Preventative Effects of Rosiglitazone on Restenosis After Coronary Stent Implantation in Patients With Type 2 Diabetes

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OBJECTIVE — Despite the popularity of coronary stenting in coronary artery disease (CAD), restenosis remains a challenging clinical problem. This study evaluated the efficacy of rosiglitazone for preventing in-stent restenosis in type 2 diabetic patients.

RESEARCH DESIGN AND METHODS — We conducted a prospective, randomized, case-controlled trial involving 95 diabetic patients with CAD who were randomly assigned to either the control or rosiglitazone group (48 and 47 patients, respectively). Quantitative coronary angiography (QCA) was performed at study entry and again at 6-month follow-up. The primary end point was the restenosis rate, which was determined by QCA.

RESULTS — Eighty-three patients (45 patients with 55 lesions in the control group and 38 patients with 51 lesions in the rosiglitazone group) completed follow-up angiography. Rosiglitazone treatment for 6 months reduced fasting insulin concentration. The high-sensitivity C-reactive protein concentration was significantly reduced in the rosiglitazone group compared with that in the control group (from 2.92 ± 1.98 to 0.62 ± 0.44 mg/l, $P < 0.001$ vs. from 2.01 ± 1.33 to 1.79 ± 1.22 mg/l, P = NS). However, the baseline and follow-up glucose and lipid concentrations were not different between two groups. The rate of in-stent restenosis was significantly reduced in the rosiglitazone group compared with the control group (for stent lesions: 17.6 vs. 38.2%, $P = 0.030$). The rosiglitazone group had a significantly lower degree of diameter stenosis (23.0 ± 23.4% vs. 40.9 ± 31.9%, $P = 0.004$) compared with the control group.

CONCLUSIONS — We demonstrated that treatment with rosiglitazone significantly reduces in-stent restenosis in diabetic patients with CAD who underwent coronary stent implantation.

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Abbreviations: CAD, coronary artery disease; hsCRP, high-sensitivity C-reactive protein; MLD, minimal lumen diameter; PPAR, peroxisome proliferator–activated receptor; QCA, quantitative coronary angiography; TZD, thiazolidinedione; VSMC, vascular smooth muscle cell.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

See accompanying editorial, p. 2764.

Coronary artery disease (CAD) secondary to atherosclerosis is the leading cause of death in patients with type 2 diabetes (1). Although a coronary stent implant is recognized to be a useful treatment for CAD (2), in-stent restenosis is still a significant clinical problem (3), and the restenosis rates in nondiabetic patients who receive stent implants are still 20–40% after 6 months (4–6). Furthermore, stenting of the native coronary arteries in diabetic patients is associated with a significantly higher in-stent restenosis rates up to 32–66%, regardless of the treatment modality for diabetes (3,7), resulting in a higher rate of morbidity and mortality compared with those for nondiabetic patients. Although many pharmacological therapies, such as conventional antiplatelet drugs, anticoagulants, and the like, have been investigated in an attempt to reduce restenosis, the majority of trials have been disappointing (8–11).

The thiazolidinediones (TZDs) are a new class of compounds for treating type 2 diabetes. In addition to the hypoglycemic effect, nonhypoglycemic effects relating to a reduction of cardiovascular risks have been described, including a decrease in blood pressure (12), a correction of dyslipidemia (13,14), an improvement in inflammation (15), and a decrease in the carotid artery intima-media thickness (16). Each of these effects is an important target to prevent or treat atherosclerosis and restenosis. It has been reported that TZDs reduce neointimal tissue proliferation after coronary stent implantation in patients with type 2 diabetes (17–19). We designed a prospective, randomized, controlled study to verify the hypothesis that rosiglitazone, another member of the TZD class, reduces the rate of restenosis in type 2 diabetic patients who have undergone coronary stenting.

RESEARCH DESIGN AND METHODS

— Ninety-five patients with previously treated diabetes (oral hy-

poglycemic agents or insulin) who had recent acute myocardial infarction or stable or unstable angina and underwent coronary stent implantation at the Cardiovascular Center, Severance Hospital, Yonsei University College of Medicine, were recruited in this study. The exclusion criteria were as follows: patients previously treated with TZDs, patients with ejection fractions <35%, patients with a liver or renal dysfunction or a pregnancy, and patients with lesions of reference vessel diameter <2.75 mm. The study was approved by the ethics committee of Yonsei University College of Medicine, and informed consent was obtained from each subject.

