First clinical experience with a new flexible low profile metallic stent and delivery system

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We report the first clinical use of a new, flexible, low profile, balloon-expandable metallic stent and delivery system (ACS Multi-Link®). The stent, designed in an effort to overcome the shortcomings of existing stents, has a low metal mass, superior scaffolding properties and favourable rheological characteristics. It also allows side branch access and is delivered via an innovative stent catheter. Ten stents were used to treat 10 patients with threatened abrupt closure after balloon angioplasty. All were successfully deployed, with a satisfactory angiographic result in nine. The patient with an unsatisfactory angiographic result proceeded to uneventful coronary bypass surgery. There were no other procedural or in-hospital complications. One patient developed restenosis and one had an intra-cerebral bleed following a fall. This new stent thus appears safe and effective when used to treat threatened abrupt closure. Due to its favourable characteristics, it may be well suited for reduction of restenosis. A multi-centre European registry (WEST) for primary implantation in 100 consecutive patients has now been completed.

Key Words: Stents, threatened abrupt closure, coronary angioplasty.

Introduction

Percutaneous transluminal coronary angioplasty is an effective treatment for selected patients with symptomatic coronary artery disease. However, despite major improvements in angioplasty technology and operational techniques, certain limitations remain. Firstly, abrupt coronary closure complicates between 2% and 8% of cases and is the major cause of in-hospital morbidity and mortality[1-3]. Secondly, long-term success is compromised by the occurrence of restenosis in approximately 30% of patients within the first 6 months[4,5].

Intracoronary stents were developed with the aim of preventing abrupt closure and restenosis after angioplasty, thus improving the safety and success of the technique[6], but stent technology is still in its infancy and all the currently available stents exhibit important shortcomings. However, a new metallic stent developed by ACS (Advanced Cardiovascular Systems, Inc., Santa Clara, California) has been designed to incorporate the most desirable positive features whilst avoiding the negative features of currently available stents. In animal studies the stent was accurately and safely deployed in 26 canine arteries with no delivery failures. Angiographic follow-up revealed Thrombolysis In Myocardial Infarction (TIMI), grade 3 angiographic patency at 3 days (n = 5), 2 weeks (n = 5), one month (n = 5), 6 months (n = 10) and one year (n = 1). There were no deaths and no acute thrombotic events[8]. We present the results of the first clinical use of the ACS Multi-Link® stent[7] and compare specific features of the new stent with those of existing stents.

Methods

The stent

The new product is a flexible, low profile, balloon-expandable stent made of stainless steel. It is comprised of individual corrugated rings, interconnected by a number of bridges (Fig. 1), comes in different lengths and sizes and does not shorten significantly with expansion. It is mounted on the balloon of a modified coronary dilatation catheter. The PE 600® balloon is wrapped in an innovative fashion and is covered by a protective elastic membrane. Proximal and distal radiopaque markers on the balloon identify the position of the mounted stent. A retractable sleeve covers the entire dilatation catheter, including the stent and balloon, and has a platinum marker at its most distal point (Fig. 2). Sleeve withdrawal can be performed with one hand by means of a specially designed manipulator[7] (Fig. 3).
A new stent and delivery system

Figure 1 The ACS Multi-Link® stent consisting of a number of balloon expandable corrugated rings which are linked by bridges. The stent is shown in the unexpanded (upper part) and expanded state (lower part).

Figure 2 ACS Multi-Link® stent mounted on an elastic membrane which covers the delivery balloon. The stent is protected by a retractable sheath, the distal extremity of which has a radiopaque metal marker for identification purposes.

