# Eluting stents: an effective, promising solution?

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**Recent studies with eluting stents showed encouraging results in preventing in-stent restenosis. We report a case of a patient in whom the implantation of carbon-coated and eluting stents in two different vessels was associated with different angiographic results.**

**A diabetic hypertensive 67-year-old woman with an acute inferior myocardial infarction underwent direct coronary angioplasty on the right coronary artery with the implantation of two carbon-coated stents. In view of the severity of an additional lesion of the left anterior descending coronary artery and diabetes, coronary angioplasty and stenting with an eluting stent was performed in this vessel.**

**Five months later the patient presented with acute pulmonary edema and an increase in troponin I levels. A new coronary angiography showed a long subtotal in-stent restenosis of the right coronary artery, whereas the left anterior descending coronary artery was normal. Our case report suggests that eluting stents should be considered a precious and effective tool in preventing in-stent restenosis.**

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## Introduction

Despite technical advancements in devices, restenosis is the most important long-term limitation of stent implantation for coronary artery disease[1].

Although in ideal coronary lesions in-stent restenosis (ISR) rates are 10-20%, the real ISR rates are much higher (30-60%), occurring in patients with complex lesions, in diabetic patients or after percutaneous treatment of ISR[2].

The rationale of the most recent approaches to restenosis, a particularly refractory form of neointimal proliferation (e.g. brachytherapy and immunosuppressive agents), arises from the similarity between tumor cell growth and the proliferation which characterizes intimal hyperplasia[3].

Recently, some studies with drug-eluting stents containing the immunosuppressive agent sirolimus and the antimitotic paclitaxel have shown encouraging results in preventing ISR with no difference in adverse effects when compared to standard stents[4-6].

We report a case of a patient in whom the implantation of carbon-coated and eluting stents in two different vessels was associated with different angiographic results at 5 months.

## Case report

In August 2002, M.M., a 67-year-old female with an acute inferior myocardial infarction was referred to our catheterization laboratory for direct coronary angioplasty within 6 hours of symptom onset. Her past medical history was characterized by insulin-dependent diabetes mellitus and mild hypertension. The patient referred recurrent chest pain at rest and on minimal exercise in the week before admission.

At admission in the cath-lab, the ECG showed sinus bradycardia with a 3 mm ST-segment elevation in the inferior leads and a 2 mm ST-segment depression in the anterior leads. At physical examination the patient was in Killip class I.

Coronary angiography revealed an acute occlusion of the dominant right coronary artery (RCA) in its mid segment (Fig. 1, left panel), and a long (> 15 mm) subtotal mid left anterior descending (LAD) stenosis (Fig. 1, right panel). At quantitative angiographic analysis, the basal reference vessel diameter of the LAD was 2.42 mm, the lesion length was 12.45 mm, and the stenosis was 97.47%.

There were no lesions on the left circumflex artery. A collateral circulation from the left coronary artery to the distal part of the RCA was present.

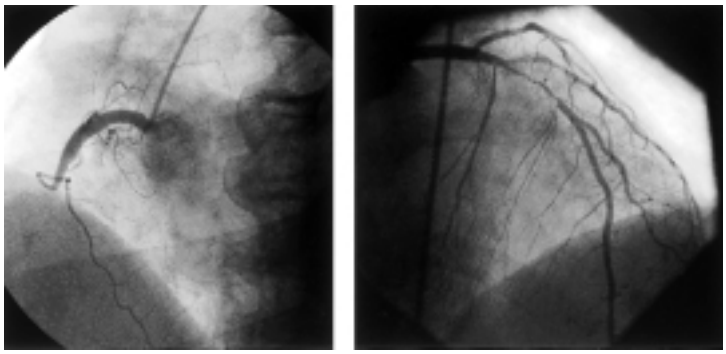

**Figure 1.** *Coronary angiography showed an acute occlusion of the dominant right coronary artery in its mid segment* (left panel)*, and a long (> 15 mm) subtotal mid left anterior descending coronary stenosis* (right panel).

