Randomized Comparison of Success and Adverse Event Rates and Cost Effectiveness of One Long Versus Two Short Stents for Treatment of Long Coronary Narrowings

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Long stents of high flexibility and low profile have become widely available. Treatment of long coronary lesions by 1 long stent may require less interventional efforts and reduce the rate of restenosis due to a lack of overlapping stent segments. This study sought to evaluate the use of 1 long stent compared with 2 short stents for treatment of long coronary lesions. One-hundred twenty-four patients with a coronary lesion 20 to 40 mm in length, in a vessel 2.5 to 4.0 mm in diameter, were randomly assigned to treatment with 1 long stent (GFX II stents or S670 of 24, 30, or 40 mm lengths; n = 62) or 2 stents (GFX II or S670 stents, n = 62) of equal length. Procedural success, interventional costs, as well as long-term clinical and angiographic outcomes were evaluated. Lesion characteristics were similar for the 2 treatment groups. Stent placement was possible as assigned by randomization in 61 of 62 cases (98%) in the 1-long-stent group and 100% of cases in the 2-short-stents group. There was crossover to successful short-stent placement in 1 case. The in-hospital success rate was 97% for the 1-long-stent group and 98% for the 2-short-stents group. Acute angiographic results were similar for both groups after intervention. The angiographic restenosis rate at 6 months was 38.5% in the 1-long-stent group and 37.5% in the 2-short-stents group (p = 0.919). Intervention time was less, and the need for a contrast agent had a tendency to be lower in the long-stent group. Procedural costs were significantly less in the long-stent group. In conclusion, 1 long stent can be used with identical procedural success and adverse event rates as 2 short stents in long, atherosclerotic coronary lesions. The restenosis rate is not reduced by the use of 1 long stent compared with 2 stents. However, long stent placement is highly cost effective. ©2002 by Excerpta Medica, Inc.

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This prospective, randomized trial evaluated acute procedural and long-term clinical and angiographic outcomes, as well as procedural costs and efforts involved with the treatment of patients with native coronary lesions of 20 to 40 mm in length by either 1 long stent or 2 stents of similar length.

METHODS

Patients: One hundred twenty-four patients with a lesion of 20 to 40 mm in length, in a native coronary artery 2.5 to 4.0 mm in diameter, were included in this randomized, multicenter trial. Patients with symptomatic coronary artery disease were eligible for this study. Patients with restenotic lesions, lesions in an ostial location, heavily calcified lesions, and lesions in extremely tortuous vessels were excluded. This study was approved by the local ethical committees, and each patient provided written informed consent for the study.

Stent implantation and treatment after stenting: All 124 lesions were treated with GFX II or S670 stents (Medtronic AVE, Santa Rosa, California). The GFX II and S670 stents have a sinusoidal ring design with a crossing profile of 0.060 to 0.062 in. Stents were implanted according to standard protocols. Dilation before stent implantation was not required, and the operator was allowed to perform direct stent placement, if possible. During intervention patients received aspirin and intravenous heparin. Additional abciximab was given to 5 patients. Therapy after the procedure consisted of 250 mg ticlopidine twice daily or 75 mg clopidogrel once daily, plus 100 mg/day aspirin for 4 weeks. Aspirin was given indefinitely. The aim of the intervention was to cover the whole lesion length ("shoulder to shoulder") using coronary

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*A list of participating institutions and investigators appears in the Appendix.

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TABLE 1 Baseline Clinical Characteristics

	1 Long Stent (n = 62)	2 Short Stents (n = 62)	p Value
Age (yrs)	62.8 ± 9.7	63.3 ± 8.8	0.372
Men	53 (85%)	48 (77%)	0.496
Systemic hypertension	20 (32%)	17 (27%)	0.695
Diabetes mellitus	11 (18%)	15 (24%)	0.509
Hyperlipidemia	19 (31%)	16 (26%)	0.691
Cigarette smoker	41 (66%)	41 (66%)	1.000
Unstable angina pectoris	15 (24%)	9 (14%)	0.262
Prior myocardial infarction	34 (55%)	32 (52%)	0.717
Prior coronary bypass grafting	1 (2%)	4 (6%)	0.366

stent placement. The length of the required stent(s) was defined by on-line quantitative coronary angiography (QCA) measurement. After the operator decided which stent length should be used, each patient was randomized for implantation of either 1 long coronary stent (lesions 20 to 24 mm, stent 24 mm; lesions 24 to 30 mm, stent 30 mm; lesions 30 to 40 mm, stent 40 mm) or 2 stents (lesions 20 to 24 mm, 2 stents of 12 mm; lesions 24 to 30 mm, 1 stent of 18 mm and 1 stent of 12 mm; lesions 30 to 40 mm, 1 stent of 24 mm and 1 stent of 18 mm). Sixty-two patients were assigned to the 1-long-stent group and 62 patients to the 2-short-stents group. It was our intention to bring the stent edges together as close as possible or to have a minimal stent overlap for the 2-short-stents group.