Beginning 1 day before the scheduled angioplasty, the subjects were randomly assigned to two treatment groups. The rosiglitazone group (47 patients with 62 lesions) was treated with 8 mg rosiglitazone before undergoing catheterization and 4 mg daily thereafter, combined with conventional antidiabetic therapy (sulfonylurea, metformin, and/or an α-glucosidase inhibitor or insulin). The control group comprised 48 patients with 60 lesions who were treated with conventional antidiabetic therapy only. With the exception of the study medication, rosiglitazone, both groups had their conventional antidiabetic medication titrated to achieve a comparable glycemic control, with a target HbA_{1c} <7.0%. When indicated, the patients were treated with sufficient medications, such as an ACE inhibitor, HMG (3-hydroxy-3-methylglutaryl)-CoA reductase inhibitor, β-blocker, or calcium channel blocker. In addition, the protocol recommended treatment with antiplatelet medications, including aspirin, ticlopidine, or clopidogrel, for 6 months. During the follow-up period, the doses of antiplatelet and hypolipidemic agents were not changed. However, the doses of antihypertensive agents were adjusted for blood pressure control, which was targeted at <130/85 mmHg.

Before the coronary stent implantation and follow-up angiography, respectively, all participants underwent a standard examination, including measurements of fasting plasma glucose, total cholesterol, HDL cholesterol, triglyceride, nonesterified fatty acids, high-sensitivity C-reactive protein (hsCRP), and insulin concentrations and measurements of blood pressure, height, weight, and waist and hip circumference, by the same investigator. However, in patients with acute myocardial infarction, fasting plasma glucose and hsCRP concentrations were measured 1 week after coronary stenting.

A clinical follow-up was performed at 1, 3, and 6 months and an angiographic follow-up at 6 months. The angiographic end point was the rate of restenosis, the percentage stenosis, and the in-stent minimal lumen diameter (MLD) at the angiographic follow-up, as determined by quantitative coronary angiography (QCA). The clinical end points included the incidences of death, acute or subacute thrombosis, and the target lesion revascularization.

Stent implantation

Balloon angioplasty and stent implantation were performed according to standard clinical practice by the femoral approach. At least 3 days before the procedure, patients were treated with 325 mg aspirin once daily and 250 mg ticlopidine twice or 75 mg clopidogrel once daily. A bolus of 100 units/kg heparin was administered after sheath insertion, and supplemental doses were then given to maintain an activated clotting time of >300 s. The stent size, the need for predilation, and the final size of the balloon for stent implantation were chosen by the operator to obtain a close-to-zero angiographic residual stenosis. Various types of stents were used at the discretion of operator. Stents used were as follows: Arthos (amg International), Arthos Inert (amg International), BX Velocity (Cordis, Johnson & Johnson), Coroflex (B. Braun Mesungen), and Express (Boston Scientific). There was no significant difference in the selection of coronary stent type for both groups.

Quantitative angiographic analysis

QCA was performed using an online quantitative coronary angiographic system (ANCOR 2.3; Siemens, Munich, Germany), by a single individual who was blinded to the patient's treatment assignment. A contrast-filled nontapered catheter tip was used for calibration. Baseline coronary angiography was performed in multiple projections. The MLD of the treated coronary segments, the reference diameter, the percent diameter stenosis, and the lesion length on the baseline angiogram were determined in the view that demonstrated the lesion to be most severe and not foreshortened. Baseline and follow-up cine angiograms were evaluated in the same view. We defined the restenosis as percent diameter stenosis >50% at the time of follow-up angiography. Lumen loss was defined as the difference between MLD immediately after the procedure and MLD at 6 months.

Assays

The plasma glucose concentrations were determined using the glucose oxidase method. The insulin concentrations were measured by a radioimmunoassay using the double-antibody method and a commercially available radioimmunoassay kit (Linco Research, St. Charles, MO). The total cholesterol and triglyceride concentrations were measured enzymatically. The nonesterified fatty acid concentrations were measured by an enzymatic calorimetric method. The hsCRP concentrations were quantified using a nephelometer II (Dade Behring Diagnostics, Marburg, Germany).

Statistical analysis

All continuous variables are expressed as means ± SD. The statistical analyses were performed using the SPSS 10.0 software package (SPSS, Chicago, IL). The effects between two groups were analyzed by an independent samples *t* test, and the comparisons between before and after treatment were analyzed by a paired *t* test. The dichotomous variables are reported as percentages along with the 95% CIs, and the comparisons were performed using a Pearson χ^2 test. The angiographic and procedural characteristics were determined using a lesion-based assessment. A two-sided value of $P < 0.05$ was considered significant. Any patients who discontinued the assigned treatment were excluded from the final analysis.

