Coronary stent thrombosis in bare metal stents

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ABSTRACT

Objective: The incidence of coronary stent thrombosis has reduced with improved techniques and drugs. Nevertheless, clinical trials may not reflect real world practice due to the selective inclusion criteria, regional variations and more complex patients treated in day-to-day practice. We examined the frequency, predisposing factors and outcome of stent thrombosis in unselected patients undergoing bare metal stents.

Methods: All patients undergoing stent implantation are entered into a prospective database. We reviewed the incidence of stent thrombosis in our database for all patients with at least 6 months of follow up.

Results: From December 1996 through to December 2002, 1140 consecutive patients underwent a coronary stenting. Stent thrombosis occurred in 9 (0.8%) patients; 7 (78%) presented within 30 days of the procedure, while 2 had late stent thrombosis occurring after 30 days. The vessel was left anterior descending artery in all, 8 (89%) had a recent anterior myocardial infarction prior to the intervention and the mean stent length was 25 mm.

Conclusion: The incidence of stent thrombosis is approximately 1% in the current era of intervention. Longer stent length in the left anterior descending artery following a recent myocardial infarction, seems to be associated with stent thrombosis.

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Stent thrombosis has been the most dreaded complication associated with coronary artery stenting carrying a very high morbidity and mortality.[1] The incidence of stent thrombosis has been reduced from 10% initially to 3.5% in the Benestent trial to approximately 1% in the modern era due to high-pressure balloon inflation, elimination of warfarin and dual antiplatelet therapy.[2] However, clinical trials may not truly reflect the current incidence of this complication, due to continuously changing practice of interventional cardiology, strict inclusion criteria of clinical trials, local patients and practice variations in a developing country. We sought to study the incidence of stent thrombosis, the predisposing factors and the outcome in an unselected population representing every day practice in a medium volume center.

Methods. Patients undergoing percutaneous coronary artery intervention (PCI) with stenting are entered prospectively in a database. The data include patient's demographics, risk factors, metabolic data, angiographic variables and procedural outcome. We reviewed our database for patients who had at least 6 months follow-up and had stent thrombosis.

Patients underwent a coronary artery stenting using standard techniques and commercially available bare metal stents. Pre-dilation with a balloon or direct stenting with or without post-dilatation, and pressures used was at the discretion of the operators, as was the use of abciximab.[3] Intra-vascular ultrasound (IVUS) was not used. Intravenous heparin was used to maintain an activated clotting time of approximately 300 seconds throughout the procedure. The antiplatelet

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Table 1 - Baseline and procedural characteristics.

Patient	Year of event	Age	Sex	Diabetes	Prior MI	Location of MI	Time from MI to PCI (days)	Vessel	Stent size (mm)	Pressure (mm Hg)	Stents (n)	Total stent length (mm)
1	1996	60	M	Yes	Yes	anterior	8	LAD	3	10	1	15
2	1998	71	M	Yes	Yes	anterior	3	LAD	3	16	1	25
3	1997	68	M	No	Yes	anterior	60	LAD	3	18	2	25
4	1998	48	M	Yes	Yes	anterior	31	LAD	2.5	16	2	32
5	2001	54	M	Yes	Yes	anterior	23	LAD	3	20	2	40
6	2000	63	F	Yes	No	-	-	LAD	3.5	12	1	25
7	1998	71	M	Yes	Yes	anterior	10	LAD	4	12	1	25
8	1999	43	M	No	Yes	anterior	1	LAD	3	16	1	16
9	1998	58	M	Yes	Yes	anterior	5	LAD	3	14	2	21

MI - myocardial infarction, PCI - percutaneous coronary intervention, LAD - left anterior descending artery

Table 2 - Treatment and outcome of stent thrombosis.

Patient	Time to event from PCI (days)	Treatment	Death	Q wave MI	CABG
1	30	PCI	No	No	Yes
2	4	PCI	No	Yes	Yes
3	3	PCI	No	Yes	No
4	35	PCI	No	Yes	No
5	5	PCI	No	Yes	No
6	68	PCI	No	Yes	No
7	13	PCI	No	Yes	No
8	1	PCI	No	Yes	No
9	4	Thrombolysis	No	Yes	No

PCI - percutaneous coronary intervention, MI - myocardial infarction, CABG - coronary artery bypass surgery

regimen consisted of aspirin 300 mg daily indefinitely and ticlopidine 250 mg twice daily orally (prior to year 2000) or clopidogrel 300 mg oral bolus and then 75 mg (after year 2000), for 4 weeks. Post PCI, heparin was not used and low molecular weight heparin was used at the discretion of the operator. Stent thrombosis was defined angiographically as presence of thrombus within the stent, or total occlusion of the stent site, or when a myocardial infarction occurred in the territory of the treated vessel.[4] Unexplained sudden death within the first 30 days following stent implantation was also considered to be due to stent thrombosis. Results are presented as mean ± standard deviation or a percentage of the total.

