Prospective randomized comparison of early and late results of 4 different stent designs

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Background Late results of interventional procedures using coronary stents are largely determined by the rate of restenosis. So far, few data are available addressing the effect of stent design on this crucial variable and on early and late adverse events after stent implantation.

Methods From 1996 through1998, a total of 965 lesions in 925 patients with coronary artery disease were randomized to treatment with 1 of 4 different stent designs (Micro stent II [M] AVE, Düsseldorf, Germany; Sito [S] Sitomed, Rangendingen, Germany; Pura Vario [PV], Devon, Hamburg, Germany; Inflow [ID] Inflow Dynamics, München, Germany). The primary end point of the study was the degree of diameter stenosis measured by quantitative coronary angiography 6 months after stent implantation.

Results Diameter stenosis at 6 months follow-up was not different in the 4 study arms (M 40.3 ± 24.1, S 42.8 ± 27.0, PV 42.6 ± 26.9 and ID 42.3 ± 26.8, $P = .7$). No significant differences could be detected in net lumen gain and late lumen loss, resulting in comparable restenosis rates (≥50% diameter stenosis) at follow-up (M 26.0%, S 30.5%, PV 31.3%, and ID 28.7%, $P = .7$). Early adverse events like stent loss, stent thrombosis, periinterventional acute myocardial infarctions and emergency coronary artery bypass graft also showed no significant differences. Multivariate regression analyses revealed reference vessel diameter <3.0 mm, overall stented length, a history of bypass grafting, localization of the target lesion in the left anterior descending coronary artery, type C lesions, dissection before stent implantation, and diabetes mellitus to be independent predictors for restenosis.

Conclusion Stent design does not have significant influence on development of restenosis. Adverse event rates were similar with all stent types used in this trial. (Am Heart J 2003;146:134-41.)

Prevention of restenosis after successful percutaneous transluminal coronary angioplasty (PTCA) still remains a major problem, although implantation of stents has led to a reduction of restenosis in different studies.[1,2] So far, however, few data analyzing the effect of stent design on this crucial variable are available. In a retrospective, nonrandomized study we found a significant difference in restenosis rate between the Palmaz-Schatz-stent and the AVE-Micro-Stent.[3] This was the reason to perform a prospective, randomized trial to evaluate whether noncoated modern stent designs of the slotted tube type or a corrugated ring system in principle may influence angiographic follow-up results and adverse events after stent implantation.

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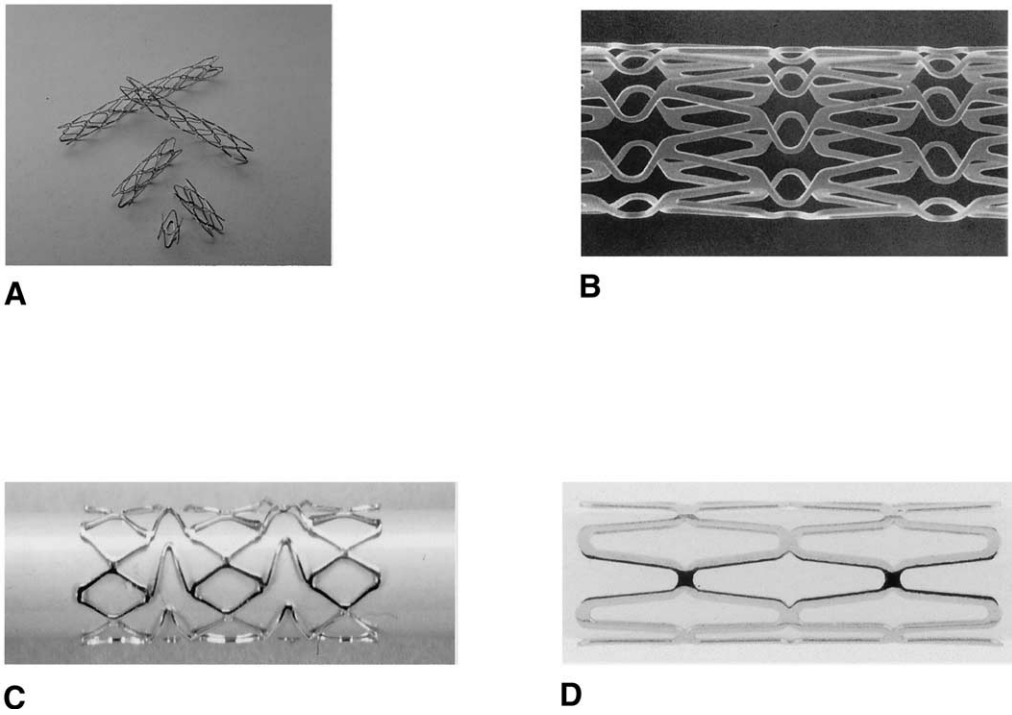
Methods