Figure 3 Stent delivery catheter with integrated manipulator for sheath retraction. The stent can be freed from the protective sheath by a one-hand action by pressing the security button in the upper mid portion of the manipulator.

guiding catheter of internal diameter 0.080 inch, an over-the-wire catheter system capable of being steered, and standard angioplasty techniques. In the event of an abrupt closure or a threatened abrupt closure following balloon angioplasty, an attempt to improve the angiographic appearance by prolonged balloon inflation was usually performed before a stent was deployed. Once the decision was made to proceed to stent implantation, the standard balloon dilatation catheter was removed using the routine exchange technique. The stent delivery system was then introduced via the guiding catheter and advanced down the coronary artery over the angioplasty guide wire. Correct positioning of the stent was aided by the radiopaque markers at the proximal and distal ends of the balloon, which also indicate the proximal and distal ends of the stent. Once positioned, the protective sleeve was retracted and the platinum marker, previously seen under fluoroscopy at the distal tip of the catheter, was seen to lie proximal to the balloon markers (Fig. 2). Accurate positioning of the stent was again confirmed prior to its deployment. The stent was expanded with a single balloon inflation to 7 atmospheres for 30 s and following stent deployment, the delivery system was removed. Additional balloon inflations with a standard angioplasty balloon catheter were performed within the stent as necessary to achieve a satisfactory angiographic results (stent:artery ratio of 1.0—1.1:1.0).

Patient selection

Patients with an unsatisfactory PTCA (abrupt closure, threatened abrupt closure or significant dissection with persistent stenosis greater than 50% following balloon angioplasty of a native coronary artery) were considered for entry into the study. For this preliminary study, only the 15 mm stent mounted on a 3.5 balloon was available. Hence only patients with target lesions of less than 15 mm in length, in vessels 2.75 mm to 3.25 mm in diameter, were suitable for inclusion.

Procedure

Percutaneous transluminal coronary angioplasty was performed via the femoral approach using an 8 Fr.

Medication

All patients received aspirin (150 mg) and a calcium channel antagonist within the 24 h prior to the angioplasty procedure. At the start of the angioplasty, heparin 15 000 IU was given intra-arterially. Prior to stent implantation, an infusion of Dextran 40 was commenced (200 ml over 30 min followed by 50–100 ml . h⁻¹). The activated clotting time was checked and the stent was...
not deployed until the activated clotting time was greater than 300 s. Additional boluses of heparin were given as necessary to maintain the activated clotting time >300 s throughout the procedure. Immediately prior to stent delivery, 1–2 mg of intracoronary isosorbide dinitrate were given. Following the procedure, patients were maintained on aspirin, a calcium channel antagonist and dipyridamole (200 mg per day). The Dextran infusion was continued until a total of 500–1000 ml had been given. All patients received heparin for at least 5 days. Once effective oral anticoagulation was obtained (international normalized ratio (INR) >2-5), patients were switched from intravenous heparin to subcutaneous low molecular weight heparin (5000 U b.d.). Patients were discharged once stable oral anticoagulation was established (INR 2-5–3-5).

Statistical analysis

Values are expressed as mean ± SD.

Ethics

The study protocol was approved by the Hospital Ethics Committee. All patients were potential candidates for coronary artery bypass surgery and gave informed written consent to the implantation of the ACS stent in the event of a suboptimal result following percutaneous transluminal coronary angioplasty.

Results

Patient population

Between 8 July 1993 and 25 August 1993, the new stent was implanted in 10 out of 62 coronary angioplasty procedures. Each patient received a single stent. Six patients had single-vessel disease and four had multi-vessel disease. All patients had good left ventricular function (left ventricular ejection fraction ≥60%). The target lesion was in the left anterior descending vessel in four patients (40%), the circumflex artery in two (20%), and the right coronary artery in four (40%). No patient had previously undergone angioplasty to the same site. The mean luminal diameter reduction prior to the procedure was 88 ± 8%, as assessed by visual inspection in standard orthogonal views. The lesion characteristics were classified using the American College of Cardiology/ American Heart Association Task Force classification. Two lesions (20%) were type A, five (50%) type B and three (30%) type C.