In-hospital and 6-month follow-up clinical outcomes: Procedural success was defined as a $<$30% final diameter stenosis in the treated lesion and the absence of major clinical complications (in-hospital death, Q-wave myocardial infarction, or emergency coronary bypass surgery). Procedural success was further characterized by the ability to perform the procedure according to randomization. All patients were monitored for 6 months after the procedure for any major adverse cardiac event (MACE)—defined as death of any origin, myocardial infarction, or a need for revascularization. Baseline clinical demographics, in-hospital complications, and the occurrence of any MACE during follow-up were verified by independent hospital chart reviews and source documentation. Patients with successful intervention and no MACE $\leq$30 days after the procedure were considered eligible for an angiographic follow-up.

Quantitative angiographic analysis: Standard qualitative morphologic criteria were used to assess the lesion length, eccentricity, calcification, and angulation. The development of postprocedural complications (such as dissections, abrupt closure, distal embolization, postprocedural thrombus, and impaired anterograde flow) was recorded.

Off-line QCA analysis was performed using an automated edge-detection algorithm at the angiographic core laboratory of the University Aachen, Germany (CAAS II System, PieMedical, Maastricht, The Netherlands). The operator performing the analysis of follow-up angiograms was unaware of the assigned stent implantation technique used to treat the lesion. The determined parameters were lesion length, reference diameter, minimal lumen diameter (MLD), and diameter stenosis. Acute lumen gain was determined as the improvement in MLD (postintervention MLD minus preintervention MLD). Late lumen loss was calculated as postintervention MLD minus follow-up MLD. Angiographic restenosis was defined as a diameter stenosis of $\geq$50%. In addition to the MLD and the reference lumen diameter, the lumen diameter of 3 sites within the stented segment was evaluated at follow-up: the proximal stent segment as defined by a length of 5 mm up to the proximal stent edge, the middle part of the stented segment as defined by a length of 10 mm at the center of the stented segment, and the distal stent segment as defined by a length of 5 mm up to the distal stent edge.

Procedural efforts and costs: The number of angioplasty balloons, coronary stents, the volume of contrast agent, and the time of the interventional procedure were determined in an attempt to evaluate the required efforts of the interventional procedure. In addition, an estimation of the interventional costs of the procedure as performed. In this approximation, the price of an angioplasty balloon was assumed to be €250, the price of a coronary stent to be €750, and the price of 1 hour of intervention time (including laboratory room and personal costs) to be €600.

Statistical analysis: Statistical analysis was performed using SPSS 10.0 (SPSS Inc., Chicago, Illinois). Continuous data are presented as mean ± SD. Qualitative data are presented as frequencies. Comparisons between groups were performed using chi-square statistics and Fisher's exact test for categorical variables, paired and unpaired *t* tests for continuous variables, or factorial analysis of variance. Significant differences were defined as a p value $<$0.05.

RESULTS

There were no differences in baseline patient characteristics between the 2 groups as listed in Table 1.

Acute angiographic results: There were no differences in preprocedural morphologic and quantitative angiographic lesion characteristics between the 2 treatment groups (Table 2). Specifically, 7% of lesions in the 1-long-stent group and 9% of lesions in the 2-short-stents group demonstrated signs of calcification. There were 35 occlusions that could be recanalized. Angiography demonstrated a similar postintervention MLD and similar acute lumen gain for both treatment groups.