RESULTS — Ninety-five patients were enrolled in this study: 48 patients randomly assigned in the control group and 47 patients randomly assigned in the rosiglitazone-treated group. The stent implantation was successful in all patients. However, 12 patients (3 in control group and 9 in rosiglitazone group) were lost to follow-up for the following reasons: the loss of follow-up and the nonattendance of the angiography (4 patients), the refusal of follow-up angiography (3 patients), transfers to other institutions for

Table 1—*Baseline anthropometric and demographic characteristics of subjects*

	Control	Rosiglitazone	P
n (M/F)	45 (34/11)	38 (24/14)	0.240
Age (years)	59.9 ± 9.3	60.9 ± 9.3	0.850
Diabetes duration (years)	7.2 ± 3.8	7.5 ± 4.9	0.982
BMI at baseline (kg/m^2)	24.8 ± 3.35	24.9 ± 2.96	0.871
Weight (cm)	68.1 ± 11.0	67.6 ± 10.0	0.914
Waist (cm)	87.2 ± 7.5	88.4 ± 6.5	0.859
Systolic blood pressure (mmHg)	140.1 ± 15.4	144.1 ± 16.2	0.307
Diastolic blood pressure (mmHg)	84.2 ± 14.3	85.5 ± 16.9	0.449
Fasting glucose (mmol/l)	8.34 ± 1.58	8.90 ± 1.91	0.386
HbA_{1c} (%)	7.72 ± 1.13	7.79 ± 1.30	0.931
Fasting insulin (pmol/l)	35.7 ± 18.0	40.2 ± 19.4	0.973
Total cholesterol (mmol/l)	4.94 ± 1.26	4.93 ± 0.97	0.873
HDL cholesterol (mmol/l)	1.06 ± 0.28	1.01 ± 0.28	0.623
Triglyceride (mmol/l)	1.80 ± 0.62	1.89 ± 0.69	0.498
Free fatty acid (μmol/l)	580.3 ± 101.7	669.2 ± 127.4	0.347
hsCRP (mg/l)	2.01 ± 1.33	2.92 ± 1.98	0.202
Acute myocardial infarction (%)	31	26	
Unstable angina (%)	40	42	
Treatments			
HMG-CoA reductase inhibitor	34 (75.6)	33 (86.8)	0.266
ACE inhibitors	34 (75.6)	29 (76.3)	0.791
Calcium channel blocker	22 (48.9)	15 (39.5)	0.380
β-Blocker	36 (80.0)	36 (94.7)	0.197
Aspirin	45 (100)	37 (97.4)	0.458
Ticlopidine	17 (37.8)	16 (42.1)	0.822
Cilostazone	28 (62.2)	22 (57.9)	0.822
Sulfonylurea	26 (57.8)	16 (42.1)	0.189
Biguanide	19 (42.2)	22 (57.9)	0.189
α-Glucosidase inhibitor	3 (6.7)	0	0.244
Insulin	0	3 (7.9)	0.112

Data are means ± SD or *n* (%).

reasons of being at a distance from their place of residence (3 patients), cancer (1 patient), or self-withdrawal of rosiglitazone (1 patient). Thus, 83 patients (45 patients with 55 lesions in the control group, and 38 patients with 51 lesions in the rosiglitazone group) completed the follow-up angiography and were included in the analyses. Rosiglitazone was well tolerated in all patients in the rosiglitazone group. No patient had significant side effects, such as an elevation in the liver enzyme levels.

The anthropometric and demographic characteristics of the 83 patients are listed in Table 1. The age, sex, BMI, waist circumference, and blood pressure between both groups were similar. In addition, there were no significant differences in the various treatment modalities except for rosiglitazone in both groups.

Although the fasting plasma glucose and HbA_{1c} concentrations were significantly improved in both groups after 6 months, there were no significant differences in the glycemic control between two groups, either at baseline or at follow-up (Table 2). There were no statistically significant differences in the insulin, total cholesterol, triglyceride, and HDL cholesterol concentrations at baseline between the two groups (Table 1). After 6 months of treatment, the fasting plasma concentration of HDL cholesterol increased and the insulin and triglyceride concentrations declined significantly

Table 2—*Biochemical characteristics of subjects at baseline and follow-up angiography*