Indication for stent implantation

All 10 patients received a stent for suboptimal results with a visible coronary dissection following balloon angioplasty. The dissections were classified according to the National Heart, Lung, and Blood Institute classification for intimal tears. Nine (90%) were of type B (parallel tracts or double lumen separated by a radiolucent area during contrast injection with minimal or no persistence after dye clearance) and one (10%) type C (contrast occurring outside the coronary lumen with persistence of contrast in the area after clearance of dye from the coronary lumen). A suboptimal angiographic result was associated with coronary dissection in all 10 patients (residual stenosis post balloon dilatation ≤40%). Patients were thus considered to be at high risk of abrupt vessel closure.

Stent deployment

Stent deployment was accomplished successfully in all patients in so far as the stent was accurately delivered to the target location, subsequently expanded and the
A new stent and delivery system

Follow-up angiogram of a stent implanted in a bend in the circumflex coronary artery. The flexible stent conforms well to the tortuous anatomy. There is no significant intimal hyperplasia.

delivery catheter removed. In one patient this required two attempts: stent delivery was unsuccessful on the first occasion as it was not possible to cross the lesion with the stent delivery system. The whole delivery system was successfully withdrawn and the lesion further dilated with a conventional balloon catheter. On second passage the stent delivery system crossed successfully and stent deployment was achieved. Following deployment, additional balloon inflations within the stent were performed in three patients. Balloon rupture at inflation pressures of between 5 and 12 atmospheres occurred in two of these.

Angiographic results

A satisfactory angiographic result was obtained in nine patients, in whom stenting completely resolved the intimal dissection and reduced the residual stenosis to <20%. Figure 4A illustrates the effect of stenting in one such patient. The baseline angiogram in this 66-year-old man with Canadian Heart Association grade 3 angina revealed a tight, proximal left anterior descending coronary artery lesion in a bend overlying the origin of the first septal branch. After balloon dilatation, a type B dissection was seen with extravasation of contrast outside the vessel lumen and a residual diameter stenosis of 80%. Following stent implantation, the intimal dissection was no longer visible and the luminal diameter was no different from the reference diameter. The patient with an unsatisfactory result was a 68-year-old man with grade 3 angina and long-term steroid medication for asthma. He had disease of both the left anterior descending artery and its diagonal branch. The lesion in the left anterior descending artery was attempted first but following balloon dilatation a type C dissection was visible in the proximal vessel. A stent was successfully deployed at this site but on subsequent angiography the dissection had extended distally beyond the stent. Attempts to further dilate within the stent and to improve the angiographic appearances of the distal dissection failed, due to repeated balloon rupture.

Complications

The patient with the unsatisfactory angiographic result was asymptomatic with TIMI grade 3 flow down the distal vessel, but it was decided to proceed to coronary artery bypass surgery the same day in view of the residual dissection and additional coronary artery disease. The surgery was uneventful and the postoperative electrocardiogram showed no new Q waves. The patient made an uncomplicated recovery. Overall, there were no deaths, no evidence of myocardial infarction (as determined by electrocardiographic changes and cardiac enzymes), no subacute stent thrombosis and no major bleeding complications prior to discharge. The mean hospital stay was 6 ± 3 days (range 4 to 12 days) including the surgical patient.

Follow-up

One patient (No. 2) developed intra-cerebral bleeding following a fall at his home 12 days after the procedure. The day before the accident, his international normalized ratio (INR) was above the optimal therapeutic range. The patient retained a neurological deficit. One patient (No. 8) complained of recurrent angina 6 weeks after the procedure and had PTCA for a 90% soft within-stent restenosis at 10 weeks. He has remained free of symptoms ever since. All others had a follow-up angiogram at 6 months with views identical to the implant procedure (Fig. 4C). No significant angiographic restenosis could be detected.