The patient was pre-treated with i.v. aspirin 500 mg and weight-adjusted heparin (70 U/kg bolus to an activated clotting time > 250 s).

Direct coronary angioplasty was performed on the RCA: the guidewire was easily advanced in the occluded portion of the RCA and after the partial reopening the vessel showed widespread disease with several stenoses in the mid and distal segments. After pre-dilation with a 3.0/20 mm-long balloon, two carbon-coated stents (Sorin Biomedica, Vercelli, Italy, 3.5 mm diameter, 32 mm long; Sorin Biomedica, Italy, 3.5 mm diameter, 12 mm long) were deployed overlapping the distal and the proximal markers of both stents and expanded at high pressure (14 atm). At the end of the procedure, a good angiographic result in the mid and distal segments of the RCA was accompanied by TIMI 3 distal flow. At quantitative analysis the stenosis in the RCA was 12.73%.

In view of the severity and length of the mid LAD lesion and owing to the presence of diabetes, coronary angioplasty with balloon pre-dilation and stenting was performed even in this vessel. In particular, we performed two balloon inflations at 6 and 8 atm respectively with a 2.5 × 20 mm long balloon. Thereafter, we implanted an eluting stent (sirolimus, Cypher Cordis 3.0/33 mm long) able to cover the previously dilated segment in its entirety with a good angiographic result as confirmed by quantitative analysis (Fig. 2, right panel) which documented a residual stenosis of 8.1%.

The hospital course was uneventful and the patient was discharged 6 days later with a left ventricular ejection fraction of 45% associated with moderate mitral regurgitation. She was prescribed lifelong aspirin (325 mg daily), ticlopidine (250 mg twice daily) for 6 months, carvedilol, ACE-inhibitors, and insulin.

Five months later, in January 2003, the patient was again admitted to our hospital because of an acute pulmonary edema associated with an increase in plasma troponin I levels.

A new coronary angiography showed a long subtotal ISR of the RCA (Fig. 3, left panel); the LAD and the left circumflex artery were normal (Fig. 3, right panel). In particular, no angiographic images of intimal proliferation were detectable at the site of implantation of the eluting stent in the mid LAD.

Intravascular ultrasound (IVUS) (Fig. 4) confirmed an impressive in-stent proliferation in the RCA and the lack of intimal proliferation of the LAD (Fig. 5). Quantitative angiographic analysis showed a significant late loss (1.93 mm) in the stented segment of the RCA and a late loss of 0.54 mm in the stented segment of the LAD.

The RCA was again successfully treated by several inflations with a 3.5/10 mm long cutting balloon.

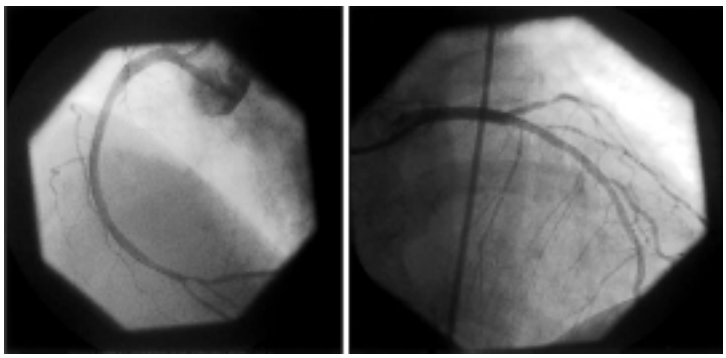

**Figure 2.** *At the end of direct coronary angioplasty on the right coronary artery a good angiographic result in the mid and distal segments of this vessel was associated with TIMI 3 distal flow* (left panel). *After eluting stent implantation in the mid left anterior descending coronary artery, a good angiographic result was obtained* (right panel).