	Control (*n* = 45)		Rosiglitazone (*n* = 38)	
	Baseline	Follow-up	Baseline	Follow-up
Fasting glucose (mmol/l)	8.34 ± 1.58	6.87 ± 1.52*	8.90 ± 1.91	7.35 ± 1.89*
Δ from baseline (mmol/l)		−2.03 ± 1.43		−1.68 ± 1.17
HbA_{1c} (%)	7.72 ± 1.13	7.23 ± 0.93†	7.79 ± 1.30	7.17 ± 0.98†
Δ from baseline (%)		−0.75 ± 1.07		−0.61 ± 1.15
Fasting insulin (pmol/l)‡	35.7 ± 18.0	34.2 ± 18.9	40.2 ± 19.4	34.5 ± 19.7†
Δ from baseline (pmol/l)		−1.4 ± 15.3		−5.8 ± 16.4
Total cholesterol (mmol/l)	4.94 ± 1.26	4.44 ± 0.88†	4.93 ± 0.97	4.34 ± 0.84†
Δ from baseline (mmol/l)		−0.50 ± 0.94		−0.59 ± 0.93
HDL cholesterol (mmol/l)	1.06 ± 0.28	1.14 ± 0.27	1.01 ± 0.28	1.12 ± 0.21†
Δ from baseline (mmol/l)		0.08 ± 0.22		0.11 ± 0.21
Triglyceride (mmol/l)	1.80 ± 0.62	1.43 ± 0.69	1.89 ± 0.69	1.34 ± 0.44*
Δ from baseline (mmol/l		−0.29 ± 0.57		−0.55 ± 0.56
Free fatty acid (μmol/l)	580.3 ± 101.7	548.8 ± 95.6	669.2 ± 127.4	492.0 ± 101.4*
Δ from baseline (μmol/l)		−31.5 ± 72.5		−177.2 ± 92.9§
hsCRP (mg/l)	2.01 ± 1.33	1.79 ± 1.22	2.92 ± 1.98	0.62 ± 0.44*§
Δ from baseline (mg/l)		−0.52 ± 1.72		−2.31 ± 2.14§

*$P < 0.001$, †$P < 0.05$ vs. baseline; ‡analyses except for insulin-treated patients; §$P < 0.05$ vs. control group.

Table 3—*Angiographic and procedural characteristics and clinical outcomes*

	Control	Rosiglitazone	P
n	45	38	
No. of stents	1.22 ± 0.47	1.32 ± 0.53	0.395
Baseline ejection fraction (%)	55.1 ± 11.4	54.3 ± 10.1	0.800
Stented coronary vessels			0.501
Left anterior descending coronary artery	27	26	
Left circumflex artery	11	9	
Right coronary artery	17	14	
Left main coronary artery		2	
Stent type (%)			0.293
Arthos	20.0	17.6	
Arthos inert	14.6	21.6	
BX velocity	23.6	27.5	
Coroflex	18.2	17.6	
Express	23.6	15.7	
Stent diameter (mm)	3.24 ± 0.42	3.29 ± 0.41	0.861
Stent length (mm)	18.40 ± 4.75	20.28 ± 5.73	0.160
Reference diameter (mm)			
Before	3.15 ± 0.49	3.16 ± 0.49	0.901
After	3.17 ± 0.41	3.20 ± 0.45	0.822
Follow-up	3.14 ± 0.48	3.18 ± 0.47	0.722
Minimal lumen diameter (mm)			
Before	0.65 ± 0.41	0.83 ± 0.57	0.066
After	3.10 ± 0.43	3.13 ± 0.48	0.891
Follow-up	1.91 ± 1.05	2.49 ± 0.88	0.009
Diameter stenosis, in stent (%)			
Before	80.1 ± 13.4	74.4 ± 14.9	0.068
After	2.5 ± 4.3	2.3 ± 4.4	0.920
Follow-up	40.6 ± 31.9	23.0 ± 23.4	0.004
Distal edge (mm)			
Before	3.06 ± 0.43	2.99 ± 0.47	0.664
After	3.07 ± 0.40	3.02 ± 0.47	0.752
Follow-up	3.07 ± 0.39	3.01 ± 0.38	0.684
Lesion length (mm)	16.48 ± 5.16	19.02 ± 6.09	0.033
Acute gain (mm)	2.48 ± 0.57	2.29 ± 0.51	0.129
Late lumen loss (mm)	1.20 ± 0.97	0.65 ± 0.73	0.005
Loss index	0.49 ± 0.42	0.29 ± 0.31	0.014
Restenosis (% of stents)	21 (38.2)	9 (17.6)	0.030
Death (%)	0	0	—
Subacute stent thrombosis (%)	0	2.6	0.481
Target lesion revascularization (%)	20.0	10.5	0.244
Percutaneous coronary intervention (%)	13.3	10.5	0.458
Coronary-artery bypass grafting (%)	6.7	0	0.499
Major adverse cardiac events (%)*	20.0	10.5	0.244

