 1 (1.8%), LMT plus 2-vessel disease was seen in 2 (3.6%), and LMT plus 3-vessel disease was seen in 5 (9.1%) patients. In a daily coronary conference held within our institution, CABG was recommended for 17 patients, percutaneous coronary intervention (PCI) was recommended for 25 patients, and aggressive medical therapy alone was recommended for 13 patients. For all patients with LMT disease, coronary revascularization was indicated. Of 18 patients without LMT