Randomized Comparison of a Titanium-Nitride-Oxide–Coated Stent With a Stainless Steel Stent for Coronary Revascularization

The TiNOX Trial

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Background—Stent coating with titanium-nitride-oxide has been shown to reduce neointimal hyperplasia in the porcine restenosis model. We designed a prospective, randomized, clinical study to investigate the safety and efficacy of titanium-nitride-oxide–coated stents compared with stainless steel stents.

Methods and Results—Ninety-two patients with de novo lesions were randomly assigned to treatment with titanium-nitride-oxide–coated stents (n=45) or stainless steel stents of otherwise identical design (n=47; control). Baseline characteristics were similar in both groups. At 30 days, no stent thromboses or other adverse events had occurred in either group. Quantitative coronary angiography at 6 months revealed lower late loss (0.55±0.63 versus 0.90±0.76 mm, $P=0.03$) and percent diameter stenosis (26±17% versus 36±24%, $P=0.04$) in lesions treated with titanium-nitride oxide–coated than in control stents. Binary restenosis was reduced from 33% in the control group to 15% in the titanium-nitride oxide–coated stent group ($P=0.07$). Intravascular ultrasound studies at 6 months showed smaller neointimal volume in titanium-nitride-oxide–coated stents than in control stents (18±21 versus 48±28 mm^3, $P<0.0001$). Major adverse cardiac events at 6 months were less frequent in titanium-nitride-oxide–coated stents than in control stent–treated patients (7% versus 27%, $P=0.02$), largely driven by a reduced need for target-lesion revascularization (7% versus 23%, $P=0.07$).

Conclusions—Revascularization with titanium-nitride-oxide–coated stents is safe and effective in patients with de novo native coronary artery lesions. Titanium-nitride-oxide–coated stents reduce restenosis and major adverse cardiac events compared with stainless steel stents of otherwise identical design. **(*Circulation*. 2005;111:-.)**

Key Words: stents ■ restenosis ■ revascularization

Restenosis has been the principal limitation of percutaneous coronary interventions, associated with an increased need for repeat revascularization and thus considerable healthcare cost.[1–3] Although bare-metal stents eliminate constrictive arterial remodeling and elastic recoil, neointimal hyperplasia typically exceeds that seen after balloon angioplasty alone, resulting in in-stent restenosis in approximately 20% to 30% of patients.[4,5]

Modifications in stent geometry,[6] strut thickness,[7] and surface material[8] have been shown to influence the restenosis rate after bare-metal stent implantation. Stent coating has been used to reduce restenosis, but the use of some materials, ie, gold,[9–11] has unexpectedly been shown to be associated with an increase in both late loss and need for repeat revascularization compared with stainless steel. A potential mechanism for this observation was found in experimental data, which revealed increased inflammatory reactions in gold-coated as opposed to stainless steel stents. More recently, patients with nickel allergy have been reported to be at increased risk for restenosis after stent implantation.[12] Nickel constitutes an important component of stainless steel, which again suggests that stent material plays an important role in the vascular repair mechanisms after stent-mediated arterial injury.

Titanium, a material frequently used for biomedical implants, features superior biocompatibility compared with stainless steel, gold, or other surface coatings.[13,14] As a nitride-oxide alloy, titanium can be easily deployed by

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physical vapor deposition on the surface of stainless steel stents. In vitro examinations of titanium-nitride-oxide showed diminished platelet adhesion and fibrinogen binding compared with stainless steel. In addition, neointimal hyperplasia was reduced by ≈50% for titanium-nitride-oxide–coated compared with stainless steel stents in the porcine restenosis model at 6 week follow-up.[15] To further explore the potential of titanium-nitride-oxide for stent coating, we performed a prospective randomized trial comparing safety and efficacy of titanium-nitride-oxide–coated stents with stainless steel stents of otherwise identical design for revascularization of patients with de novo native coronary artery lesions.