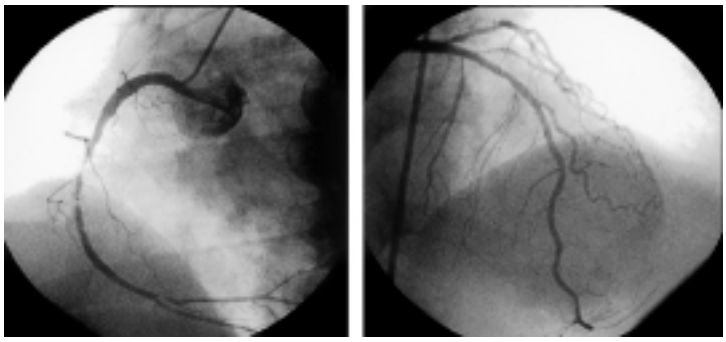

**Figure 3.** *New coronary angiography (January 2003) showed a long subtotal in-stent restenosis of the right coronary artery* (left panel). *The left anterior descending coronary artery was normal* (right panel). *In particular, no angiographic images of intimal proliferation were detectable at the site of eluting stent implantation in the mid left anterior descending coronary artery.*

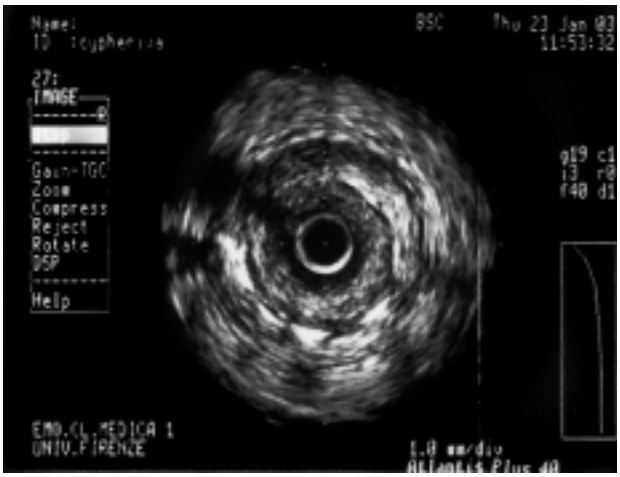


**Figure 4.** *Intravascular ultrasound confirmed an impressive in-stent proliferation in the right coronary artery.*

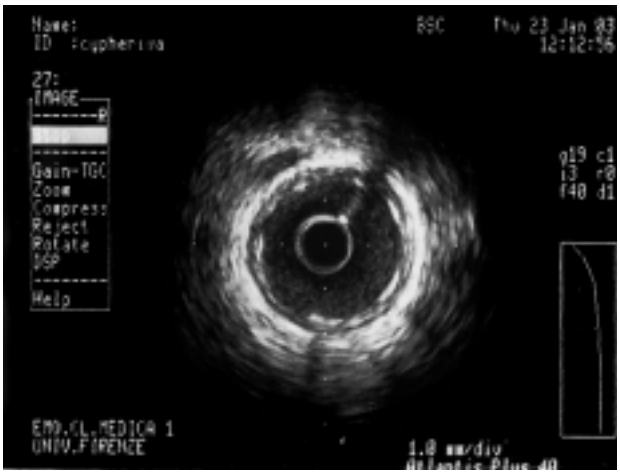


**Figure 5.** *Intravascular ultrasound confirmed the lack of intimal proliferation in the left anterior descending coronary artery.*

The procedure was uneventful and the patient was discharged 3 days later on lifelong aspirin (325 mg daily), ticlopidine (250 mg twice daily) for almost 6 months, ACE-inhibitors, carvedilol, and insulin.

## Discussion

Since the introduction of coronary angioplasty by Gruntzig, the only widely accepted means of reducing coronary restenosis has been the implantation of coronary stents[7].

Restenosis is a complex process involving both mechanical and biological mechanisms[8-10]. It has been demonstrated that stenting reduces the mechanical components of restenosis (elastic recoil and negative remodeling), but it stimulates the cellular mechanisms leading to ISR. Poor results have been generally obtained with mechanical and radiation-based treatments in all types of ISR[11-16]. Thus, the prevention of ISR appears better and more rational than treatment and, in the last years, the concept of using stents coated with agents that could potentially inhibit neointimal hyperplasia has emerged.

