Initial and Follow-Up Results of the European Seaquence™ Coronary Stent Registry

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The primary objective of the present study was to assess the feasibility and the safety of the Seaquence™ stent (CathNet-Science) deployment for the treatment of coronary artery disease and the event-free survival of patients treated with this coronary stent. The study was conducted as a multicenter, prospective, observational registry. Patients with stable or unstable angina pectoris who were candidates for percutaneous coronary intervention with elective stenting of one single de novo lesion in a native coronary artery ≥3 mm in diameter were included in the study. Clinical follow-up was performed at 1 month and 9 months. Major adverse coronary events (MACE), that is, cardiac death, myocardial infarction, and target vessel revascularization (re-PTCA or CABG), were recorded over a period of 9 months. Using this stent, a 99% in-hospital success rate was achieved. A total of 17 patients presented MACE (8.7%) during the whole follow-up period and target lesion revascularization was needed for 14 (7.1%) patients. Using multivariate analysis only some clinical parameters (patients treated for unstable angina, with a history of CABG or of female gender) were found as independent predictors of MACE after coronary stenting. Procedural related factors, angiographic characteristics, or reference diameter were not found to influence clinical outcome. Because the study was performed in patients with a high proportion of complex lesions (relative high-risk nonselected population with nearly one third calcified lesions, many long and type B2 and C lesions) we can conclude that the coronary Seaquence™ stent can be considered as a stent of reference in routine practice.
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Introduction

In the recent years, coronary stenting has gained an incredible speed of development due to the excellent immediate and long-term results obtained by its use in different settings of coronary artery disease.[1,2,3,4,5] More than 20 companies are competing for markets, making stents from different materials and with various physical properties. It is suspected that the structure and the material of the stent can influence long-term results after coronary stenting.[6,7] Recent recommendations on stent manufacturing, implantation, and utilization suggest that different steps might be respected before

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clinical unrestricted application could be delivered.[8] However, at least in Europe, several available stents used in routine practice have never been evaluated for middle or long-term clinical outcome. The primary objective of the present study was to assess the feasibility and the safety of the Seaquence™ stent (CathNet-Science) deployment for the treatment of coronary artery disease and the event free survival of patients treated with this coronary stent. For this purpose, the occurrence of all major adverse cardiac clinical events (MACE) after stent implantation were assessed in a prospective multicenter European registry.

Methods

Design. The study was conducted as a multicenter, prospective, observational registry. Patients with stable or unstable angina pectoris were selected for this study in different European centers between April 1999 and October 1999. Clinical follow-up was performed at 1 month and 9 months. Major adverse coronary events (MACE), that is, cardiac death, myocardial infarction, and target vessel revascularization (re-PTCA or CABG) were recorded over a period of 9 months.

Selection of Patients. Patients with stable or unstable angina pectoris who were candidates for percutaneous coronary intervention with elective stenting of one single de novo lesion in a native coronary artery ≥3 mm in diameter were included in the study (Table 1). Written consent was obtained for each patient. The study was conducted according to the principles of the Declaration of Helsinki.

Stent Type. The Seaquence™ stent is a stainless steel 316L tubular stent of the balloon expandable type made from a series of linked ring with a repeating «S» shape; it incorporates a system of various strut widths for homogenous stent deployment and a minimal recoil rate of <5% for all sizes. Stents are available in different lengths from 8 mm to 28 mm, in diameter from 2.5 mm to 4 mm, and are loaded on an over-the-wire semicompliant, low profile balloon delivery system with high-pressure resistance (to a rated burst pressure of 16 atm and average burst pressure of 22 atm), requiring a standard guiding catheter of 6F.

Stent Placement Procedure and Subsequent Antiplatelet Management. After stent deployment, patients received aspirin (>100 mg/day) and ticlopidine (250 mg × 2 per day) or clopidogrel (300 mg the first time and 75 mg per day during 1 month). Levels of cardiac enzymes at inclusion and at 12–24 hours after implantation were systematically collected.

Table 1. Inclusion and Exclusion Criteria

Inclusion criteria
■ Patients with stable or unstable angina pectoris
■ Patients who are eligible for coronary dilatation and stent implantation
■ Procedure on one lesion (multivessel disease only if other lesions do not require treatment)
■ De novo lesion in a native vessel
■ Written informed consent obtained
Noninclusion criteria
■ Myocardial infarction within 3 days prior to inclusion
■ Life expectancy less than 1 year or factors making clinical follow-up difficult
■ Contraindication to an emergency coronary by-pass surgery
■ Acute or chronic renal impairment
■ Severe hepatic disease
■ Intolerance or contraindication to aspirin, ticlopidine or clopidogrel drug therapy
■ Severe left ventricular failure (ejection fraction <30%)
■ Cardiogenic shock
Excusion criteria related to angioplasty
■ Intended angioplasty to more than one lesion or of a coronary by-pass graft
■ Treatment of a restenotic lesion
■ Intended angioplasty in a true aorto-ostial lesion
■ Unprotected left-main coronary artery disease
■ Very long lesion (>38 mm)
■ Bifurcating lesion or heavily calcified
■ Total occlusion (TIMI 0)

