
Direct Stent Implantation Using the EXPRESS™ Coronary Stent System: Results of a Multi-Center Feasibility Study

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The aim of this prospective, multicenter, single arm study was to assess the safety and feasibility of EXPRESS™ Coronary Stent implantation in native coronary arteries without balloon predilatation. Forty-two patients with de novo or restenotic lesions were enrolled, of which 38 were eligible for analysis. The coronary lesions were predominantly complex, occurring in arteries with a mean reference diameter of 2.80 ± 0.49 mm. Technical and procedural success were achieved in 89.5% and 84% of the cases respectively. The mean minimal lumen diameter increased from 1.08 ± 0.26 mm to 2.55 ± 0.44 mm and diameter stenosis decreased from $61 \pm 7\%$ to $13 \pm 8\%$. The primary endpoint of major adverse cardiac events at 30 days was 2.6% and was limited to only one event (target vessel revascularization, nontarget lesion). No other MACE were observed during the three-month follow-up period. Based on the findings of this study, direct stenting with the EXPRESS™ Stent appears feasible and is well tolerated. (J Intervent Cardiol 2003;16:491–497)

Introduction

Within the field of percutaneous coronary intervention (PCI), coronary stenting has replaced percutaneous transluminal coronary angioplasty (PTCA) as the dominant treatment for coronary artery disease and stents have become an essential component of the interventional cardiologist's armamentarium for treating coronary artery disease.¹ Compared with PTCA alone or provisional stenting (i.e., stenting undertaken only if suboptimal results are obtained after PTCA), elective stenting results in superior clinical outcomes in the months after PTCA in a wide variety of patient subgroups and lesion types.¹

Direct coronary stenting, i.e., stent implantation without predilatation, has been proposed as a method to

reduce procedure time, decrease radiographic exposure time, and to reduce procedural costs.^{2–9} Additionally, it has been suggested that vessel injury is reduced in the setting of direct stenting and therefore, the incidence of dissection.¹⁰

The EXPRESS™ Coronary Stent System was designed to treat a wide range of vessel sizes while providing high flexibility during deployment and maintaining stent conformation to the vessel wall after implantation. This prospective, multicenter, single arm study was conducted to gather data on the safety and feasibility of the EXPRESS™ Coronary Stent System when used in the setting of direct stenting and represents the first clinical report on the EXPRESS™ Stent.

Methods

Patient Selection. Patients eligible for enrollment had ischemic coronary artery disease (CAD) in which

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a planned stenting procedure of a single de novo lesion or a restenotic lesion in a native coronary artery was indicated. For patients who had a previous percutaneous revascularization, the prior intervention had to have occurred more than 2 months from the time of enrollment. Target lesions needed to have a diameter stenosis of 50–90% and have ≤ 18 mm in length to permit a single stent to completely cover the lesion in a vessel with a reference diameter (visual inspection) of ≥ 3.0 and ≤ 4.0 mm.

Patients with the following were excluded as per the protocol: unprotected left main coronary artery disease, bifurcation lesions, saphenous vein or arterial grafts, visible intraluminal thrombus, ostial lesions, severely calcified lesions, lesions with severe angulation ($>90^\circ$ bend immediately proximal to the target lesion) or excessive tortuosity making it unsuitable for stent delivery and deployment. Patients with planned multilesion PCI (within the target vessel), severe left ventricular dysfunction (ejection fraction $< 30\%$), and contraindications to aspirin and/or ticlopidine and clopidogrel were also excluded.

The study was conducted in accordance with the Declaration of Helsinki on Biomedical Research Involving Human Subjects.¹¹ Written ethical committee approval of the protocol and informed consent was obtained prior to patients entering the study. The study protocol required that all patients receive detailed information concerning the trial from the local investigator or other authorized personnel before study entry. Written informed consent was obtained from all patients.