Study design and inclusion/exclusion criteria

The study was performed between October, 1996 and October, 1998 in 925 consecutive patients who were referred to the heart center of Leipzig (tertiary refer center) for evaluation of coronary artery disease. Study protocol was approved by the ethics committee of the University of Leipzig. Patients between 18 and 80 years of age were eligible if they had ≥1 de novo coronary lesion in different vessels and after they gave written informed consent. Lesions in different vessels were randomized independently; with 2 lesions in 1 vessel, only the proximal lesion was randomized, and it was decided that the distal lesion should be treated with the same stent type. Indications for stenting were classified a 1) major dissections, 2) recoil or 3) elective stenting. The lesion was randomized to 1 of the 4 arms by sealed envelopes. The aim was to cover the lesion with 1 stent; only in exceptional cases were more stents implanted, and whenever possible they were of the same randomized type.

Figure 1



A, Micro II stent. **B**, Sito stent. **C**, Pura Vario stent. **D**, Inflow stent.

Quantitative analysis of coronary angiograms was performed before PTCA, immediately after stenting, and at 6 months (mean follow-up of 6 ± 1.2 months). Procedural success was defined as stent implantation with <30% stenosis as final result of intervention.

If the patient refused angiographic control, the referring physician or the patient himself was interviewed for adverse events and clinical status by phone.

Characteristics of stents

Four different stents, all 316 L stainless steel, were used in this trial: MICRO-Stent II (Advanced Vascular Engineering [AVE]), SITO-Stent (SITOmed GmbH), PURA-VARIO-Stent (Devon-Medical GmbH), and INFLOW-Stent (Inflow Dynamics). The Micro Stent, premounted on a semicompliant rapid-exchange PTCA-balloon catheter system, is a construction of multiple basic elements, that are formed from laser fused, 3-mm length, sinusoidal elements. The number of elements leads to the total length of the stent, which was available in lengths of 6, 9, 12, 18 and 24 mm (Figure 1, *A*). The round stent struts have a diameter of 200 μm.

All other stents were hand crimped, slotted tube stents. The Inflow-Dynamics stent consists of sinusoidal struts that are arranged in a 90 degree angle (Figure 1, *D*). All struts have an oval-formed cross-section with a strut diameter of 85 μm in the central part and 75 μm at the end of the stent. To make the 15 and 23 mm stents more flexible, they are divided in subsegments with 2 connections in between.

The Sito-Stent has a multicellular design (Figure 1, *B*) with high flexibility despite a closed profile. The struts with rounded edges have a diameter of 100 μm.

The Pura-Vario-Stent is also a laser-cut, mesh stent (Figure 1, *C*) with rounded struts in a diameter of 120 μm.

The difference between all the stents used in this study is the principal design, the thickness and form of the struts, and the fact that the Micro stent (a corrugated ring design) was the only premounted stent system, whereas all other stents in this trial were hand crimped stents. More details are described in Table I.

Medical treatment

All patients received 15,000 IU heparin and 500 mg ASA (acetylsalicylic acid) immediately before PTCA, followed by ASA 100 mg/day. In patients with planned PTCA, ticlopidine was started 1 day before the intervention; in all other patients with prima vista PTCA, ticlopidine was started immediately after the procedure for 4 weeks. Between October 1996 and April 1997, ticlopidine was given 250 mg once daily, and thereafter it was given with a loading dose of 500 mg 3 times.[4] A total blood count was obtained after 2 weeks.

Quantitative coronary angiography

Coronary angiograms were obtained in 2 orthogonal views after intracoronary injection of 0.2 mg nitroglycerin. Quantitative analysis was performed in the projection showing the

Table I. Stent characteristics

	Micro II	Sito	Pura-Vario	Inflow
Principal design	Modular design with crown-like segments, punctually linked, rounded wire	Slotted tube with multicellular rectangular design	Slotted tube with multiple segments	Slotted tube modified articulation
Strut diameter	200 μm	100 μm	120 μm	75/85 μm
Metallic surface area	8.4%	11%-18%	9.9%	14%-28%
Shortening	2%	<5%	2.9%	17%
Length (mm)	9/12/18/24	9/16/26/32	7/11/15/19	7/9/11/15/23
Diameters (mm)	2.5-4.0	2.5-4.0	2.5-4.0	2.5-4.0
Recoil	<5%	<5%	<3%	<5%
Flexibility	+++	+++	++	+
Recrossability	++++	+++	+++	+++
X-ray contrast	+++	(+)	+	−/++
Premounted	Yes	No/yes	No/yes	No

From: Personal communication, G. Strupp, Fulda, Germany: Bauarten and Eigenschaften koronarer Stents, 2000.

highest degree of stenosis with a computer assisted quantitative angiographic system (MEDIS: Medical Imaging Systems, Version 3.0, Nuenen, The Netherlands) as described elsewhere.[5] Minimal lumen and reference diameter were measured, and acute gain, late lumen loss, and net gain, as well as the corresponding percent values, were calculated.

