

## The incidence of late stent thrombosis after successful cypher stent implantation

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**Background:** Stent thrombosis is a rare but devastating complication of coronary stent implantation. Coronary stent deployment is associated with a low incidence of acute and sub-acute thrombosis. However, late stent thrombosis has been recognized clinically. The aim of this prospective study was to evaluate the incidence of late stent thrombosis in patients receiving sirolimus-eluting stents.

**Patients and Methods:** One hundred patients (132 lesions) who underwent implantation of sirolimus eluting stents were selected. All patients were pre-medicated with 325 mg of aspirin, which was continued indefinitely. Anti-thrombotic regimens, including intravenous heparin and a loading dose of clopidogrel (300 mg) were given in the catheterization laboratory and clopidogrel 75 mg/day was continued for at least 6 months. In patients allergic to clopidogrel, ticlopidine at a dose of 250 mg twice daily was prescribed as a substitute. Late stent thrombosis was defined as myocardial infarction characterized by anginal symptoms with ST-elevation on the electrocardiogram and creatine kinase-MB elevation >3 times the upper limit of normal with angiographic documentation of partial or total stent occlusion more than 30 days after sirolimus eluting stent implantation (while the stented segment was the culprit lesion).

**Results:** Complete 2 year follow-up was available for all patients. Between 30 days to 2 years after sirolimus-eluting stent implantation, 2 patients (2%) experienced late stent thrombosis at a mean time of 420 days (range 360 to 480).

**Conclusions:** This study reports a very late stent thrombosis after 20 months of sirolimus eluting stent implantation and 15 months after cessation of clopidogrel treatment, despite continued aspirin administration. This study also implies the possible need for long term antiplatelet therapy among patients receiving sirolimus eluting stents.

**Keywords:** Sirolimus eluting stent, Stent, Thrombosis

### Introduction

Stent implantation is the most commonly used technique of percutaneous coronary intervention. Coronary stent deployment is associated with a low incidence of acute

thrombosis. The incidence of acute and sub-acute coronary stent thrombosis, defined as stent thrombosis within 30 days of deployment, has been reduced to <1% to 2% as a result of improved deployment techniques that fully appose stent to vessel wall and the use of antiplatelet agent. However, it is likely that late stent thrombosis defined as thrombosis 30 days after stent deployment has been under recognized clinically, and its pathological

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descriptions remain unclear. Whether it occurs early or late, stent thrombosis is associated with either death or nonfatal myocardial infarction<sup>1, 2, 3</sup>. Morphological substrates observed as a pathological mechanisms of fatal late coronary stent thrombosis in humans include stenting across major arterial side branches, radiation therapy, plaque disruption in the arterial segments adjacent to stents, stenting of necrotic lipid-rich plaques with plaque prolapse, and diffuse in-stent restenosis. A common pathological finding in all of these clinical events was incomplete neointimal healing<sup>4</sup>. The aim of this study was to assess the incidence of late stent thrombosis during prospective follow-up of sirolimus eluting stent implantation.

### **Patients and Methods**

This study comprised all patients who underwent implantation of sirolimus eluting stents (Cypher, Cordis Corp) at Faghihi Hospital from April 10, 2004 through April 31, 2006 .

### **Medical Therapy**

All patients undergoing percutaneous coronary intervention were premedicated with 325 mg of aspirin, which was continued indefinitely. Anti-thrombotic regimens, including intravenous heparin, a loading dose of clopidogrel (300 mg) was given in the catheterization laboratory, with clopidogrel 75 mg/d prescribed for 6 months. In patients allergic to clopidogrel, ticlopidine at a dose of 250 mg twice daily was a surrogate medication.

### **Data Collection and Study End Point**

Baseline clinical and procedural data were collected prospectively. Late stent thrombosis

was defined as myocardial infarction, characterized by anginal symptoms with ST-elevation on the ECG or creatine kinase-MB elevation >3 times the upper limit of normal with angiographic documentation of partial or total stent occlusion more than 30 days after sirolimus eluting stent implantation with the stented segment as the culprit lesion. All events were adjudicated by 2 independent observers independently. The primary end point of the present analysis was the incidence of stent thrombosis between 30 days to 2 years after sirolimus eluting stent implantation.

## **Results**

### **Patient Characteristics**

A total of 132 sirolimus eluting stent were placed in 100 patients to treat 132 lesions. Baseline characteristics of the study population are presented in Table 1. Review of initial angiography of patients with late stent thrombosis confirmed normal (TIMI 3) Epicardial flow and the absence of residual dissection or stenosis in all cases.

### **Incidence of late stent thrombosis and 2 years outcomes**

Complete 2 year follow-up was available for all patients. Between 30 days to 2 years after sirolimus eluting stent implantation, 2 patients ( 2% ) experienced late stent thrombosis from 360 to 480 days (mean time = 420 days). In all cases, stent thrombosis was confirmed by angiography. Of these 2 patients, 1 had a repeat percutaneous coronary intervention and 1 presented to surgeon for coronary artery bypass graft. In all patients anti-platelet therapy (Aspirin + Clopidogrel or Aspirin + Ticlopidine) was continued for a total of 6 months after stent

**Table 1.** Baseline Characteristics and Procedural Data of the Study Population

Patients (n=100)	
Female/Male	28/72
Previous MI	42
Smoking	53
Dyslipidemia	62
Diabetes mellitus	26
Arterial hypertension	69
Previous CABG	5
Total stent length, mm	24.0 ± 12.6
Stent diameter, mm	3.0 ± 0.5
TIMI 3 flow at completion of procedure	100

MI=myocardial infarction; CABG= coronary artery bypass graft, Mean±SD

implantation. Aspirin administration was continued indefinitely.

### Discussion

All patients undergoing implantation of sirolimus eluting stents demonstrated a 2% incidence of late stent thrombosis. Danenberg et al.<sup>5</sup> identified 8 of 994 (0.8%) patients with coronary stents presenting with AMI within

35 to 400 days (mean time=141 days) after stenting (with the stented segment as the culprit lesion). Heller et al.<sup>6</sup> observed late stent thrombosis (AMI >30 days after implantation) in 12 (0.65%) of the patients under study, while no particular coronary angiographic finding at the time of initial stenting or any specific stent types were linked to late stent thrombosis. In their study, the patients presented from 33 to 270 days (73 ± 23 days) after stenting. Finally, Wang et al.<sup>7</sup> reported late stent thrombosis in 9 of 1191(0.76%) patients within 39 to 211 days (mean presentation= 109 days). In our study, late stent thrombosis was found in 2 of 100 patients (2%) with a mean presentation of 420 days (range: 360 to 480). The present study reports a very late stent thrombosis after 20 months of sirolimus eluting stent implantation and 15 months after cessation of clopidogrel administration, despite sustained aspirin uptake. This implies the possible need for long term use of antiplatelet medication among patients receiving sirolimus eluting stents.

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