*Major adverse cardiac events were defined as death, Q-wave myocardial infarction, or target lesion revascularization.

from baseline in the rosiglitazone group, although these changes were not significantly different from those in the control group (Table 2). The fasting serum nonesterified fatty acid and hsCRP concentrations after treatment decreased significantly in the rosiglitazone group and remained unchanged in the control group. Particularly, hsCRP concentration in the rosiglitazone group decreased significantly from baseline (from 2.92 ± 1.98 to 0.62 ± 0.44 mg/l, $P < 0.001$) and versus control (1.79 ± 1.22 mg/l at follow-up, $P < 0.05$).

Angiographic data

There were no significant differences in the target vessels, the stent types, the stent diameter and length, the angiographic reference diameter, and the MLD between the two groups (Table 3). The rate of restenosis was 17.6% in the rosiglitazone-treated group and 38.2% in the control group ($P = 0.03$). This reduction in the rosiglitazone group was associated with improvement in the MLD at follow-up (2.49 ± 0.88 mm in the rosiglitazone group vs. 1.91 ± 1.05 mm in the control group, respectively, $P = 0.009$). Rosiglitazone treatment significantly reduced the diameter stenosis after 6 months (23.0 ± 23.4 vs. 40.4 ± 31.9% in the control group, $P = 0.004$) (Fig. 1). More patients in control group than in the rosiglitazone-treated group underwent target lesion revascularization (nine in the control group and four in the rosiglitazone group), although this difference was not statistically significant ($P = 0.244$).

CONCLUSIONS — This study demonstrated that rosiglitazone significantly reduced restenosis rate in the 6 months after coronary stenting in the type 2 diabetic patients. These effects were independent of glycemic control, since there were no significant relationships between the restenosis percentage and the changes in glucose concentrations and because the glycemic indexes were similar in the two groups, either at the baseline or at the follow-up angiography.

Because the proliferations of neointimal tissue and/or the medial vascular smooth muscle cells (VSMCs) are pivotal to the pathophysiology of a postintervention restenosis (20,21), inhibiting cellular proliferation for preventing an in-stent restenosis is a rational strategy. Although numerous therapies, including mechanical or pharmacological approaches, to block or inhibit the pathological processes of vascular proliferation have been studied, clinical trials have generally failed to recapitulate the efficacy documented in animal studies (8–11). Considering this point of view, brachytherapy (22,23) and drug-eluting stents (24,25) are the most promising new therapies for preventing a restenosis. However, some limitations prevent these therapies from becoming widely used. Therefore, easy and safe approaches to reducing the restenosis rate are needed.

TZDs directly improve insulin resistance and hyperglycemia, acting via the nuclear transcription factor peroxisome proliferator–activated receptor (PPAR)-γ

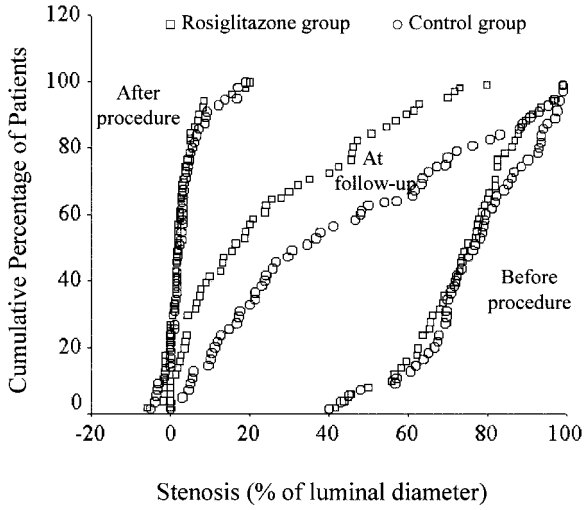

Figure 1—*Cumulative distribution curves for percent stenosis of the luminal diameter in the rosiglitazone and control groups. The distributions were similar at baseline and immediately after stent implantation. At 6 months, the mean degree of stenosis in the rosiglitazone group was significantly lower than that in the control group.*

(26). Recent reports have established the presence of PPAR-γ in human endothelial cells, VSMCs, monocytes and macrophages, and human arterial lesions, all of which have important pathogenetic roles in atherosclerosis (27,28). This finding suggests that PPAR-γ agonists may directly affect the molecular mechanisms involved in atherosclerosis and restenosis. The activation of PPAR-γ in vascular cells inhibits the growth factor–induced proliferation and migration of VSMCs (29) or monocytes (30). In our in vitro and animal studies, rosiglitazone effectively led to a dose-dependent attenuation of VSMCs migration induced by the platelet-derived growth factor and inhibited neointimal proliferation after a carotid artery balloon injury in a type 2 diabetic animal model (unpublished data).