Device and Stent Procedure. The EXPRESSTM Coronary Stent System consists of a balloon-expandable stent premounted on a high-pressure delivery catheter. The stent is laser cut from 316L stainless steel tubing into a specific geometric pattern. The pattern consists of a multitude of radial expandable elements with varying amplitude, which are interconnected by longitudinally oriented elements. The interconnected elements are offset along the length of the stent to maintain a balance of longitudinal forces along the stent. For the purpose of this study, the EXPRESSTM Coronary Stent System was intended to provide permanent structural support and to increase arterial lumen diameters in an atherosclerotic lesion of native coronary arteries by stent implantation without balloon predilatation.

Patients were required to receive clopidogrel (75 mg/day) or ticlopidine (250 mg twice a day) at least 24 hours prior to the catheterization. If the patient

was not on clopidogrel treatment on the day of the procedure, a loading dose of 300 mg was given at least 4 hours prior to catheterization. Coronary angiography and intervention were performed according to local standard clinical practice. Following the insertion of the arterial sheath, an initial bolus of heparin was administered, and repeated as needed to maintain an activated clotting time of ≥ 250 seconds throughout the interventional portion of the procedure. After performing the preprocedure angiography, visual angiographic assessment or on-line quantitative coronary angiography (QCA) was utilized to determine lesion eligibility. An EXPRESSTM stent of sufficient length (2–4 mm longer than the shoulder-to-shoulder measured lesion length) to cover the lesion and correct diameter (a stent to distal reference vessel ratio of 1.1:1.0) was chosen from the available stent matrix. The stent was advanced over the guidewire to the target lesion site and positioned across the lesion using the two radiopaque markers on the delivery balloon catheter. If the initial attempts at direct stenting failed, investigators were instructed to remove the EXPRESSTM delivery system and perform predilatation with an undersized balloon and then reattempt stent delivery and deployment. Stents were to be deployed at pressures between the labeled nominal pressure and up to 2 atmospheres greater than nominal pressure (9–11 atmospheres). Adequate stent deployment was evaluated visually, as well as, by on-line QCA. Angiographic criteria for optimal stent expansion were achieved when the diameter stenosis within the stent was $< 30\%$ by QCA. If the angiographic appearance of the target lesion was suboptimal, investigators were obliged to perform additional in-stent post-dilatation with a high pressure noncompliant balloon of appropriate length and diameter until the target of 30% or less residual stenosis was reached. Heparin was discontinued on completion of the procedure, and the vascular sheath was removed according to institutional practice. Patients were treated with acetylsalicylic acid ≥ 75 mg/day and clopidogrel (75 mg/day) for 30 days or ticlopidine (250 mg twice a day) for at least 2 weeks. ReoPro could be used at the operators' discretion in high-risk cases (diabetes, unstable angina, etc.).

Clinical Follow-Up. At hospital discharge, patients' anginal class was assessed, an electrocardiogram (ECG) was recorded and adverse events plus cardiac medication documented. Measurements of biochemical markers (creatine kinase, CK; CK-MB; Troponin) were also performed. Patients were instructed to return to the hospital at 30 days for further eval-

uation (angina status, ECG, cardiac medications, and event documentation). They were also contacted via telephone at 3 months postprocedure to assess angina status, cardiac medications, and the occurrence of any major adverse cardiac events.

Endpoints. The primary endpoint of the study was major adverse cardiac events (MACE) at 30 days (MACE defined as death, myocardial infarction (both Q wave and non-Q wave infarctions), coronary artery bypass graft or target vessel revascularization). Secondary endpoints included procedural success (defined as successful direct stenting with a final diameter stenosis of <30% by off-line QCA at the target site, without occurrence of MACE at the time of hospital discharge), technical success (defined as successful delivery and deployment of the stent to the target lesion, without balloon rupture, embolization, guidewire fracture, or use of a device outside the treatment strategy). Other secondary endpoints included angiographic measurements (in-stent and vessel segment minimal lumen diameter and the percentage diameter stenosis postprocedure), procedure time, fluoroscopy time, anginal status at 1 month, and MACE at 3 months.