End points

The primary end point of the study was diameter stenosis at 6 months. This end point was chosen because 1) minimal luminal diameter (MLD) alone, though it reflects quite well the neointimal proliferation process inside the stent, is less valid to compare angiographic results as it has to be related to the vessel size for clinical decisions like target vessel revascularization, and 2) reference diameters tend to increase after stent implantation as a result of flow dependent vasodilatation.[6]

Secondary end points were restenosis (lumen reduction of ≥50%), rate of reintervention at the target lesion (repeat intervention or CABG), myocardial infarction (Q-wave infarction with creatine kinase twice normal or non–Q-wave infarction) and stent thrombosis (acute within 48 hours, subacute <28 days), as well as mortality in the first 48 hours and during follow-up.

Statistical analysis

The study was designed to detect a 10% difference in diameter stenosis at follow-up between the best and worst study arm with a power of 90% on a 5% level of significance. The target number of lesions to be randomized was calculated to be 1000 lesions, including a drop out rate of 15%. The calculation was based on an expected diameter stenosis of 30% ± 26%.[3]

Patients were valuable for final angiographic analysis with respect to the primary end point if a control angiography after >4 months had been performed or restenosis was proven before. However, for analysis of clinical events, all patients with angiographic or telephone follow-up were considered.

Results are expressed as mean ± SD or as proportions. For categorical data, global tests were performed using the χ^2 test. For continuous data, analysis of variance was used, accounting for the number of groups. A multivariate analysis of restenosis at follow-up using logistic regression was performed. All statistics were performed with the SPSS version 8.0 (SPSS Inc, Chicago, Ill).

Results

Baseline characteristics

The study population consisted of 925 patients (686 men [83.2%] and 239 women [16.8%]). Mean age was 61.7 ± 10.3 years. Baseline characteristics were well balanced between the 4 study arms and are shown in Table II.

Stent implantation

A total of 965 lesions were randomized. Because the production of the Micro stent II was stopped in October 1997, this arm had to be stopped after 176 lesions. In 240 of the lesions, implantation of >1 stent was performed, resulting in a total of 1301 stents implanted. A total of 1140 stents were randomized devices, 161 stents were used additionally, due to insufficient results with the randomized stents, including only 30 stents (28 GFX and 2 Jostent) with a different design, which had no statistical influence on general analysis. There were 886 patients with 1, 38 with 2, and 1 patient with 3 lesions randomized. Multiple interventions as well as multiple stenting were well distributed among the 4 study arms.

Angiographic results

Figure 2 shows the eligibility of lesions for statistical analysis. A total of 959 lesions were available for implantation results. Three lesions, all in the PU-VA stent

