

## COMPARISON OF BARE METAL VERSUS DRUG ELUTING STENTS

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## ABSTRACT

**Objectives:** To compare the frequency of stent thrombosis (acute and subacute) between bare metal stents and drug eluting stents in 1 month follow up. **Duration:** Six months from 12th January 2017 to 11th July 2017. **Sample size:** 300 consecutive patients of coronary artery disease undergoing PCI with bare metal or drug eluting stents (150 patients of each type of stent). **Methods:** After fulfilling the inclusion criteria 300 patients of coronary artery disease were studied. The total number of males in the study population was 254 (85%) with mean age  $51 \pm 9.814$  years while female patients were 46 (15%) with mean age  $55.83 \pm 9.518$  years. Smoking was the commonest risk factor in males while hypertension was commonest in females. 52% patients were admitted with initial diagnosis of unstable angina and 44% patients as acute myocardial infarction. 80% patient showed single vessel coronary artery disease on angiography. Half of the study population was deployed bare metal stents while half was deployed drug eluting stents. Acute stent thrombosis was not documented in our study. All the patients were advised to take regularly dual antiplatelet therapy following PCI. **Results:** Out of 300 patients, 3 patients developed subacute stent thrombosis which had initial diagnosis of unstable angina with single vessel coronary artery disease and PCI to LAD was done in all the three patients. 2 patients were deployed bare metal stents while one patient was deployed drug eluting stent. All the 3 patients were deployed stents having length of more than 20 mm. 2 patients who were deployed bare metal stents took regular antiplatelet therapy but they were readmitted within 8 days following PCI; one patient presented with acute myocardial infarction and second patient as a case of unstable angina. 3rd patient who was deployed drug eluting stent took irregular dual antiplatelet therapy due to intolerable gastrointestinal problem and he was readmitted on 29th day following PCI as a case of acute myocardial infarction. Out of 3 patients, 2 were hypertensive. In our study population not a single death was documented. The frequency of acute and subacute stent thrombosis in our study was 1% in one month follow up. **Conclusion:** Stent thrombosis is more common in patients of unstable angina with long lesions following PCI with bare metal stents. Patients with poor compliance to dual antiplatelet therapy following PCI have more risk of stent thrombosis. Commonest presentation of stent thrombosis is acute myocardial infarction.

**KEYWORDS:** Acute and subacute, PCI, LAD.

## INTRODUCTION

Coronary artery disease (CAD) is the most common cause of cardiovascular death all over the world. It is most commonly due to atherosclerosis.<sup>[1]</sup>

The prevalence of CAD & its associated morbidity and mortality increase as age advances.<sup>[2]</sup> CAD has been shown to be more prevalent in males than females.<sup>[3]</sup>

Symptomatic CAD was initially treated with coronary artery bypass grafting (CABG). Then Percutaneous Transluminal Coronary Angioplasty (PTCA) was used as alternative to CABG for symptomatic patients who have focal lesion in proximal coronary vessels. But it soon became evident that two major issues limited the wide

spread use of PTCA. First, abrupt vessel closure resulting from angioplasty induced dissection and thrombus formation. Second, development of restenosis either clinically or identified as recurrent arterial narrowing by routine repeat angiography.<sup>[4]</sup>

The use of Percutaneous Coronary Intervention (PCI) to treat CAD has expanded dramatically over the past two decades.<sup>[4]</sup> Intracoronary stents have become an important addition to the current practice of angioplasty. Initially bare metal stents (BMS) were used but it was soon evident that risk of restenosis was increased. So, there was the need of such stents which can reduce the risk of restenosis. Sustained local delivery of several agents like sirolimus & paclitaxel from a stent coating

system (drug eluting stent system) has been very effective in suppressing the local neointimal proliferation that causes angiographic and clinical restenosis.<sup>[5]</sup>

Several randomized trials have demonstrated that drug eluting stent (DES) implantation decreases restenosis rate.<sup>[6]</sup> But drug eluting stents are associated with incomplete endothelialisation which may be caused by delayed healing and/or a hypersensitivity reaction due to the synthetic polymer used in its composition and/or the active drug.<sup>[7]</sup> So, stent thrombosis remains the major complication limiting late outcome after angioplasty with drug eluting stents.