Methods

Patient Population

Patients who were at least 18 years of age with stable or unstable angina pectoris or signs of myocardial ischemia were eligible for the study. De novo lesions in native coronary arteries with a lesion length <15 mm, a reference vessel diameter of 2.5 to 3.5 mm, and a diameter stenosis of at least 50% by visual estimate suitable for percutaneous coronary intervention were treated. No more than 2 target lesions were treated in a single patient, and the second lesion had to be located in another major epicardial coronary artery. Exclusion criteria included acute myocardial infarction; severe heart failure; cardiogenic shock; restenotic lesions; a target lesion of the left main or in a vessel with thrombus, or severe calcification; severe comorbidities with a life expectancy of <1 year; lack of informed consent; or unwillingness to undergo coronary angiography during follow-up. The study was conducted according to the declaration of Helsinki and was approved by the institutional review boards of all participating institutions. Written informed consent was obtained from all patients.

The study was a prospective, single-blind, randomized, multicenter trial performed in 5 centers in Switzerland (n=3) and Germany (n=2). Patients were randomly assigned to receive either a titanium-nitride-oxide–coated stent or an uncoated, stainless steel stent of otherwise identical design. Randomization was performed by means of sealed envelopes supplied to each participating center from the study coordinating center. The stents were visually distinguishable through the dark-surface appearance of the titanium-nitride-oxide–coated stents, which left the patient but not the implanting physician unaware of which stent would be implanted.

Stent Coating With Titanium-Nitride-Oxide

A commercially available stainless steel stent with a tubular slotted design (OMEGA, Qualimed Inc) was used in this study. Unmodified stainless steel stents served as controls. Coating of stainless steel stents was performed by physical vapor deposition of titanium in a prespecified gas mixture of nitrogen and oxygen in a vacuum chamber. Titanium-nitride-oxide–coated stents were then immersed in an albumin solution to prevent oxidation of the surface coating and sterilized. Titanium-nitride-oxide–coated stents and uncoated control stents were shipped to the participating sites and stored at room temperature.

Stent Implantation Procedure

All patients were pretreated with aspirin (100 mg daily) and received intravenous heparin (100 IU/kg) during the procedure. Oral clopidogrel was administered as a loading dose of 300 mg before or immediately after the procedure and was continued at a daily dose of 75 mg for 1 month. The use of glycoprotein IIb/IIIa antagonists was left to the discretion of the operator.

The stent implantation procedure was standardized according to the following guidelines: (1) predilation of the lesion with a standard balloon dilation catheter was mandatory in all patients, with a target balloon-to-artery ratio of 1:1. (2) Stent length (10, 14, or 17 mm) was chosen to cover the entire lesion with a single stent. (3) Stents were manually crimped on a balloon dilation catheter. (4) Stents were then advanced into the predilated lesion and expanded by adjusting the balloon inflation pressure to achieve an angiographic appearance of the expanded stents that was slightly larger than the reference vessel segment. (5) More than 1 stent could be implanted into the lesion in case of incomplete lesion coverage, edge dissection, or otherwise suboptimal result.

Quantitative Coronary Angiography

Coronary angiograms were analyzed by the angiographic core laboratory at the German Heart Center, Technical University, Munich, Germany. Angiograms were viewed offline with the automated edge-detection system CMS (Medis Medical Imaging System). The operators performing the quantitative coronary analysis were unaware of the treatment allocation. The contrast-filled, nontapered tip of the guiding catheter was used as a scaling device to obtain absolute dimensions. The same views and calibration techniques were used during follow-up examinations. Measurements of the target lesion at baseline, immediately after stent implantation, and at 6-month angiographic follow-up were obtained in at least 2 orthogonal views after intracoronary administration of 0.1 to 0.2 mg of nitroglycerin. The analyzed segment comprised the stent segment and the proximal and distal stent edges, defined as 5 mm proximal or distal to the stent. End-diastolic frames showing maximal severity of stenosis were chosen for measurements of minimal luminal diameter and percent diameter stenosis. Late loss in luminal diameter was defined as the difference in minimal luminal diameter immediately after stent implantation and that measured at follow-up. Binary restenosis was defined as stenosis of ≥50% at follow-up examination.