Quantitative Coronary Angiographic Measurements. Coronary angiography was performed before and after the stent deployment procedure according to a standard acquisition procedure that allowed for subsequent computer assisted-quantitative coronary angiography analysis. The quantitative analysis of the treated lesion has been carried out with the QCA-CMS Medis System (Medical Imaging System, Nuenen, the Netherlands). The analysis system determines the minimal luminal diameter (MLD), the mean reference diameter, and the percentage of stenosis at the treated site.[9] The diameter of the catheter was used to convert the images from pixels to millimeters as previously detailed. Quantitative angiographic analysis was performed in the Core Lab of the University Hospital of Caen.

Clinical Follow-Up. Clinical follow-up at 1 and 9 months and CRFs were monitored by Quintiles Company. All MACE as previously defined were systematically recorded during the on-site follow-up visits in each center. At each monitoring visit, CRFs

were inspected for completeness, accuracy, and verified against source documents.

Statistical Analysis. All categorial variables were presented as percentage with their absolute number. Continuous variables are presented as means ± SD. Event free survival distributions are estimated by using the Kaplan-Meier method. A proportional hazard model (Cox's model) was used to assess the effects of various covariates and cofactors on the event-free survival times. These variates and factors were fitted using a forward stepwise selection procedure, which excluded variables from the model unless they were significant at the 5% level. The variables assessed were: BMI, age, sex, prior myocardial infarction (MI)/PTCA/CABG, stable versus unstable angina, coronaropathy[1,2,3] (vessel disease), LVEF (< or > 40%), smoking history, dyslipidemia, diabetes, hypertension, family history of CAD, type of lesion, TIMI grade flow before and after stenting, calcification of arteries, size of dilated artery, length of stenting, CK level at hospital discharge, and outcome of stenting procedure.

Results

In Hospital Results. One hundred and ninety-six patients from 16 European centers (listed in the Appendix) were included in the study. Baseline characteristics of the study population are detailed in Table 2. Patients were mainly males (78%) and the mean age of the study population was 63 ± 10 years ranging from 35 years to 87 years. About 20% of patients were diabetic and nearly 50% of the patients were treated for acute coronary syndromes.

Table 2. Baseline Clinical Characteristics ($n = 196$)

Mean age ± SD (years)	63 ± 11
Male (%)	152 (78)
Dyslipidemia (%)	114 (58)
Diabetes (%)	38 (19)
Smoking (%)	109 (56)
Hypertension (%)	114 (58)
Familial history (%)	56 (29)
Previous MI (%)	66 (34)
Previous PTCA (%)	26 (13)
Previous CABG (%)	6 (3)
Silent ischemia (%)	20 (10)
Stable angina (%)	92 (47)
Unstable angina (%)	89 (46)

Table 3. Angiographic Characteristics

LVEF (% ± SD)	64 ± 12
Type of disease (%)	
One vessel	58
Two vessel	25
Three vessel	17
Lesion type (ACC/AHA classification) (%)	
A	23
B1	36
B2	35
C	7
Calcification in vessel dilated (%)	55 (28)
Reference diameter (mm ± SD)	
Before procedure	3.33 ± 0.42
After procedure	3.37 ± 0.42
Diameter stenosis (% ± SD)	
Before	70 ± 10
After	11 ± 7
Minimal luminal diameter (mm ± SD)	
Before	1 ± 0.38
After	3 ± 0.42
Procedure results	
Procedural success rate (%)	99
TIMI 3 after stenting (%)	100
Distribution of vessel segments stented (%)	
1. RCA	40
2. LAD	36
3. Cx	18

Clinically, nearly half of the patients had unstable angina (89 patients out of 196); the majority of these were classified, according to Braunwald classification, as class B (67 patients (75%)), the remaining as class A (15 patients) or C (seven patients).