Procedural efforts and costs: The use of angioplasty balloons and the number of angioplasties before stent placement were similar between the 2 groups. The number of applied stents was significantly higher in the 2-short-stents group. There was a slight trend toward less intervention time and a strong trend toward less use of a contrast agent in the 1-long-stent

TABLE 2 Baseline Angiographic Data

	1 Long Stent	2 Short Stents	p Value
Coronary artery			
Right	40	40	1.000
Left anterior descending	16	19	0.691
Left circumflex	6	3	0.490
Total occlusions	17	18	0.932
Artery calcium	5 (8%)	6 (10%)	0.872
Lesion length (mm)	26.2 ± 6.0	27.8 ± 6.6	0.156
Preintervention			
Reference diameter (mm)	3.04 ± 0.65	3.04 ± 0.51	0.990
MLD (mm)	0.83 ± 0.64	0.70 ± 0.61	0.206
Postintervention			
Reference diameter (mm)	3.07 ± 0.57	3.13 ± 0.50	0.562
MLD (mm)	2.70 ± 0.52	2.72 ± 0.52	0.831
Acute diameter gain (mm)	1.88 ± 0.81	2.02 ± 0.79	0.304

TABLE 3 Procedural Data and Interventional Efforts

	1 Long Stent	2 Short Stents	p Value
Diameter stent deployment balloon (mm)	3.17 ± 0.35	3.25 ± 0.34	0.261
Maximal implantation pressure (atm)	11.8 ± 1.9	12.0 ± 1.9	0.505
Total stent length (mm)	32.1 ± 9.7	32.8 ± 10.4	0.720
No. of stents	1.31 ± 0.64	2.16 ± 0.41	<0.001
No. of balloons pre-stent	0.99 ± 0.53	1.03 ± 0.71	0.664
No. of angioplasties pre-stent	1.73 ± 1.28	1.46 ± 1.19	0.234
No. of balloons post-stent	0.18 ± 0.39	0.19 ± 0.40	0.932
Intervention time (h)	0.79 ± 0.41	0.91 ± 0.46	0.141
Contrast agent (ml)	165 ± 73	190 ± 70	0.056
Intervention costs (Euros)	1,577 ± 676	2,293 ± 666	<0.001

TABLE 4 Angiographic Data at Follow-up

	1 Long Stent	2 Short Stents	p Value
Follow-up minimal lumen diameter (mm)	1.55 ± 0.70	1.55 ± 0.74	0.981
Late loss (mm)	1.14 ± 0.62	1.18 ± 0.85	0.780
Net gain (mm)	0.76 ± 0.76	0.83 ± 1.06	0.744
Restenosis rate (%)	38.5	37.5	0.919
Lumen diameter proximal stent edge (mm)	2.19 ± 0.96	2.14 ± 1.02	0.842
Lumen diameter body of stented segment (mm)	1.65 ± 0.76	1.66 ± 0.83	0.946
Lumen diameter distal stent edge (mm)	1.95 ± 0.99	1.91 ± 0.86	0.883

group. Overall, estimated procedure costs based on the use of angioplasty balloons, coronary stents, and procedure time were significantly lower in the 1-long-stent group (Table 3).

In hospital and 6-month follow-up clinical outcomes: All lesions of the 2-short-stents group were treated as assigned. The successful placement of a long stent was possible in 61 of 62 (98%) cases in the 1-long-stent group. In 1 patient, lesion placement of 1 long coronary stent could not be achieved, and there was a crossover to the successful placement of 2 short stents. Additionally, 13 patients in the 1-long-stent group had >1 stent implanted (5 cases due to dissections at a stent edge and 8 cases due to the incomplete coverage of the lesion by 1 stent). Direct stent placement was possible and attempted in 9 cases of the 1-long-stent group and 12 cases of the 2-short-stents group. Procedural success was 62 of 62 cases (100%) in the 2-short-stents group and 60 of 62 cases (97%) in the 1-long-stent-group ($p = 0.479$). There was 1 myocardial infarction due to vessel dissection in the 1-long-stent group, and there was 1 crossover to short stent placement. The in-hospital success rates were similar, with 61 of 62 cases (98%) in the 2-short-stents group and 60 of 62 cases (97%) in the 1-long-stent group. In the period before the 6-month follow-up, MACEs occurred in 6 of 62 cases (10%) in the 2-short-stents group and in 5 of 62 cases (8%) in the 1-long-stent group.