Quantitative Intravascular Ultrasound

At follow-up, stented vessel segments were examined in a subgroup of 56 patients at 2 study sites with intravascular ultrasonography (In Vision Plus, Imaging System, Volcano Therapeutics Inc) with an automated pullback device at 0.5 mm/s. Data were stored on CD-ROM. Quantitative analysis was performed offline by an experienced investigator who was unaware of the study group and who used a dedicated software package (TapeMeasure, INDEC Systems Inc). The cross-sectional area of lumen and stent was manually traced in steps of 2 mm in the stented segment. Total stent and lumen volume were calculated as $V=\Sigma^{n}_{i=1} A_i \times H$, where V is volume, A is total stent or lumen area in a given cross-sectional image, H is thickness of the coronary artery slice, and n is the number of slices. Neointimal hyperplasia was calculated as stent volume minus lumen volume.

Study End Points and Analysis

An independent clinical research organization (IMECO AG, Zurich, Switzerland) verified all data on case record forms. Patients were evaluated by telephone interview at 30 days and clinical evaluation with an ECG and repeat coronary angiography at 6 months. The primary end point of the study was in-stent luminal late loss as assessed by quantitative coronary angiography. Secondary end points were device success, binary restenosis and minimal luminal diameter of the stented segment at 6 months, neointimal volume as assessed by intravascular ultrasound at 6 months, and a composite of major adverse cardiac events at 30 days and 6 months after the index procedure. Device success was defined as successful implantation of the assigned study stent into the target lesion with a residual stenosis <20% and TIMI 3 flow at the termination of the procedure. Major adverse cardiac events were a composite of death, Q-wave or non–Q-wave myocardial infarction, clinically driven revascularization of the target lesion by either CABG surgery or repeat percutaneous coronary intervention, and stent thrombosis. A non–Q-wave myocardial infarction was defined by ischemic chest pain with an increase in the creatine kinase (CK) level to more than twice the upper limit of normal, accompanied by an increased level of CK-MB or troponin, and the absence of new Q waves on the ECG. Q-wave myocardial infarction was defined as the development of new Q

TABLE 1. Clinical Characteristics

	TiNOX (n=45)	Control (n=47)	*P*
Age, y	65±10	64±13	0.97
Male gender, n (%)	34 (76)	32 (68)	0.49
Previous myocardial infarction, n (%)	19 (42)	18 (38)	0.80
Cardiovascular risk factors, n (%)			
Smoking	16 (36)	21 (45)	0.40
Diabetes mellitus	15 (34)	16 (34)	0.99
Family history of CAD	17 (39)	15 (32)	0.66
Systemic hypertension	33 (73)	34 (72)	0.99
Hypercholesterolemia	38 (84)	32 (68)	0.05
Medical treatment, n (%)			
Acetylsalicylic acid	42 (93)	44 (94)	0.99
β-Blockers	27 (60)	26 (59)	0.68
ACE inhibitor	9 (20)	16 (34)	0.16
Lipid-lowering agents	29 (64)	27 (57)	0.53
Clopidogrel	15 (34)	18 (38)	0.67

TiNOX indicates titanium-nitride-oxide; CAD, coronary artery disease.

waves in at least 2 contiguous leads, accompanied by a significant increase in CK and CK-MB levels. Target-lesion revascularization was considered to be clinically driven if the stenosis of the target lesion was at least 50%, with ischemic symptoms or a functional study that indicated ischemia, or in the absence of symptoms, if the stenosis was at least 70%. Stent thrombosis was diagnosed in the presence of an acute coronary syndrome with angiographic evidence of either vessel occlusion or thrombus within the study stent.