It was previously reported that TZDs reduce neointimal tissue proliferation after coronary intervention (17–19) and that troglitazone reduces in-stent restenosis in a relatively small number of patients with type 2 diabetes (18). However, these were studies with small patient numbers, and some reports (19,31) demonstrated that TZDs did not reduce the in-stent restenosis despite reducing neointimal proliferation. Although we did not perform an intravascular ultrasound, which can greatly aid the characterization of the neointimal accumulation that cannot be studied with QCA, the present study is the first to our knowledge to demonstrate that the administration of rosiglitazone was quite effective in reducing the in-stent restenosis rate in type 2 diabetic patients.

This antirestenosis effect is likely to be independent of the known hypoglycemic action of rosiglitazone. Both groups had undergone the maximum treatments, such as ACE inhibitor, antiplatelet agents, HMG-CoA reductase inhibitor, diet control, and/or exercise, for reducing the patient's cardiovascular risks. As a result, significant improvements in fasting plasma glucose, HbA_{1c}, or total cholesterol concentrations and blood pressure (data not shown) were observed in both groups, and most characteristics between two groups were similar except for the use of rosiglitazone. Therefore, the effect of inhibiting a restenosis in rosiglitazone group might result from the additional effects associated with rosiglitazone.

We also showed that hsCRP concentrations, markers of systemic inflammation, were markedly improved in the rosiglitazone group compared with the control group. Recent studies show that the inflammatory response plays an important role not only in atherosclerosis but also in restenosis after stent implantation (32) and that TZDs reduce the levels of the multipotent immunomodulator CD40 ligand (33) and various cytokines, such as serum matrix metalloproteinase-9 or tumor necrosis factor-α (34), and inhibit the expression of the monocyte chemoattractant protein-1 receptor in lesional and circulating monocytes (35). These findings suggest that TZDs have anti-inflammatory and potentially antiatherogenic effects. Additionally, TZDs reduce the cardiovascular risks on the aspects related to insulin resistance, including lipid metabolism, vascular reactivity, endothelial function, coagulation, vessel wall, or body fat distribution. Although the precise mechanism of TZDs for preventing in-stent restenosis has not been verified in this study, except for the anti-inflammatory effect, many in vitro, animal, and human studies have illustrated the potential of using TZDs for treating or preventing in-stent restenosis and atherosclerosis. Furthermore, because most diabetic patients with CAD also are at high risk for diffuse atherosclerotic changes on a large part of the vascular system, the TZDs class will be a relatively safe and important modality not only for preventing an in-stent restenosis but also for inhibiting any undiscovered and diffuse atherosclerotic processes.

This study has additional limitations. First, this study was performed with the diabetic population having different treatment modalities and did not completely exclude the effects of the other treatments except for the TZDs. Therefore, further investigations to determine whether rosiglitazone reduces the restenosis rate and neointimal proliferation after a coronary stent implant in nondiabetic patients are warranted. Because TZDs have various nonhypoglycemic effects that can reduce cardiovascular risks, it is possible that the TZDs will benefit the nondiabetic population in reducing the restenosis rate or in preventing atherosclerotic processes. Second, it was a single-center study with a small number of patients. A large-scale, multicenter study is warranted. Finally, this study demonstrated the effect of rosiglitazone for preventing in-stent restenosis. However, that alone could not fully explain the possible effects of TZDs on atherosclerosis and/or macrovascular complications in high-risk patients with type 2 diabetes. Accordingly, further studies, such as PROactive (the Prospective Pioglitazone Clinical Trial in Macrovascular Events) (36), are needed.

In conclusion, rosiglitazone treatment in type 2 diabetic patients significantly reduced restenosis and improved the angiographic outcome 6 months after coronary stent implantation. This effect of rosiglitazone for preventing in-stent re-

stenosis is partly attributed to its anti-inflammatory properties and may present an important modality for inhibiting any undiscovered and diffuse atherosclerotic processes observed in diabetic patients.

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