Angiographic follow-up results: Angiographic follow-up was carried out in 52 patients (84%) in the 1-long-stent group and in 55 patients (89%) in the 2-short-stents group. Results of the follow-up QCA are listed in Table 4. The MLD at follow-up was similar in both groups. The restenosis rate was 38.5% in the 1-long-stent group and 37.5% in the 2-short-stents group ($p = 0.919$). The restenosis rate was 48% for the 31 lesions with long (28.6 ± 6.8 mm) total occlusions with angiographic follow-up, compared with 34% for the nonocclusions. Late loss increased with lesion length (Figure 1). There was no difference between both treatment groups at any lesion length. The lumen diameter was smallest at the body of the stented segment for both treatment groups ($p < 0.001$) (Figure 2). There was no difference between either group at any part of the stented vessel segment. Restenosis length at follow-up was shorter than the initial stenosis length (13.2 ± 9.7 mm). There was no difference between the 2 groups in restenosis length at follow-up.

DISCUSSION

This study demonstrates that the use of 1 long stent: (1) is highly feasible for treatment of long coronary lesions, (2) results in a restenosis rate that is comparable with the use of 2 shorter stents of similar total stent length, (3) is associated with a trend toward shorter procedure length and use of contrast agent, and (4) is more cost-effective than the use of 2 coronary stents.

Long-lesion angioplasty: Treatment of short atherosclerotic lesions in relatively large vessels as well as restenotic lesions with metallic slotted-tube stents has been shown to improve acute and long-term outcomes by catheter-based interventions.[1–5] The optimal treatment of long coronary lesions is still not well defined, with most data relating to the placement of multiple short stents.[6–9] Long coronary lesions are traditionally

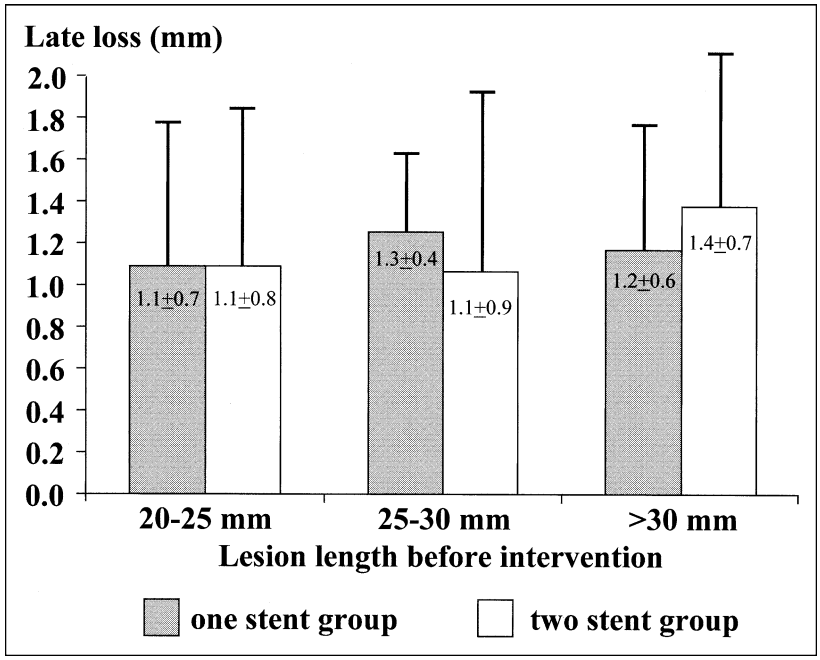

FIGURE 1. Late loss for different lesion lengths treated by either 1 long stent or 2 short stents.