Angiographic Analysis. Coronary angiography was performed in at least two orthogonal projections chosen to optimally assess the target lesion. Identical views were obtained before and after coronary intervention following intracoronary administration of 0.1–0.2 mg nitroglycerin. All angiograms were sent to the core laboratory (Cardialysis, Rotterdam, The Netherlands) for analysis. The computer based CAAS II system was used to perform off-line quantitative analysis of angiograms as previously described.¹² Visual assessments included TIMI flow, lesion eccentricity, calcification, thrombus, lesion length, and dissection grade.

Statistical Analysis. Descriptive statistics were calculated for all relevant variables. For categorized variables, the data are presented as counts and incidence rates. For continuous variables, the data are presented as mean \pm standard deviation. The statistical analysis was performed on all 42 patients enrolled in the study. All study parameters were also evaluated in the “intention-to-treat” group (N = 38) and, according to the protocol, in a subgroup in which direct stenting was successful (N = 33). As this was a nonrandomized trial, no statistical reference to internal or external populations was made.

Results

Baseline Characteristics. From May to June of 2001, 42 patients were enrolled at 7 European Centers (see Appendix). In violation of the protocol, predilatation was performed in 4 of the 42 patients before direct stenting was attempted. These patients are not included in the “intention-to-treat” analysis as there was no intention to treat the lesion according to the protocol. Subsequent to QCA, the target lesions in these four patients were found to be unacceptable for direct stenting for various reasons (lesion eccentricity, impossibility to cross without predilatation (multiple irregularities, lesion tortuosity), a diameter stenosis more than 90%, and the investigator’s decision). The remaining 38 patients were included in the “intention-to-treat population” (Fig. 1).

Baseline demographic, clinical, and lesion characteristics for the “intention-to-treat” population, as well as for the “successful direct stenting” population, are shown in Tables 1 and 2, respectively.

Procedural Outcome. Technical success was not achieved in four additional patients. In two patients predilatation was performed, after attempting direct stenting. In the third patient the study stent would not cross the lesion and another nonstudy stent was implanted. In the last of these four patients, a study stent was delivered but not deployed since the stent appeared to be too long for the lesion, and another nonstudy stent was implanted. Therefore, per protocol technical success was achieved in 34 of 38 patients in the “intention-to-treat” population. In one patient successful direct stenting could not be confirmed by the core laboratory, as the angiogram was not available. As a result, this procedure was classified as technically unsuccessful even though, according to the judgement of the investigator, direct stenting was successfully performed. The “successful direct stenting” subgroup therefore included 33 patients. Procedural success was achieved in 32 patients as one patient in whom direct stenting was a technical success was classified by the core laboratory to be a procedural failure since the diameter stenosis after stent deployment was measured as greater than 30%.

Procedure time in both the “intention-to-treat” population and in the “successful direct stenting” group was 18 minutes (range 6–48 minutes) and the mean fluoroscopy time was 6.3 minutes (range 1.1–24.2 minutes) and 6.5 minutes (range 1.1–24.2 minutes) respectively.