Results are shown as mean±SD or as proportions (%). Differences between groups were compared with an unpaired *t* test for continuous variables and Fisher exact test for categorical variables. Statistical significance was assumed with a probability value <0.05. All data were analyzed with the use of SPSS version 11.[16] The sample size of the study was based on the hypothesis that late loss by quantitative coronary angiography would be decreased by 0.4 mm with a common SD of 0.5 mm for the titanium-nitride-oxide–coated stent compared with the control stent. Detection of this difference with 80% power and a 2-sided α-error of 5% would require a sample size of 41 patients per study group. We assumed 90% adherence to the 6-month angiographic follow-up, and thus the sample size was increased to 90 patients.

A total of 92 patients were included in the study, and no patient was excluded from the analysis. All patients were solicited to undergo a control angiogram at 6 months, and 82 (89%) ultimately underwent angiographic follow-up. There were no significant differences with respect to age, number of treated lesions, and type of implanted stents between patients undergoing and those refusing angiography at 6 months. Clinical follow-up was complete in 91 patients (100%) at 1 month, and 6 patients (6.6%) were lost to follow-up at 6 months.

Results

Clinical characteristics were well balanced between the 2 groups and were notable for a high prevalence of diabetes (33%; Table 1). A total of 96 native coronary artery lesions were treated, with angiographic characteristics summarized in Table 2. There was no difference with regard to the treated target vessel between the 2 groups; however, there was a lower prevalence of type A lesions (9% versus 31%, $P=0.03$) in the titanium-nitride-oxide group compared with the control group (Table 2). Device success after predilation of the lesion

TABLE 2. Lesion Characteristics

	TiNOX	Control	*P*
No. of lesions	47	49	
Target vessel, n (%)			0.10
LAD	25 (53)	15 (30)	
RCA	12 (26)	20 (41)	
LCx	10 (22)	14 (29)	
ACC/AHA class, n (%)			0.03
Type A	4 (9)	15 (31)	
Type B1	18 (39)	10 (20)	
Type B2	22 (48)	21 (43)	
Type C	3 (7)	3 (6)	

TiNOX indicates titanium-nitride-oxide; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery; and ACC/AHA, American College of Cardiology/American Heart Association.

was 46 (100%) and 49 (100%) in lesions treated with a titanium-nitride-oxide–coated and control stent, respectively. There were no differences between groups with respect to lesion length (9.9±3.5 versus 10.0±4.5 mm, $P=0.90$), reference vessel diameter (2.85±0.39 versus 2.91±0.40 mm, $P=0.45$), stent-to-lesion length (1.64±0.55 versus 1.66±0.54, $P=0.90$), maximal inflation pressure (12.4±2.5 versus 12.7±2.2 bar, $P=58$), and number of implanted stents per lesion (1.2±0.4 versus 1.1±0.3, $P=0.33$).

Quantitative Coronary Angiography

Reference vessel diameter, minimal luminal diameter, and percent diameter stenosis were similar for both groups at baseline (Table 3). At 6-month follow-up, the primary end point of late loss was significantly lower in lesions treated with a titanium-nitride-oxide–coated stent than in those treated with a control stent (0.55±0.63 versus 0.90±0.76 mm, $P=0.03$). Percent diameter stenosis (26±17% versus 36±24%, $P=0.04$) and binary angiographic restenosis (15% versus 33%, $P=0.07$) were lower in titanium-nitride-oxide–coated stents than in control stents. No edge effect proximal or distal of the stent was observed in either group, and there were no differences in the pattern of restenosis between stent groups (Table 3). The cumulative distribution of percent diameter stenosis for both stent groups is depicted in the Figure.

Intravascular Ultrasound

There were no differences in stent volume between groups. Lumen volume (116±32 versus 90±42 mm^3, $P=0.01$) was significantly larger and neointimal volume (18±21 versus 48±28 mm^3, $P<0.0001$) significantly smaller in titanium-nitride-oxide–coated stents than in control stents (Table 4).