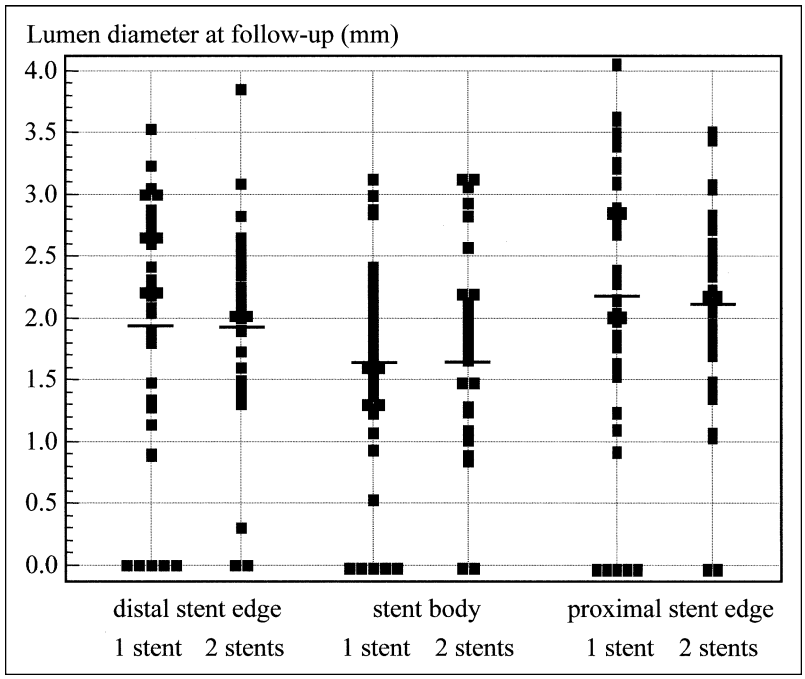

FIGURE 2. Mean ± SD of the follow-up lumen diameter at the proximal stent edge, the middle part of the stented vessel segment, and the distal stent edge of lesions treated by 1 long coronary stent compared with 2 short stents.

considered to be complex lesions with a higher procedural risk as well as a higher restenosis rate.[10–12] Because the use of stents has almost equalized long lesions compared with short lesions regarding the procedural risks, there is abundant evidence that conventional stenting of long lesions is independently associated with an increased restenosis risk.[13–16] In a study of 2,736 lesions, Kastrati et al[15] reported a restenosis rate of 28% for lesions <15 mm, and a restenosis rate of 37% for long lesions (≥15 mm, p <0.001). Kobayashi et al[16] reported that recurrence rates for stented lesions increased proportionally with lesion length: 24% for lesions up to 20 mm, to 47% for lesions >35 mm in length (p <0.01). Additional risk factors of restenosis after long-lesion stenting may be gaps between stents and the overlap segment of 2 adjacent stents. Equivalent repeat revascularization rates after the use of stents ≥25 mm in length compared with stents <20 mm in length have been reported.[17] However, the average lesion length in the group treated with 1 stent of ≥25 mm length was only 13 mm. This finding may indicate that the stent length is of less importance than the actual lesion length for subsequent restenosis.

In the setting of long dissections, the use of long stents has proven to be equivalent to multiple short-stent placements.[18] However, tight coronary lesions and dissections are likely to react differently to stent placement. Suboptimal results after initial intervention or the elective primary success rate was found to be high in a registry on the use of long coronary stents for large dissections.[18] Angiographic follow-up was obtained in 73% and it indicated a restenosis rate of 27%.

Spot stenting of the tightest spots within long coronary lesions has been suggested to reduce restenosis of long lesions compared with complete stent coverage. A significantly reduced restenosis and revascularization rate has been reported for spot stenting compared with the total coverage of stents.[19] However, the technique is more laborious and the use of intravascular ultrasound has been recommended to optimize this approach. Because several operators may either not be willing or are unable to perform this demanding technique, there have been controversial reports on the use of spot stenting compared with complete coverage of the lesion length by stents regarding the reduction of restenosis. Ormiston et al[20] reported in a study on 120 long coronary lesions that mildly diseased segments containing <25% stenosis at baseline are unlikely to develop stenosis at follow-up. This result is explained by the known importance of lesion plaque burden for subsequent intimal hyperplasia proliferation, with a correlation of intimal hyperplasia to plaque burden

before stent placement.[21] Total coverage of the lesion has been proposed as result of this study because of easier performance versus the spot stenting technique.

The restenosis rates in this study agree with those previously reported for long coronary lesions. Treatment of long total occlusion was associated with a higher restenosis rate. The restenosis rate was not altered by the implantation of 1 long stent compared with 2 short stents. Furthermore, segmental analysis demonstrated similar lumen loss at the body of the stented vessel length for 1 long stent compared with 2 short stents, indicating that a slight overlap does not result in an excess of lumen loss. Thus, the study indicates that the number of stents is not an independent factor for increasing the likelihood of restenosis, whereas the lesion length is the dominant factor. This finding is different from a previous report by Kastrati et al.[15] However, although these investigators reported that an overlap region increased restenosis, stent overlap as well as gaps between stents were avoided in the present study.

APPENDIX

In addition to the investigators, the following institutions and investigators participated in the IMPULSE study—Data coordinating center: Gesellschaft für Qualitätssicherung in der klinischen Forschung mbH, Selm, Germany, K. Stahl. Study investigators: Dr. P. Sick, Herzzentrum Leipzig, Leipzig, Germany; Dr. R. Bach, Klinikum Weißer Hirsch, Dresden, Germany; Dr. K. Kücheler; AK St. Georg, Hamburg, Germany.

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