Discussion

Abrupt closure following balloon angioplasty is associated with major complications. Simpfendorfer et al.[1] studied a group of 32 patients with abrupt closure of whom 41% required coronary surgery and 43% suffered Q-wave myocardial infarction. Ellis et al.[9] examined 140 similar patients and reported an in-hospital mortality of 3%. Fifty-five percent of patients underwent coronary surgery and 81% sustained some evidence of myocardial damage. Abrupt closure is usually caused by coronary dissection. Moreover, patients with coronary dissection but without abrupt closure may develop this complication after leaving the catheterization laboratory[1,2]. In a study of 3500 consecutive elective coronary
angioplasty procedures, the strongest predictor of a major complication was the appearance of an angiographically visible intimal dissection. Such dissection was associated with a 6.5-fold increase in the risk of a major complication (death, emergency coronary surgery or myocardial infarction). Both intimal dissection and residual stenosis after balloon angioplasty are independent predictors of abrupt closure. Recently, these patients with 'threatened' abrupt closure have been treated by intracoronary stenting in an attempt to reduce ischaemic complications. Coronary stents provide an intravascular scaffold capable of sealing dissection flaps and reducing the residual stenosis after balloon angioplasty. The Palmaz-Schatz stent (Johnson & Johnson) with more than 100,000 stents having been implanted worldwide. By far the most frequently used stent until now is the Palmaz-Schatz stent covered by a retractable sheath. This stent is a slotted tube stent and is either manually crimped onto a standard balloon catheter before use or supplied on a stent delivery system. The main disadvantages of this design. The Strecker stent, also made of tantalum and thus radiopaque, is formed of a network of wires akin to chicken-fencing. The stent is designed to combine flexibility with ease of placement. The flexible balloon-expandable stents (Gianturco-Roubin, Wiktor, Strecker) were designed to combine flexibility with ease of placement. None of them, however, is supplied with a protective sheath to prevent damage to the stent and embolization from the carrier balloon and they all suffer from reduced resistance to external radial forces leading to recoil after placement. This is important as the initial luminal gain after stenting appears to determine the amount of restenosis. All flexible coil stents have large gaps between wires. The advantages of the Gianturco-Roubin stent are its flexibility and the fact that it does not shorten during expansion. Its disadvantages are its recoil and relatively loose geometry. The flexible balloon-expandable stents are the weakest predictor of a major complication could be attributed to the early learning curve of implantation strategy and management errors.

**Stenting for abrupt closure and threatened abrupt closure**

Most clinicians have grouped together the results of stenting for abrupt closure with those for threatened abrupt closure. Comparisons between different studies and various stents should, however, be treated with caution as the patient populations vary and the definitions used are inconsistent. Randomized comparative trials have yet to be performed. Allowing for these limitations, our results using the ACS MultiLink stent for threatened abrupt closure are similar to the published series with alternative stents. Stent deployment was successful in all patients except one who had a residual dissection distal to the stented area and in whom surgery was considered the most prudent option. In-hospital stent thrombosis did not occur. While this is very encouraging the numbers studied were small.

**Positive and negative features of the various types of metallic coronary stents**

A number of technological problems have been experienced with existing intracoronary stents

**The Palmaz-Schatz stent**

By far the most frequently used stent until now is the Palmaz-Schatz stent (Johnson & Johnson) with more than 100,000 stents having been implanted worldwide. This stent is a slotted tube stent and is either manually crimped onto a standard balloon catheter before use or supplied on a stent delivery system. The main disadvantages of this stent are its lack of flexibility, its shortening with expansion, and the fact that side branch access is almost impossible. The design most frequently used has two articulated segments joined by a single filament in order to increase its flexibility. A new spiral articulation with reduced flexibility is now in clinical use. Successful deployment can be achieved in about 95% of patients. Failure of stent delivery is more common in tortuous vessels, target lesions located at a bend point and target lesions in the circumflex artery, and when there is evidence of dissection after the initial angioplasty. In such cases, the operator is forced to withdraw the stent-loaded balloon, resulting in stent embolization in up to 3% of patients. Johnson & Johnson manufactured their stent delivery system in an attempt to circumvent this problem. This consists of a ready mounted Palmaz-Schatz stent covered by a retractable sheath. The sheath protects the stent during its passage through the guiding catheter and proximal artery and is withdrawn once the stent is positioned. Experience has shown, however, that only a minority of stents are well deployed using the stent delivery system and that further dilations within the stent are usually necessary using a different balloon. Studies with the original articulation have suggested that restenosis is likely to develop in the gap.