Results. From December 1996 to December 2002, 1140 patients underwent a coronary artery stenting. Nine patients (0.8%) had stent thrombosis. Seven of the 9 patients had sub-acute stent thrombosis (≤ 30 days) and 2 patients had late (>30 days) stent thrombosis.

The baseline clinical, angiographic and procedural characteristics of these patients are presented in **Table 1**. Eight of the 9 patients (89%) had a recent ST elevation anterior myocardial infarction. Seven of these 8 patients had an anterior wall motion abnormality with reduced left ventricular function. The mean time between the myocardial infarction and the stent procedure was 18 ± 20 days. The left anterior descending artery was the culprit vessel in all the patients. The mean stent diameter was 3.0 mm, and the mean balloon deployment pressure was 15 mm Hg. Four of the 9 patients (44%) received multiple stents and the mean stent length was 25 ± 8 mm. Two patients were non-compliant with the antiplatelet therapy; one stopped aspirin due to perceived aspirin allergy despite in-hospital treatment and the second patient stopped ticlopidine for unclear reasons. No patients received abciximab, and one patient received post-procedural treatment with low-molecular weight heparin.

The presentation of stent thrombosis was chest pain and 7 ruled in for an acute myocardial infarction with ST elevation on the electrocardiogram and cardiac enzyme elevation. Eight of the 9 patients (89%) were treated with immediate re-intervention and balloon angioplasty, while one patient was treated with thrombolytic therapy at an outside hospital prior to transfer and did not require intervention. Two patients required a coronary bypass surgery after the repeat intervention, as the PCI result was deemed suboptimal (**Table 2**).

Discussion. The incidence of stent thrombosis in this consecutive series of "real world" patients with routine dual antiplatelet therapy is 1%, which is comparable with data from larger-volume centers and clinical trials. The implication of this study is that placing long stents in the left anterior descending artery that supplies infarcted myocardium might be at high risk of stent thrombosis despite high-pressure deployment.

The original stent studies reported an incidence of 3.5% of sub-acute stent thrombosis.[2] The higher rate of thrombosis was attributed to the use of warfarin anti-coagulation and to the relatively low-pressure stent deployment (10 atmospheres in the Benestent trial). Colombo et al,[5] demonstrated a decline in stent thrombosis rates to 1.6% with the use of IVUS guided high-pressure stent inflation.[5] Others subsequently showed the same low rate of incidence of stent thrombosis with high-pressure stent deployment without IVUS use (1.8%).[6,7] Randomized controlled trials have now proven the superiority of dual-antiplatelet therapy over warfarin anti-coagulation.[8,9] Other recent registry data with combined antiplatelet therapy and high-pressure inflation, report stent thrombosis rate comparable to ours.[4]

Initial studies reported early stent thrombosis, occurring within 30 days post stent implantation. The brachytherapy trials first reported the phenomenon of late (>30 days) stent thrombosis.[10] Subsequent review of stent registries has confirmed this phenomenon of late stent thrombosis in non-brachytherapy treated stent patients.[11] This phenomenon of late thrombosis was not recognized in the earlier studies due to its infrequent occurrence, as many earlier stent trials did not follow patients beyond 30 days and in the early studies, events beyond 30 days were not classified as stent thrombosis. In our study, 2 of the 9 patients presented with late stent thrombosis. Thus, longer-term treatment with aspirin and clopidogrel may be prudent, consistent with the recommendations of clopidogrel reduction of events during extended observation trial investigators.[12]

There are no consistent predictors of stent thrombosis across studies. Multiple stents,[4] bailout stenting, unstable angina,[13] residual dissections,[14] and low ejection fraction were identified as predictors of stent thrombosis in individual studies.[15] The striking finding in our study is that stent thrombosis was seen only in the left anterior descending artery mainly in post-infarction patients. Whether this is due to heightened thrombogenicity of the post infarction plaque or abnormal flow in the vessel supplying infarcted myocardium is open to speculation.[15] At our institution, this has lead to a more aggressive antiplatelet therapy with abciximab and post-procedural enoxaparin in such patients.[16] This might have contributed to the temporal decrease in the incidence of stent thrombosis.

The most important limitation of this study is that it underestimates the actual incidence of stent

thrombosis, considering only the patients who returned to the hospital are available for analysis. Any patient dying at home, or presenting at another hospital may not be included in the database if the event were not reported to us. Thus, late stent thrombosis is liable to be underestimated. Such limitation is germane to all non-trial observational registries.[11] The relatively low number of events precludes the use of multivariate logistic regression analysis to evaluate the predictors of thrombosis. Despite this limitation, it is remarkable that 8 out of 9 patients had stent thrombosis, following intervention for an anterior myocardial infarction.

In conclusion, the early and late stent thrombosis in bare metal stents in the current era of dual antiplatelet therapy and high-pressure inflation occurs in 0.8% of patients. This will serve as a baseline for comparison with stent thrombosis rates in drug eluting stents.[17] Further studies are needed to assess if IVUS guidance, long-term antiplatelet therapy, low molecular weight heparin would help further reduce this complication.

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