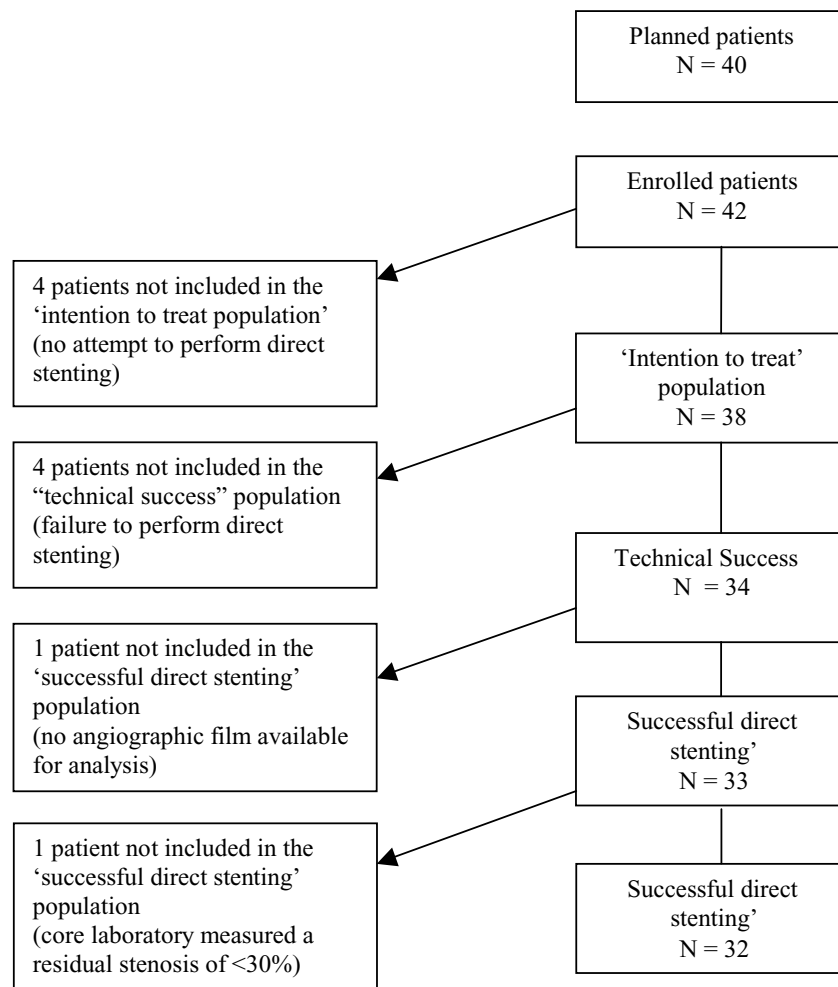


Figure 1. Analysis population.

Angiographic measurements in the “intention to treat” group showed that the mean minimal lumen diameter increased from 1.08 ± 0.26 mm preprocedure to 2.55 ± 0.44 mm postprocedure. The mean diameter stenosis decreased from $61 \pm 7\%$ preprocedure to $13 \pm 8\%$ postprocedure. The postprocedural characteristics and QCA data are shown in Tables 3 and 4.

Clinical Follow-Up. Due to a protocol violation (significant lesion in the target vessel other than the target lesion that requires treatment), one (2.6%) MACE was reported in the “intention-to-treat” population, which was a target vessel revascularization (non-target lesion), one day postprocedure. In the “successful direct stenting” group, no MACE occurred within the 3-month postprocedure follow-up period.

No MACE was reported during the same follow-up period for the four patients excluded from the analysis (excluded due to predilatation being performed before attempting direct stenting).

At baseline, all patients had either angina or silent ischemia. At one month follow-up only 4 patients (10.5%) had angina, all of which were stable. At the 3-month follow-up time point, three (7.9%) patients had stable angina.

Discussion

Publications of several studies, with patient populations varying between 61 and 3,653, have