Clinical Follow-Up

Clinical events during 6-month follow-up are shown in Table 5. At 30 days, no adverse events and no stent thrombosis had occurred. At 6 month follow-up, a significantly higher incidence of major adverse cardiac events was found in patients assigned to control compared with titanium-nitride-oxide–coated stents (27% versus 7%, $P=0.02$). This difference was largely driven by the more frequent need for target lesion

TABLE 3. Quantitative Coronary Angiography Data

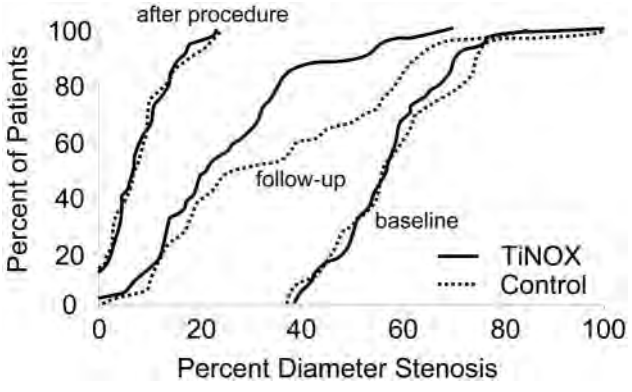
	TiNOX	Control	*P*
No. of lesions	47	49	
Lesion length, mm	9.9±3.5	10.0±4.5	0.90
Reference vessel diameter, mm	2.85±0.39	2.91±0.40	0.45
Before procedure			
Minimal lumen diameter, mm	1.18±0.40	1.21±0.46	0.77
Diameter stenosis, %	72±11	70±11	0.75
After procedure			
Minimal lumen diameter, mm	2.65±0.40	2.73±0.39	0.34
Diameter stenosis, %	10±5	9±5	0.81
Follow-up			
No. of patients	40	42	
No. of lesions	42	43	
Minimal lumen diameter, mm			
Proximal edge	2.53±0.62	2.59±0.63	0.68
In-stent	2.10±0.63	1.82±0.80	0.09
Distal edge	2.47±0.47	2.46±0.64	0.93
Diameter stenosis, %	26±17	36±24	0.04
Late loss, mm	0.55±0.63	0.90±0.76	0.03
Binary (>50%) restenosis, n (%)	6 (15)	14 (33)	0.07
Pattern of restenosis, n			0.73
Focal	2	5	
Diffuse	4	9	
Proliferative or total occlusion	0	0	

TiNOX indicates titanium-nitride-oxide.

revascularization in control compared with titanium-nitride-oxide–coated stents (23% versus 7%, $P=0.07$).

Discussion

Stent coating with titanium-nitride-oxide reduced angiographic and ultrasonic measures of restenosis compared with stainless steel control stents of otherwise identical design in this prospective, randomized, multicenter trial. The favorable effect on restenosis was associated with fewer major adverse cardiac events at 6 months, mainly driven by a reduced need for target-lesion revascularization. At the same time, titanium-nitride-oxide–coated stents demonstrated an excellent safety profile comparable to that of uncoated control stents.



Cumulative distribution curve for percent diameter stenosis stratified according to stent type. TiNOX indicates titanium-nitride-oxide.

TABLE 4. Follow-Up Intravascular Ultrasonography Data

	TiNOX	Control	*P*
No. of patients	28	27	
No. of lesions	28	27	
Stent volume, mm^3	134±30	138±47	0.69
Lumen volume, mm^3	116±32	90±42	0.01
Neointimal volume, mm^3	18±21	48±28	<0.0001

TiNOX indicates titanium-nitride-oxide.