Table II. Baseline characteristics of the randomized lesions

	Micro II (n = 176)	Sito (n = 259)	Pura-Vario (n = 263)	Inflow (n = 267)	*P*
Age (mean ± SD)	62.3 ± 9.2	61.9 ± 10.5	61.8 ± 10.9	61.6 ± 10.4	.92
Height cm (mean ± SD)	170.3 ± 7.8	169.7 ± 8.9	170.7 ± 8.9	170.2 ± 8.6	.64
Mass kg (mean ± SD)	79.6 ± 13.0	80.3 ± 13.9	80.2 ± 13.3	80.6 ± 13.6	.91
CHD (%)					
1-Vessel	82 (46.6)	123 (47.5)	111 (42.2)	119 (44.6)	
2-Vessel	68 (38.6)	92 (35.5)	98 (37.3)	98 (36.7)	.76
3-Vessel	26 (14.8)	44 (17.0)	54 (20.5)	50 (18.7)	
CCS-classification before (%)					
CCS 1	59 (33.5)	94 (36.3)	81 (30.8)	94 (34.0)	
CCS 2	53 (30.1)	87 (33.6)	83 (31.6)	77 (28.8)	.79
CCS 3	39 (22.2)	46 (17.8)	63 (24.0)	62 (23.2)	
CCS 4	25 (14.2)	32 (12.4)	36 (13.7)	34 (12.7)	
Sex (%)					
Female	43 (24.4)	73 (28.2)	56 (21.3)	78 (29.2)	.15
Male	133 (75.6)	186 (71.8)	207 (78.7)	189 (70.8)	
Previous interventions (%)					
PTCA	29 (16.5)	34 (13.1)	30 (11.4)	27 (10.1)	.23
Bypass	7 (4.0)	7 (2.7)	13 (4.9)	10 (3.7)	.62
Risk-factors (%)					
Hypertension	121 (68.8)	164 (63.3)	163 (62.0)	170 (63.7)	.52
Diabetes mellitus	44 (25.0)	69 (26.6)	75 (28.5)	72 (27.0)	.88
Hyperlipoproteinemia	80 (45.5)	124 (47.9)	123 (46.8)	125 (46.8)	.97
Smoking	68 (38.6)	82 (31.7)	97 (36.9)	89 (33.3)	.39
Primary indication (%)					
Emergency	23 (13.1)	53 (20.5)	50 (19.0)	51 (19.1)	.24
Elective	153 (86.9)	206 (79.5)	213 (81.0)	216 (80.9)	
Localization of lesion (%)					
LAD/diagonals*	80 (45.5)	115 (44.4)	115 (43.7)	117 (43.8)	
RCX/marginals*	42 (23.9)	52 (20.1)	42 (16.0)	44 (16.5)	*.22
RCA*	49 (27.8)	92 (35.5)	98 (37.3)	102 (38.2)	
Main stem	1 (0.6)	0 (0)	1 (0.4)	1 (0.4)	
Bypasses	4 (2.3)	0 (0)	7 (2.7)	3 (1.1)	
Type of lesion (%)					
Type A	28 (15.9)	39 (15.1)	50 (19.0)	43 (16.1)	
Type B	108 (61.4)	166 (64.1)	152 (57.8)	164 (61.4)	.86
Type C	40 (22.7)	54 (20.8)	61 (23.2)	60 (22.5)	
Length of lesion					
Mean ± SD (mm)	10.5 ± 3.9	10.5 ± 4.2	10.7 ± 4.6	10.5 ± 4.3	.97
Indication (%)					
Recoil	38 (21.6)	54 (20.8)	58 (22.1)	48 (18.0)	
Dissection	111 (63.1)	167 (64.5)	172 (65.4)	168 (62.9)	.58
Elective	27 (15.3)	38 (14.7)	33 (12.5)	51 (19.1)	

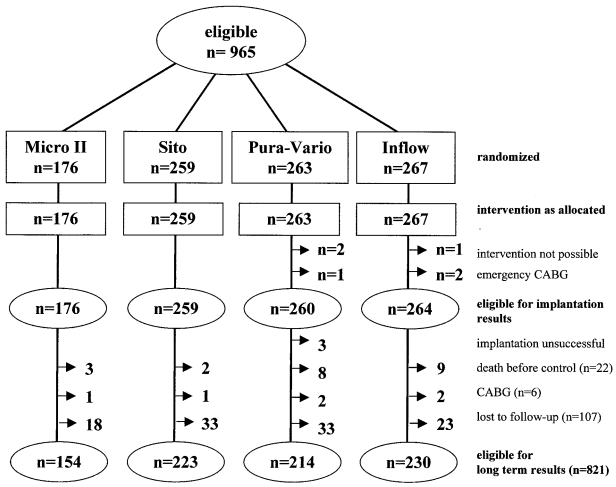
**P* value only for main vessels; left main and bypasses not included.

group, had a residual stenosis of >30% and were defined as unsuccessful implantation. Another patient showed "no reflow" after stenting in acute myocardial infarction, which resolved in the sequel, so acute gain was available for 958 lesions. Long-term angiographic follow-up was available for 821 lesions (85.1%)—well balanced among the 4 study arms.

All quantitative angiographic data were analyzed on an intention-to-treat basis with the tightest part of the lesion taken for analysis independently from the number or kind of stents implanted at this particular site. Results are shown in Table III. The primary end point diameter stenosis at follow-up was not significantly different among the 4 stent groups (Figure 3).