EXPRESS™ STENT SYSTEM FOR DIRECT STENTING

Table 1. Baseline Demographic Characteristics

	Intention to Treat N = 38	Successful Direct Stenting N = 33
Age (years)	66.2 ± 9.0	66.2 ± 9.3
Male gender	31 (81.6)	27 (81.8)
History of		
MI	11 (28.9)	9 (27.3)
Q-wave MI	8 (21.1)	6 (18.2)
CABG	1 (2.6)	1 (3.0)
PCI	12 (31.6)	10 (30.3)
Stroke	5 (13.2)	5 (15.2)
Peripheral vascular disease	1 (2.6)	1 (3.0)
Risk factors		
Diabetes mellitus/insulin dependent	1 (2.6)	1 (3.0)
Diabetes mellitus/non-insulin dependent	5 (13.2)	4 (12.1)
Hypertension	21 (55.3)	18 (54.5)
Hypercholesterolemia	20 (52.6)	17 (51.5)
Previous smoker	19 (50.0)	15 (45.5)
Current smoker	6 (15.8)	5 (15.2)
Ejection fraction	61.6 ± 11.9	62.5 ± 12.4
Angina		
Unstable (Braunwald Class), total	13 (34.2)	11 (33.3)
IB	5 (13.2)	4 (12.1)
IIB	4 (10.5)	3 (9.1)
IIIB	3 (7.9)	3 (9.1)
IC	0 (0.0)	0 (0.0)
IIC	1 (2.6)	1 (3.0)
IIIC	0 (0.0)	0 (0.0)
Stable (CCS), total	20 (52.6)	17 (51.5)
1	2 (5.3)	2 (6.1)
2	16 (42.1)	13 (39.4)
3	2 (5.3)	2 (6.1)
4	0 (0.0)	0 (0.0)
Silent ischemia	5 (13.2)	5 (15.2)

described the assessment of direct stenting.²⁻¹⁰ In some of these studies, only patients eligible for direct stenting were enrolled, and in other direct stenting was compared with predilatation. The technical success of direct stenting reported in the literature is between 87% and 98%.²⁻¹⁰ Given these data, we accordingly wished to explore the use of the EXPRESS™ Coronary Stent System for direct stenting of patients with CAD.

The 90% technical success rates demonstrated in the EXPRESS™ Direct Stenting Study is similar to the results found in the literature. Furthermore, in one of the five patients in whom direct stenting was classified as a technical failure, stent length was calculated incorrectly and upon identification of the error, the study stent was removed from the guidewire and

a non-study stent of the correct length was implanted. By definition, this was a technical failure, but if this patient were to be included in the procedural success analysis, the rate of procedural success would have been 92% (34/37).

Only one patient (2.6%) experienced a MACE consisting of re-intervention of the target vessel, non-target lesion. As previously stated, this patient was enrolled in violation of the protocol exclusion criteria (presence of a significant lesion in the target vessel other than the target lesion that requires treatment). There was no reported MACE in the four patients excluded (due to conventional stent implantation) from the intention-to-treat analysis up to 3-months postprocedure. There was also no MACE in the successful direct stenting subgroup (N = 33). These numbers are similar to those

Table 2. Preprocedure Lesion Characteristics

	Intention to Treat N = 38 N (%)	Successful Direct Stenting N = 33 N (%)
Target vessel		
RCA	13 (34.2)	12 (36.4)
LAD	14 (36.9)	11 (33.3)
LCX	11 (29.0)	10 (30.3)
Lesion type (AHA/ACC)		
A	2 (5.3)	2 (6.1)
B1	11 (28.9)	10 (30.3)
B2	25 (65.8)	12 (36.6)
C	0 (0.0)	0 (0.0)
Type of lesion		
Concentric	6 (15.8)	6 (18.2)
Eccentric type 1A	16 (42.1)	15 (45.5)
Eccentric type 1B	10 (26.3)	8 (24.2)
Eccentric type 2A	3 (7.9)	2 (6.1)
Eccentric type 2B	3 (7.9)	2 (6.1)
Calcification		
Little or none	23 (60.5)	20 (60.6)
Moderate to heavy	15 (39.5)	13 (39.4)
Thrombus		
Present	1 (2.6)	1 (3.0)
Grade of perfusion (%)		
TIMI 0, TIMI 1	0 (0.0)	0 (0.0)
TIMI 2	4 (10.5)	4 (12.1)
TIMI 3	34 (89.5)	29 (87.9)
Lesion length		
Discrete (<10 mm)	27 (71.1)	23 (69.7)
Tubular (10–20 mm)	11 (28.9)	10 (30.3)
Eccentricity		
Concentric	6 (15.8)	6 (18.2)
Eccentric	32 (84.2)	27 (81.8)
Lesion contour		
Smooth	32 (84.2)	29 (87.9)
Irregular	6 (15.8)	4 (12.1)