Of note, these beneficial results were achieved in a population with a relatively high cardiovascular risk profile. The prevalence of diabetes (34%), the most important clinical risk factor for restenosis, was similar to that reported in the SIRIUS (Sirolimus-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions) and TAXUS-IV (Treatment of de novo coronary disease using a single paclitAXel elUting Stent) trials.[17,18] The binary restenosis rate of 33% for the control group was similar to the 35% reported for the bare-metal BX Velocity stent in the SIRIUS trial. These stents have a relatively unfavorable stent design, with a strut thickness of 140 μm.[19] In contrast, the 15% binary restenosis rate for titanium-nitride-oxide–coated stents represents a 55% reduction compared with the control group. Late loss, a more appropriate measure of neointimal hyperplasia, was reduced by 39% from 0.90±0.76 mm in the control group to 0.55±0.63 mm in the titanium-nitride-oxide group, and neointimal volume was reduced from 48±28 to 18±21 mm^3 (63% reduction). To the best of our knowledge, this constitutes the first study reporting reduced restenosis attributable to a novel stent-surface material in humans.[8]

TABLE 5. Major Adverse Cardiac Events During 6 Months of Follow-Up

	TiNOX	Control	*P*
1-Month MACE			
No. of patients	45	47	
Overall, n (%)	0 (0)	0 (0)	0.99
Stent thrombosis, n (%)	0 (0)	0 (0)	0.99
6-Month MACE			
No. of patients	42	44	
Overall, n (%)	3 (7)	12 (27)	0.02
Death	0 (0)	1 (2)	0.99
Myocardial infarction	0 (0)	1 (2)	0.99
Q-wave	0 (0)	1 (2)	0.99
Non–Q-wave	0 (0)	0 (0)	0.99
TLR	3 (7)	10 (23)	0.07
PCI	2 (5)	10 (23)	0.03
CABG	1 (2)	0 (0)	0.99
Stent thrombosis	0 (0)	1 (2)	0.99

TiNOX indicates titanium-nitride-oxide; MACE, major adverse cardiac events; TLR, target-lesion revascularization; and PCI, percutaneous coronary intervention.

Impact of Stent Material on Restenosis

Modifications of stent surface and material properties have important implications for neointimal hyperplasia after stent implantation. Stainless steel constitutes the principal material in >85% of commercially available stents. The advantages of stainless steel are its excellent hoop strength, ease of processing, and low cost; however, limited visibility at the time of stent implantation and the relatively high restenosis rate fostered an interest in alternative stent materials. Furthermore, patients with nickel allergy have been found to be at increased risk for restenosis after stent implantation. Koster and colleagues[12] reported a greater need for target-lesion revascularization (100%) in patients with positive patch-test reactions to nickel than in those without nickel allergy (69%). Because inflammatory reactions at the vascular injury site have been associated with the severity of neointimal hyperplasia in experimental restenosis models, it has been hypothesized that patients with nickel allergy may have more pronounced local inflammation and thus neointimal hyperplasia.

Gold has been investigated intensively as a potential stent-surface material because of its noble material properties, its high metal density (which translates into improved radiopacity during stent implantation), and its excellent malleability; however, Kastrati and colleagues[9] reported increased binary restenosis and target-lesion revascularization in a randomized, clinical trial comparing gold-coated with stainless steel stents of identical design. These findings have been corroborated in 2 other randomized trials with gold-coated stents, which revealed increased restenosis and greater need for target-lesion revascularization.[10,11] More recently, an experimental study confirmed exaggerated neointimal hyperplasia with gold-coated stents than with stainless steel stents in the porcine restenosis model.[20] The likely mechanism was increased inflammatory cell recruitment and incomplete healing induced by gold-coated stents. These data demonstrate the importance of surface modifications for restenosis after stent implantation.