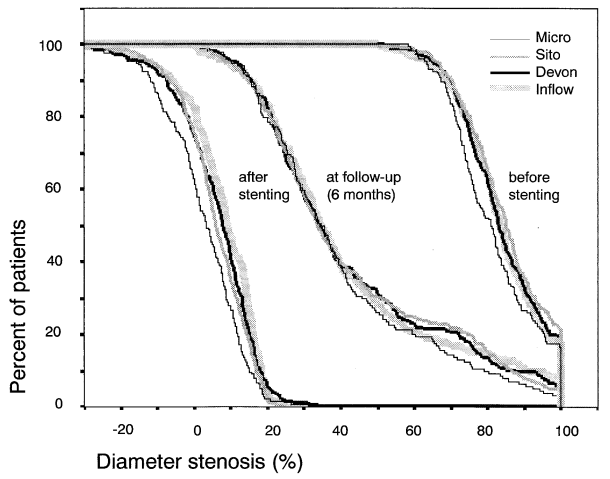
Baseline diameter stenosis in the Micro stent group was slightly but significantly lower, and mean luminal diameter, reference diameter (RD), and net gain were slightly but significantly higher than in the other groups. After stent implantation, reference diameters were comparable among all 4 study arms, whereas the MLD was slightly but significantly higher, resulting in a somewhat lower degree of diameter stenosis in the Micro stent group. At follow-up, no significant differences for RD, MLD, and degree of diameter stenosis were detectable. Late lumen loss, net gain, and increase of diameter stenosis were similar in all groups, resulting in a comparable restenosis rate and target lesion revascularization rate (Table III). There was also

Figure 2



Trial profile.

Figure 3



Diameter stenosis before stenting, immediately after stenting and at 6 months follow-up. Data are shown as a continuous frequency distribution.

no significant difference in restenosis rate among the only premounted stent system (Micro II) and the other 3 hand-crimped stent types (26.0% vs 31.1%, $P = .33$).

Acute and late outcome

Procedural success rate differed slightly but significantly among the 4 stent groups (Micro 99.4%, Sito 97.6%, Pu-Va 95.4% and Inflow 94.8%, $P = .03$).

The overall incidence of stent loss (including nonrandomized devices) or failure to reach the target lesion was not statistically different ($P = .25$); however, the number of events was too low to detect minor differences. Stent loss occurred with 3 Micro-stents, 3 Sito-stents and 6 Inflow-stents. Target lesion could not be reached or crossed with 2 Micro-stents, 3 Sito-stents, 8 Devon-stents, and 7 Inflow-stents.

Major adverse cardiac events (MACE) with regard to stent thrombosis, myocardial infarction, CABG, and target vessel revascularisation were not significantly different (Table IV). Stent thrombosis developed in 12 patients, all of whom were transferred immediately to the cath lab for successful emergency recanalization. Nine patients developed non–Q-wave myocardial infarctions; in 3 patients no infarction was observed.

Emergency CABG operation was performed in 2 patients with stent loss in the left main coronary artery (1 Micro, 1 Inflow) and in another patient with acute stent thrombosis 1 day after intervention in the Pu-Va stent group. Two other early (<28 days) and 5 late CABG operations were performed electively due to multivessel disease.

There were 14 side-branch occlusions (total or functional) during intervention (3 in the Micro, 3 in the Sito, 4 in the Devon, and 4 in the Inflow group). Four side branches were reopened successfully, 4 cases were unsuccessful, and 6 were left conservatively due to lack of symptoms.

Overall mortality was similar among the 4 stent groups (Table IV). Inclusion of patients with unstable angina or myocardial infarctions including cardiogenic shocks (18.3% of all patients) resulted in a relatively high overall mortality rate of 2.4% (22/925). Periinterventional mortality up to 48 hours was 0.6% (6/925), and long-term mortality up to 6 months was 1.7% (16/925, including 5 patients [0.5%] with noncardiac reasons [stroke, malignant diseases]).

Regression analysis

To further investigate independent predictors for restenosis, a multivariate logistic regression analysis was performed for data of 820 lesions (1 case excluded for no reflow in myocardial infarction). The analyzed variables and overall results are shown in Table V.

Discussion

The present study shows that stent design of the 4 different stents used in this trial had no impact on diameter stenosis 6 months after stent implantation. Despite less diameter stenosis and a somewhat higher initial lumen gain in the Micro-stent group, late lumen loss as well as net lumen gain were not significantly different among the 4 stent designs, resulting in comparable restenosis rates. The primary success rate was significantly higher in the premounted Micro-stent group compared with the other 3 stent designs used,