Angiographic characteristics of the patients and technical aspects of the procedures are detailed in Table 3. In Figure 1, the cumulative distribution of MLD is shown before and after stent implantation. Mean MLD before angioplasty was 1.0 ± 0.38 mm and increased up to 3.0 ± 0.42 mm immediately after stent implantation. Mean percentage of stenosis with quantitative angiographic core lab analysis was 70 ± 10% of stenosis before dilatation with a mean percentage of residual stenosis of 11 ± 7% after stent implantation. The mean maximal pressure for stent deployment was 12.2 ± 2.3 atm. Implantation was successful for 99% of all stents. The most used stent length was 18 mm (43% of patients). During the hospital stay (mean of 4.1 ± 3.7 days) there was no death, myocardial infarction, or coronary artery by-pass grafting. One patient had a repeated PTCA. At discharge, the vast majority of patients were asymptomatic, two patients had

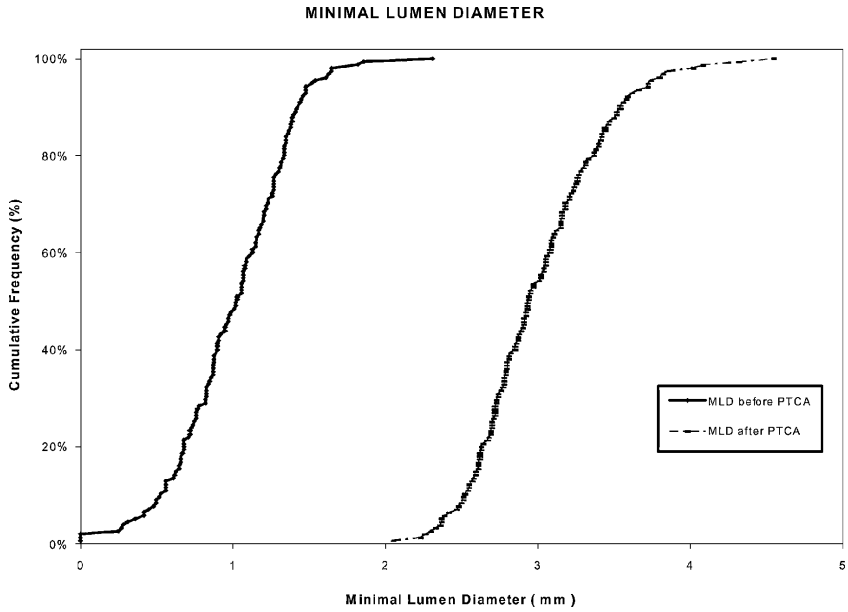

Figure 1. Minimal luminal diameter (MLD) before and after coronary stenting.

recurrent ischemia, and one had a nonserious vascular complication at the vascular access site.

Clinical Follow-Up Outcome. The follow-up time was 9 months with interim follow-up at the end of the first month after inclusion (Table 4). At 1 month, the follow-up was obtained for 97.5% of patients included; 170 (87%) were asymptomatic and one patient had presented unstable angina (classified as BII on the Braunwald scale) and other patients had stable angina. Seven patients were recorded with major adverse clinical events at this assessment: three cases of myocardial infarction and four re-PTCA.

At 9-month follow-up (available for 89% of enrolled patients), 145 (74%) were totally asymptomatic. Twenty-three patients reported stable angina well controlled by medical treatment and only 13 patients had ischemia documented with noninvasive testing at 9 months (noninvasive test realized for 87% of patients). We recorded 10 major adverse clinical events more: one MI, seven re-PTCA, three CABG (one patient had two MACE). All these data are summarized in the Table 4. The Kaplan–Meier estimate of the event free survival is given in Figure 2. A total of 17 patients presented MACE (8.7%) during the whole follow-up period and target lesion revascularization (TLR) was needed for 14 (7.1%) patients.

Analysis of the Effects of Various Covariates and Cofactors on the Event-Free Survival Time. The results of this analysis are presented in Table 5. The table shows the parameter estimates for the final model selected. Only three factors had a significant effect on the event-free survival time. These are the patients' sex, history of CABG, and type of angina (stable/unstable). The risk ratio in the table indicates the relative risk of instantaneous MACE for different levels of the three factors.

Table 4. Major Adverse Clinical Events

	Hospital Discharge	One month Follow-Up	Nine months Follow-Up
Death	0	0	0
Acute myocardial infarction	0	3	1
Re-PTCA	1	4	7
CABG	0	0	3
Patients with MACE	1	7	10

Discussion

These results clearly demonstrate that the use of the Seaquence^{TM} coronary stent is associated with a high, immediate success rate and with excellent long-term clinical outcome. The 99% in-hospital success rate achieved with this stent compares favorably with