Titanium has been widely accepted as the material of choice for biomedical implants, namely, orthopedic and dental prostheses, because of its superior biocompatibility and high corrosion resistance.[13,14,21] Although solid titanium might be used for manufacturing, the metal processing proves difficult, and manufacturing costs are prohibitive. In contrast, titanium alloys such as titanium-nitride-oxide can be used more easily and applied to stainless steel surfaces by physical vapor deposition. The thin layer of titanium-nitride-oxide proves durable even after stent expansion and can be realized at reasonable cost. Initial in vitro examinations of titanium-nitride-oxide–coated surfaces revealed reduced platelet and fibrinogen binding compared with stainless steel. More importantly, neointimal hyperplasia was reduced by 50% in the porcine restenosis model at 6 weeks compared with stainless steel stents of otherwise identical design.[15] The magnitude of reduction in neointimal hyperplasia observed with titanium-nitride-oxide–coated stents in the experimental setting was comparable to those reported by Suzuki et al[22] for sirolimus-eluting stents in pigs. The present clinical study confirms the beneficial effect of titanium-nitride-oxide–coated stents in patients with de novo native coronary artery lesions.

Titanium-Nitride-Oxide–Coated Stents in the Era of Drug-Eluting Stents

A pressing question concerns the potential role of titanium-nitride-oxide–coated stents in the new era of drug-eluting stents. Both sirolimus-eluting stents[17] and paclitaxel-eluting stents[18] have recently demonstrated dramatic reductions in binary restenosis (sirolimus 8.9%, paclitaxel 7.9%) and late loss (sirolimus 0.24 mm versus paclitaxel 0.39 mm) compared with stainless steel stents over a wide range of lesions and patients. The binary restenosis rate of 15% and the mean late loss of 0.55 mm for titanium-nitride-oxide–coated stents are favorable but clearly not sufficient to supplant drug-eluting stents.

Notwithstanding, the following strategies will help to define the utility of titanium-nitride-oxide–coated stents in future investigations. First, the combination of titanium-nitride-oxide stent coating with a modified stent design, notably a thin strut construction, may allow for further reduction in restenosis. Clinical studies comparing thick versus thin strut stent designs revealed reduced restenosis and target-lesion revascularization.[7,19] Therefore, it is of interest whether thin struts in conjunction with titanium-nitride-oxide stent coating are able to reduce late loss in an additive fashion. Optimization of stent design for restenosis reduction could become an economically attractive alternative to drug-eluting stents.

Second, coronary artery stenoses at low risk for restenosis, ie, short lesions with a reference vessel diameter >3.0 mm,[23] may be more cost-effectively treated with a titanium-nitride-oxide–coated stent. The rate of target-lesion revascularization in short lesions with large diameter was 5% for titanium-nitride-oxide–coated stents in the present study compared with 4% for sirolimus-eluting stents in the SIRIUS trial.

Third, stent thrombosis may be a particular problem for drug-eluting stents because of their thrombogenic surface.[24] Polymer coatings[25] and drugs in high doses[26] have been reported as potentially prothrombogenic, resulting in local inflammation and enhanced thrombus formation.

Study Limitations

The findings of the present study have to be interpreted in the context of the following limitations. (1) The present study was designed as a safety and efficacy trial and is therefore too small to qualify as a clinical end-point study. (2) The study included lesions <15 mm in length because of a limitation in the available stent lengths. Investigation in more complex lesions and patients will require further study. (3) The intravascular ultrasound study was performed in only 56 patients at 2 centers because of limited funding; however, given the higher sensitivity of intravascular ultrasound for neointimal volume measurements, fewer patients were required to undergo the procedure. (4) The proportion of patients lost to follow-up is relatively high given the small size of the study population. We attempted to contact all patients by phone, but some patients were inaccessible because of their move to an unknown location. (5) The study

design was single blind because of the different surface appearance of the titanium-nitride oxide–coated stent, which left the patient but not the implanting physician unaware of the allocated treatment. A comparison of titanium-nitride-oxide with drug-eluting stents may help to identify the role of this novel surface coating in the current era of drug-eluting stents.

Conclusions

Revascularization with titanium-nitride-oxide–coated stents is safe and effective in patients with de novo coronary artery lesions. Titanium-nitride-oxide–coated stents reduce restenosis and major adverse cardiac events compared with stainless steel stents of otherwise identical design.

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