Table III. QCA data

	Micro II	Sito	Pura-Vario	Inflow	*P*
RD (0) (mm)	3.2 ± 0.6	3.1 ± 0.6	3.1 ± 0.6	3.0 ± 0.6	.03
MLD (0) (mm)	0.6 ± 0.4	0.5 ± 0.4	0.5 ± 0.4	0.5 ± 0.4	.01
Diameter stenosis (0)	81.7 ± 11.9	85.1 ± 11.4	84.0 ± 11.6	83.8 ± 11.7	.03
RD (1) (mm)	3.3 ± 0.5	3.2 ± 0.6	3.2 ± 0.5	3.2 ± 0.5	.22
MLD (1) (mm)	3.1 ± 0.6	3.0 ± 0.5	2.9 ± 0.6	2.9 ± 0.5	<.005
Diameter stenosis (1)	3.0 ± 12.9	5.6 ± 9.5	6.9 ± 13.5	7.7 ± 9.9	<.005
RD (F) (mm)	3.0 ± 0.5	3.0 ± 0.5	3.0 ± 0.5	3.0 ± 0.5	.69
MLD (F) (mm)	1.8 ± 0.8	1.7 ± 0.9	1.8 ± 0.9	1.8 ± 0.9	.60
Diameter stenosis (F)	40.3 ± 24.1	42.8 ± 27.0	42.6 ± 26.9	42.3 ± 26.8	.70
Acute gain (mm)	2.6 ± 0.6	2.5 ± 0.6	2.4 ± 0.6	2.4 ± 0.5	.02
Percent acute gain	79.3 ± 16.1	79.5 ± 14.4	77.5 ± 16.1	76.1 ± 15.0	.05
Late lumen loss (mm)	1.3 ± 0.9	1.2 ± 0.9	1.2 ± 0.9	1.2 ± 0.8	.27
Percent lumen loss	37.7 ± 24.6	37.3 ± 29.6	36.2 ± 28.1	34.9 ± 28.0	.75
Net gain (mm)	1.2 ± 0.9	1.3 ± 0.9	1.3 ± 0.9	1.3 ± 0.9	.99
Percent net gain	41.5 ± 28.1	42.4 ± 27.7	42.1 ± 27.8	41.9 ± 28.5	.99
Restenosis rate (%)	26.0	30.5	31.3	28.7	.70
TLR (%)	12.0	16.4	16.6	16.1	.36

QCA data expressed as mean ± SD before PTCA (0), immediately after stenting (1) and at follow-up (F). MLD and (relative) acute gain of the Micro stent group was significantly higher before and after intervention as compared with the other stent groups; late loss and net gain as well as restenosis rate, however, were not significantly different. *TLR*, Target lesion revascularisation.

Table IV. Adverse events within 28 days and 1-6 months follow-up

	MICRO	SITO	DEVON	INFLOW	*P*-Wert
Stent thrombosis	0	4	5	3	.32
Acute	0	3	4	3	
Subacute	0	1	1	0	
Myocardial infarction*	1	3	4	3	.78
Within 28 d	0	2	4	3	.42
Fatal	0	0	1	0	
Nonfatal	0	2	3	3	
Within 1-6 m	1	1	0	0	
Fatal	1	0	0	0	
Nonfatal	0	1	0	0	
CABG	1	2	3	4	.83
Within 28 d	1	1	1	2	.93
Within 1-6 m	0	1	2	2	
Death	3	2	8	9	.17
Within 28 d	2	1	7	5	.18
Cardiac	2	1	5	4	
Noncardiac	0	0	2	1	
Within 1-6 m	1	1	1	4	
Cardiac	1	0	0	1	
Noncardiac	0	1	1	3	
Target vessel revascularization	22	42	41	39	.36
Any clinical event within 28 d	3	6	11	10	.38
MACE within 6 m (cardiac death, MI, CABG, TVR)	26	48	55	55	.36

*All Q-wave MI

which were hand crimped stents. The overall early and late major adverse event rate, however, was independent of stent design.

Restenosis

There are few data from animal studies or retrospective clinical trials demonstrating differences in restenosis with different stent design,[3,7,8] though these studies also reflect some special conditions like the articulation strut of the Palmaz-Schatz stent, which is a well-known origin for in-stent restenosis.[9] Aside from one small study comparing the Micro-stent I with the Palmaz-Schatz stent,[10] the data of our prospective, randomized trial are the first to show that there was no

Table V. Multivariate analysis for restenosis

	Odds ratio	95% CI	P
Age*	0.99	0.98-1.02	.8
Sex	1.2	0.81-1.77	.35
Hypertension	0.96	0.68-1.35	.8
Diabetes mellitus	1.44	1.01-2.07	.04
Hypercholesterinemia	0.98	0.71-1.36	.92
Smoking	0.93	0.65-1.35	.71
Previous PTCA	0.66	0.39-1.12	.12
Former CABG	2.25	1.02-4.95	.04
Severity of CAD			
2-Vessel disease	0.94	0.57-1.54	.79
3-Vessel disease	1.14	0.71-1.54	.59
LAD + diagonals	1.46	1.04-2.03	.03
Type of lesion			
Type A	0.94	0.59-1.52	.81
Type C	1.44	0.98-2.12	.06
RD before <3.0 mm	1.54	1.12-2.14	.009
Emergency intervention	0.74	0.47-1.17	.2
Dissection as indication for stenting	2.1	1.14-3.87	.02
Type of stent			
Micro	1.02	0.62-1.67	.92
Sito	1.18	0.77-1.82	.44
Devon	1.08	0.7-1.66	.72
Multiple stenting	0.69	0.34-1.39	.3
Stented length†	1.48	1.13-1.94	.004