described in the studies published by Chan, Hamon, Herz, and Wilson.^{3,6–8}

The total procedure time and radiation exposure time with direct stenting in this study were both quite low (procedure time in this study was 18 minutes, versus 32.8 minutes in the study described by Chan; radiation exposure time was 6 minutes in this study versus 6.7 minutes in Chan's study and 8.7 minutes in the study described by Figulla). The main significance of these values is the reduction of radiation exposure to patients and catheterization laboratory personnel and increased efficiency in use of the catheterization laboratory leading to a reduction in hospital costs.

Table 3. Postprocedural Characteristics

	Intention to Treat N = 38 N (%)	Successful Direct Stenting N = 33 N (%)
Thrombus Present at the treated site	1 (2.6)	1 (3.0)
Grade of perfusion		
TIMO 0, TIMI 1	0 (0.0)	0 (0.0)
TIMI 2	1 (2.6)	1 (3.0)
TIMI 3	37 (97.4)	32 (97.0)
Dissections	0 (0.0)	0 (0.0)
Procedural complications*	3 (7.9)	0 (0.0)
Additional stent in target lesion		
Reason		
DS > 50%	1 (2.6)	1 (3.0)
Ischemia and dissection type C	0 (0.0)	0 (0.0)
Dissection type D, E, or F	0 (0.0)	0 (0.0)
Other	4 [†] (10.5)	3 [‡] (9.1)
Additional lesions treated	3 (7.9)	2 (6.1)

*In two patients stent device did not cross lesion; in one patient stent size was not appropriate.

[†]Additional stents were implanted: in one patient, due to abnormal aspect distal to first stent; in another patient due to stenosis distal to first stent; in one patient due to aneurysm; and in another patient study stent was too long.

[‡]Additional stents were implanted: in one patient due to abnormal aspect distal to first stent; in another patient due to stenosis distal to first stent; and in one patient due to aneurysm.

Limitations

There are several limitations to this study including lack of randomization, small sample size, no collection of follow-up angiographic or IVUS data and a

Table 4. Quantitative Coronary Angiography (Matched Pre-Post)

	Intention to Treat N = 37*	Successful Direct Stenting N = 33
Lesion length (mm)	9.47 ± 3.53	9.68 ± 3.47
Reference diameter (mm)		
Preprocedure	2.80 ± 0.49	2.79 ± 0.51
Post-stent	2.93 ± 0.40	2.92 ± 0.42
Minimal lumen diameter (mm)		
Preprocedure	1.08 ± 0.26	1.10 ± 0.26
Post-stent	2.55 ± 0.44	2.52 ± 0.45
Diameter stenosis (%)		
Preprocedure	61 ± 7	60 ± 7
Post-stent	13 ± 8	13 ± 8
Total occlusion (N)		
Preprocedure	0	0
Post-stent	0	0

*For one patient no angiographic recordings were available.

relatively short follow-up period. However, it should be emphasized that this was a feasibility study and that the intention was only to assess the feasibility of direct stenting with the EXPRESS™ Coronary Stent System.

Recently, the TAXUS-IV trial was presented comparing the EXPRESS™ bare stent with its paclitaxel-eluting form.¹³ After nine months, the bare EXPRESS™ stent showed a markedly low TLR of 11.3% with a TVR of 12%. MACE after 9 months was 15.0% with a TVF of 14.4%. Stent thrombosis occurred in 0.8% (5/652).

Conclusions

The data from this study support the proposal that direct stenting can be performed safely with the EXPRESS™ Coronary Stent System. The technical performance and the clinical-angiographic results are in line with previously published reports on direct stenting using other devices. Additional studies including angiographic endpoints are required to fully assess use of the Express™ Coronary Stent System in direct stenting.

APPENDIX

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