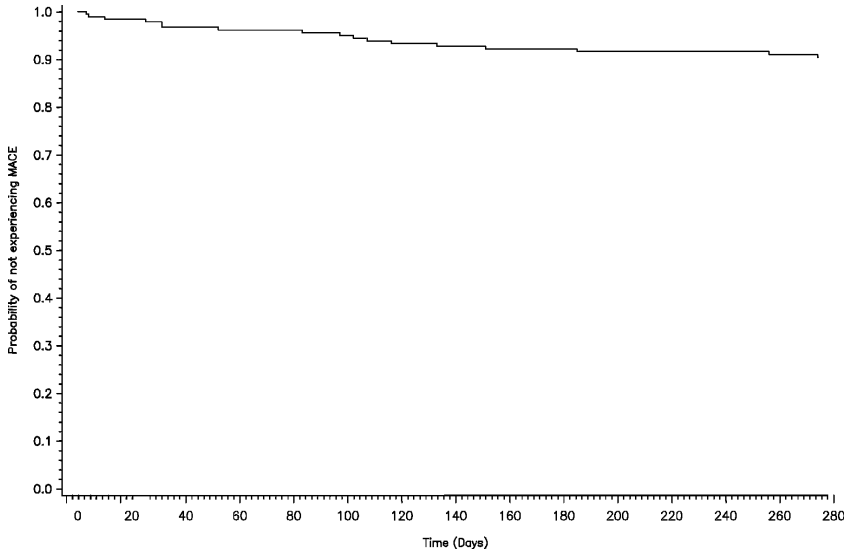

Figure 2. Event-free survival at 9 months.

the 94–98% reported for the Palmaz-Schatz stent in BENESTENT I,[1,2] II,[3,10] and START[11] trials, as well as in other trials (ISAR-STEREO,[6] STRESS[12])) involving different types of stents.[7,13,14] The majority of clinical data available today is generated by the analysis of studies using Palmaz-Schatz stent. Recent trials with new devices (AVE stent, NIR stent) show similar high success rates.[15–17] Our registry includes a relatively great number of patients with unstable angina or high-risk lesions (type B2 and C) present in more than 40% of the patients. In routine practice lesions and patients meeting Benestent/STRESS criteria account for only 25% of the patients. Given that in previous studies lesions have been highly selected with exclusion of high-risk lesions the results obtained with the Seaquence™ stent are very promising. During the initial in-hospital follow-up in our study, no death, MI, or CABG was recorded, but only one re-PTCA was recorded. During 1-month and 9-month follow-ups, the results are also encouraging; there was no death reported in this period and other MACE are at an acceptable low level: four patients with MI, three with CABG, and 11 re-PTCA. All these data are at least similar with recent data reported by other investigators.[17,18] The TLR of 7.1% is also very promising in a rather high-risk study population.

Table 5. Survival Analysis: Multivariate Analysis Using a Cox Proportional Hazards Model

	Wald chi-squared Statistic	Risk Ratio	P-Value
Patient sex	0.559	0.208	0.0050
CABG	1.092	8.107	0.0552
Stable/unstable angina	0.773	7.767	0.0080

In the present study, only some clinical parameters (patients treated for unstable angina, with a history of CABG or of female gender) were found as independent predictors of MACE after coronary stenting. Procedural related factors, angiographic characteristics, or reference diameter were not found to influence clinical outcome.

There are some limitations to the present study. As in many other studies not all patients returned to follow-up, but data from other studies suggested that this is a subgroup of patients, which are in a relatively good condition. There are also some concerns about angiographic follow-up. In Benestent II, trial of conventional PTCA versus stent placement, one half of each group had angiographic follow-up, and one half had clinical follow-up alone.[11,19] In patients undergoing angiographic follow-up, the incidence of TLR was greater (14.4 vs 9.1). In the present study, we decided to avoid systematic angiographic follow-up associated with unjustified TLR as previously discussed and recently confirmed with 1.7 times higher reintervention rate associated with planned follow-up angiography without improvement of late survival;[20] we considered clinical status more important for the patients than rigid angiographic criteria.

Conclusion

There is evidence from several published trials that elective stenting of de novo lesions in native coronary arteries improve the clinical outcome. This improvement has been clearly demonstrated with the Palmaz-Schatz stent. Before these conclusions could be extrapolated to other types of stents, well-conducted studies must be systematically mandated.

In the present study, the Seaquence™ coronary stent has been proved to be safe and effective in the treatment of coronary atherosclerotic lesions; it can be easily deployed with nearly 100% success rate. At 1-month and 9-month follow ups there are no death reported and very few MACE (especially low rate of CABG and myocardial infarction). Because the study was performed in patients with a high proportion of complex lesions (relative high-risk nonselected population with nearly one third calcified lesions, many long and type B2 and C lesions excluding chronic total occlusions) we can conclude that the coronary Seaquence™ stent can be considered as a stent of reference in routine practice.

Appendix

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Conflict of Interest Statement

The data were analyzed, presented, and reported independently of CathNet-Science. The University of Caen has received a grant from CathNet-Science for quantitative coronary angiography measurements. Investigators received honoraria for inclusion of patients in the registry. Monitoring was ensured through Europe by Quintiles and data directly transmitted to the steering committee.

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