*OR per year.
†OR per 10 mm.

difference in the primary end point diameter stenosis after 6 months or in net gain and late lumen loss, resulting in comparable restenosis rates for all slotted tube stents and the 1 corrugated ring stent used in this study. The lower diameter stenosis in the Micro-stent group had no quantitative influence on the development of neointima proliferation, which was also demonstrated in another study.[11] On the basis of these results, we conclude that strut thickness, form of strut, and the design of these 4 stents had no significant influence on neointima proliferation and thus restenosis rate. Our results, attained with stents of highly different strut thickness (75-200 μm), are in some ways opposite the results of the Intracoronary Stenting and Angiographic Results-Strut Thickness Effect on Restenosis Outcome (ISAR-STEREO) study,[12] which demonstrated a lower restenosis rate with thinner struts. It remains speculative whether, in different delivery systems, the significant difference between device success or the necessary manual correction of the lumen contour in the ISAR-STEREO study influenced the results. Kastrati et al[13] could also show that there was a significant difference in clinical outcome (primary end point: event free survival at 1 year with regard to death of cardiac origin, myocardial infarction, and target-vessel revascularization) among 5 different stent designs. Diameter stenosis and MLD at 6 months were slightly significantly different, whereas late lumen loss, loss index, and restenosis rates were also not significantly different, comparable to our results. The reasons for these small differences cannot be judged, because stent results in the Kastrati et al[13] study were given anonymously.

Adverse events

The rate of adverse events in our study with regard to stent loss, stent thrombosis, emergency CABG, and myocardial infarction due to the stenting procedure is similar to other studies.[14,15] However, there was a significant difference in primary success of implantation of the first randomized stent, with the premounted stent system being the best compared with the hand crimped stents, especially the Inflow stent. With this stent it was more difficult to reach the target lesion. This may be explained by the very thin material of the stent and the missing connections between the stent mashes, which resulted in either a higher stent-loss rate or displacement of the stent due to less secure fixation on the balloon. This demonstrates that both premounting and the stent design may have an influence on the security of stent implantation. The overall incidence of early and late adverse events (stent thrombosis, myocardial infarctions, CABG, deaths, and TVR) after successful implantation, however, was similar among all stents (Table IV).

Independent predictors for restenosis

To investigate independent predictors of restenosis, a multivariate logistic regression analysis was performed. Highly significant predictors were reference vessel diameter <3.0 mm before stent implantation, overall stented length, a history of bypass grafting, dissection as indication for the first stent, left anterior descending coronary artery lesions, type C lesions, and diabetes mellitus. These results are comparable with other studies,[16-19] which could at least partly demonstrate the same parameters that are predictive for in-stent restenosis. Prior CABG, however, which may be a sign for more severe coronary artery disease, and dissection as indication for the first stent (being a sign for greater vessel trauma and perhaps thrombus formation), has never been evaluated as an independent risk factor for restenosis in native vessels. Though endothelial dysfunction in patients with diabetes and patients with hypertension may influence restenosis, the greater than normal early formation of thrombus, rather than proliferation of smooth muscle cells, contributes to restenosis after coronary stenting in patients with diabetes mellitus; therefore, diabetes mellitus is an independent risk factor for restenosis, in contrast to hypertension.[20]

Limitations of the study

One limitation of the study is the use of some older stent designs, which are no longer available. However, the results can probably be generalized because, in general, newer stents are not very different from the older stent designs used in this study, and restenosis rates in clinical practice are quite comparable.

Blinding of the interventionalists was not possible because they were familiar with all the stents and would have realized which study arm was randomized.

The inclusion of emergency cases has led to a relatively high mortality rate in this study, mainly due to patients with cardiogenic shock. Nevertheless, the calculated minimal number of patients with angiographic reevaluation (85.1%) was reached and the results of the study are in this way very close to clinical routine.

Conclusions

Stent design seems to have minor relevant influence on the development of in-stent restenosis. Therefore, other therapeutic options, such as covering of stent struts with carbon or other materials, local drug delivery, and radiation therapy are currently being tested for their ability to reduce the risk of restenosis.