**The self-expanding stent**

The self-expanding mesh stent (Wallstent, Medinvent SA) was the first stent to be used in human coronary arteries and although this stent has been on hold for coronary use since 1990 its design does have certain advantageous features, namely its flexibility and length. The self-expanding stent also has an excellent expansion ratio, allowing 1.5 mm delivery devices to carry 6.5 mm stents. Its disadvantage is that the stent shortens with expansion making precise placement difficult, and side branch access impossible. Some of the earlier studies have reported a prohibitively high rate of stent thrombosis, but our own experience suggests that this complication could be attributed to the early learning curve of implantation strategy and management errors.

**The flexible balloon-expandable stents**

These stents (Gianturco-Roubin, Wiktor, Strecker) were designed to combine flexibility with ease of placement. None of them, however, is supplied with a protective sheath to prevent damage to the stent and embolization from the carrier balloon and they all suffer from reduced resistance to external radial forces leading to recoil after placement. This is important as the initial luminal gain after stenting appears to determine the amount of restenosis. All flexible coil stents have large gaps between wires. The advantages of the Gianturco-Roubin stent are its flexibility and the fact that it does not shorten during expansion. Its disadvantages are its recoil and relatively loose geometry. These two factors, combined with the high wire profile (diameter 150 μm), may be the cause of the relatively high restenosis rate. The advantage of the Wiktor stent is that the stent is made of tantalum and is thus radiopaque. Limited structural support and relatively thick wires with large gaps (similar to the Gianturco-Roubin stent) are the disadvantages of this design. The Strecker stent, also made of tantalum and thus radiopaque, is formed of a network of wires akin to chicken-fencing. The stent is
flexible and has relatively small gaps between the wires. However, this stent has the disadvantage of considerable recoil and there seems to be an increased risk of stent thrombosis, probably attributable to a combination of wire crossings and recoil.

The new ACS Multi-Link® stent and delivery system
This new metallic stent and delivery system is designed to reduce shortening during expansion and combine easy side branch access, flexibility, low metal surface and low strut thickness (approximately 50 μm compared with 76 μm for the original Palmaz-Schatz stent, more for the new models) with good structural support and easy, safe delivery. The stent expands only due to its innovative delivery balloon wrapping, combined with a computer-designed stress distribution in the bend points. In this pilot study, the stent delivery system readily negotiated tortuous vessels and was successfully deployed in a bend in the circumflex artery (Fig. 5). There was no failure of the stent delivery system. When indicated, the whole delivery system was successfully retracted and the stent correctly deployed on the second attempt following further balloon dilatation of the lesion. There were no instances of the delivery balloon rupturing. Following stent deployment, additional balloon inflations within the stent were attempted in three patients. This, however, resulted in balloon rupture in two of the three patients. The probable explanation for this was that the passage of the balloon catheter through the very flexible stent in a severely tortuous vessel displaced a proximal strut which then pierced the balloon. The geometry of the terminal struts has been slightly modified since this study was carried out and no further problems have arisen. In this pilot study we were limited to a maximum balloon inflation pressure of 7 atmospheres for stent deployment. Higher inflation pressures with the delivery balloon are now used and may obviate the need for further balloon crossing after the initial deployment.

Conclusions
The new ACS Multi-Link® stent and delivery system appears safe and effective when used to treat threatened abrupt closure and the results of long-term follow up are encouraging. This new stent design overcomes some of the shortcomings of existing stent technology. Much larger studies are now needed to confirm these early but favourable clinical results. A multi-centre registry (West European Stent Trial (=WEST)) for 100 primary implantations of the ACS Multi-Link® stent system is now in the process of being evaluated.

References