Stent coatings can be divided into two categories: biocompatible materials and drug-eluting coatings. Biocompatible materials currently under investigation are thought to be less thrombogenic and inflammatory and are thereby able to reduce neointimal hyperplasia. These materials include inert coatings such as carbon, gold, silicon carbide, and phosphorylcholine. Drug coatings include drugs such as heparin, corticosteroids, and antimitotic agents. These materials have been tested in animal and human studies with variable results. Both in animal and in human studies, stents coated with phosphorylcholine, heparin and corticosteroids do not exhibit a significant antiproliferative effect, whereas stents eluting antimitotic agents such as paclitaxel and sirolimus show a significant inhibitory effect on neointimal hyperplasia. There are no published animal studies evaluating stents coated with other inert materials, such as gold and silicon carbide. In human studies, gold-coated stents have been found to increase restenosis to a greater extent than uncoated stents[4,17-24].

In our case report, 5 months after the first procedure, we observed an ISR type III-IV in the RCA previously treated with two Carbostents and the absence of ISR in the LAD treated with a rapamycine-eluting stent.

The Carbostent is a non carbon-coated stent characterized by a turbostatic carbon coating with an innovative multicellular design that should provide a high thromboresistance and improved biocompatibility. Experimental results in porcine coronary arteries showed minimal early platelet deposition and mild-long term neointimal hyperplasia and the absence of an inflammatory response after Carbostent implantation[25]. Few data are so far available on Carbostents in humans. Antoniucci et al.[26] observed that Carbostent implantation in native coronary arteries is associated with a low rate of 6-month restenosis in patients with stable and unstable angina. On the other hand, we implanted a Carbostent during acute myocardial infarction, which is a different clinical setting.

Moreover, several variables are known to increase the risk of ISR:

• individual risk factors: diabetes, a history of prior ISR, genetic factors, allergic reactions to the stent components;

• procedure-related factors: greater length of the stent, number of stents used, lesions in small or in chronically occluded vessels, at the vessel ostium, into the vein graft, and the post-procedural minimum lumen diameter achieved[7].

Our patient is diabetic and diabetes is a well-known individual risk factor associated with greater restenosis after successful angioplasty. In fact, diabetic patients exhibit a high propensity to thrombosis since hyperglycemia is associated with endothelial dysfunction, accelerated platelet deposition and overexpression of several growth factors[27,28].

However, in our report, the different results between the two vessels obviously cannot be determined by different individual risk factors.

With regard to procedure-related factors, the stents in the RCA were longer than the eluting stent in the LAD but the vessel diameter was greater in the RCA than in the LAD. Besides, IVUS performed during the second angiography showed a correct ratio between the vessel and stent-diameter and a correct apposition of the stent in both the coronary arteries. IVUS also documented that the lesion in the middle LAD had been completely covered by the drug-eluting stent, which represents a technical aspect that is known to reduce ISR[29]. Since IVUS demonstrated that the conventional and eluting stents were correctly positioned, the mechanical factors accounting for restenosis are supposed to be equal in both vessels. Moreover, the extensive distribution of the ISR in the RCA suggested a greater involvement of biological than of procedure-related mechanisms in its development. Among the factors contributing to the development of ISR, one should bear in mind the presence of thrombus in the RCA[30-33] and the absence of ISR in the vessel treated with an eluting stent strongly suggests that the local release of immunosuppressive drug is responsible for the lack of intimal proliferation.

In our patient, the second coronary angiography was performed because of the development of pulmonary edema 5 months after the first procedure, that is probably too early to detect a "delayed" ISR which could be associated with eluting stent implantation[3]. This is the reason why a new angiographic control has been planned.

In conclusion, our case report suggests that eluting stents are a precious and effective tool in preventing ISR.

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