Results were dependent on stent design: there was a significant difference in the primary success rate between the premounted stent system and the other stents used in this study. However, overall adverse events, such as stent loss, stent thrombosis, myocardial infarctions, and emergency CABG, were comparable, though there was a trend to higher rate of stent loss or displacement with the Inflow stent. Therefore, and with regard to patient security, premounted stent systems are preferred for routine patient treatment, which is already clinical practice.

With regard to the independent predictors of restenosis in this study, aggressive predilatation should be avoided so as to reduce dissections as an independent risk of restenosis, and primary stenting should be used in suitable lesions. Treatment of diabetes mellitus should also be optimized.

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References

1. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group [see comments]. N Engl J Med 1994;331:489–95.
2. Fischman DL, Leon MB, Baim DS, et al, Stent Restenosis Study Investigators. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease [see comments]. N Engl J Med 1994;331:496–501.
3. Sick P, Schumann E, Zindler G, et al. Comparative studies of the rate of restenosis after implantation of Palmaz-Schatz and AVE-Micro stents [in German]. Z Kardiol 1997;86:1000–9.
4. Berglund U, Lindahl T. Enhanced onset of platelet inhibition with a loading dose of ticlopidine in ASA-treated stable coronary patients. Int J Cardiol 1998;64:215–7.
5. Hausleiter J, Nolte CW, Jost S, et al. Comparison of different quantitative coronary analysis systems: ARTREK, CAAS, and CMS. Cathet Cardiovasc Diagn 1996;37:14–22, discussion 23..
6. Foley JB. Alterations in reference vessel diameter following intracoronary stent implantation: important consequences for restenosis based on percent diameter stenosis. Cathet Cardiovasc Diagn 1995;35:103–9.
7. Rogers C, Edelman ER. Endovascular stent design dictates experimental restenosis and thrombosis. Circulation 1995;91:2995–3001.
8. Tominaga R, Harasaki H, Sutton C, et al. Effects of stent design and serum cholesterol level on the restenosis rate in atherosclerotic rabbits. Am Heart J 1993;126:1049–58.
9. Ikari Y, Hara K, Tamura T, et al. Luminal loss and site of restenosis after Palmaz-Schatz coronary stent implantation. Am J Cardiol 1995;76:117–20.
10. Menafoglio A, Eeckhout E, Debbas N, et al. Randomised comparison of Micro Stent I with Palmaz-Schatz stent placement for the elective treatment of short coronary stenoses. Cathet Cardiovasc Diagn 1998;43:403–7.
11. Goldberg SL, di Mario C, Hall P, et al. Comparison of aggressive versus nonaggressive balloon dilatation for stent deployment on late loss and restenosis in native coronary arteries. Am J Cardiol 1998;81:708–12.
12. Kastrati A, Mehilli J, Dirschinger J, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. Circulation 2001;103:2816–21.
13. Kastrati A, Dirschinger J, Boekstegers P, et al. Influence of stent design on 1-year outcome after coronary stent placement: a randomized comparison of five stent types in 1,147 unselected patients [see comments]. Catheter Cardiovasc Interv 2000;50:290–7.
14. Altmann DB, Racz M, Battleman DS, et al. Reduction in angioplasty complications after the introduction of coronary stents: results from a consecutive series of 2242 patients. Am Heart J 1996;132:503–7.
15. Valdes M, Pinar E, Pascual D, et al. Complications at the first month following various types of intracoronary stents, implanted with high pressure without intracoronary ultrasonography or anticoagulation. Rev Esp Cardiol 1996;49:432–8.
16. Bauters C, Hubert E, Prat A, et al. Predictors of restenosis after coronary stent implantation. J Am Coll Cardiol 1998;31:1291–8.
17. Eeckhout E, van Melle G, Stauffer JC, et al. Can early closure and restenosis after endoluminal stenting be predicted from clinical, procedural, and angiographic variables at the time of intervention? Br Heart J 1995;74:592–7.
18. Kastrati A, Schomig A, Elezi S, et al. Predictive factors of restenosis after coronary stent placement. J Am Coll Cardiol 1997;30:1428–36.
19. Moscucci M, Piana RN, Kuntz RE, et al. Effect of prior coronary restenosis on the risk of subsequent restenosis after stent placement or directional atherectomy. Am J Cardiol 1994;73:1147–53.
20. Carter AJ, Bailey L, DeVries J, et al. The effects of uncontrolled hyperglycemia on thrombosis and formation of neointima after coronary stent placement in a novel diabetic porcine model of restenosis. Coron Artery Dis 2000;11:473–9.