The reported incidence of stent thrombosis with bare metal stents is 1.2%.<sup>[8]</sup> The incidence of stent thrombosis with drug eluting stents ranged between 0% to 2.7% in different studies.<sup>[9]</sup> Following DES implantation, mortality was significantly higher in patients with stent thrombosis compared with those without stent thrombosis (31% versus 3%).<sup>[9]</sup>

## METHODS

The study was conducted in Emergency ward, Coronary care units and Cardiology ward of the Punjab Institute of Cardiology Lahore, which is a tertiary care centre. It is a cross sectional study with non probability, purposive sampling technique. The duration of study was six months, from 12th January 2017 to 11th July 2017. Sample size was 300 consecutive patients of coronary artery disease undergoing PCI with bare metal or drug eluting stents (150 patients of each type of stent).

**Inclusion Criteria:** All the new patients of coronary artery disease (unstable angina, NSTEMI or acute myocardial infarction) were included in the study. There angiography and PCI was done. They were followed for any ischemic chest pain till 30 days following stent implantation.

**Exclusion Criteria:** All the patients presenting with ischemic chest pain after 30 days of stent implantation were excluded from the study.

**Stent thrombosis:** was defined as partial or total thrombotic occlusion of stent, documented by coronary angiography after stent implantation. According to timing it has following types.<sup>[9]</sup>

**Acute Stent Thrombosis:** was defined as stent occlusion intraprocedural or within 24 hrs of stent implantation.<sup>[9]</sup>

**Subacute Stent Thrombosis:** was defined as stent occlusion after 24 hrs till 30 days following stent implantation.<sup>[9]</sup>

## Data Collection and Follow Up

The patients of coronary artery disease were admitted through emergency and out patient department of Punjab Institute of Cardiology Lahore for angiography. After

informed consent, 300 patients of coronary artery disease were taken for PCI or angioplasty. PCI of 150 patients was done with bare metal stent while rest of the 150 patients with drug eluting stent. All patients were given antiplatelet therapy (aspirin 150mg and 600mg clopidogrel) 2–4 hours before angioplasty as loading dose. Following angioplasty, all patients were prescribed antiplatelet therapy (aspirin 150mg once daily and clopidogrel 75mg twice daily) and all patients were admitted for 24 hours in the hospital so that patients developing ischemic chest pain with in 24 hours (acute stent thrombosis) should be collected for the study. All other patients who remained asymptomatic for 24 hrs during the hospital stay following angioplasty were discharged on the same antiplatelet therapy and advised for follow up after every two weeks.

Patient developing ischemic chest pain with in 30 days following angioplasty (subacute stent thrombosis) during follow up were also collected for the study. All patients with acute stent thrombosis (as already admitted) and subacute stent thrombosis during follow up, were admitted and reassessed by detailed history, clinical examination and investigation (electrocardiography and cardiac enzymes). Angiography was done with in 24 hours of ischemic chest pain to confirm the diagnosis of stent thrombosis as ischemic chest pain might be due to partial or total occlusion of other coronary vessel.

## Data Analysis

Data was analyzed by SPSS-10 software. Variables of the study were age, gender, coronary vessel in which stent implanted, type of stent used, risk factors, antiplatelet therapy following angioplasty, angiographic diagnosis of stent thrombosis and type of stent thrombosis. Numerical variable like age were calculated by mean and standard deviation. Qualitative variables like gender, vessel in which stent implanted, type of stent used, risk factors, antiplatelet therapy following angioplasty, angiographic diagnosis of stent thrombosis and type of stent thrombosis were calculated by frequency and percentage.

Investigations like electrocardiography and cardiac enzyme were presented in a form of frequency distribution table. Frequency and percentage were calculated for stent thrombosis and its types (acute or subacute). These variable were further associated with type of stent used (bare metal or drug eluting) during PCI, age, gender, vessel in which stent implanted, risk factors and post angioplasty antiplatelet therapy. If the associations found significant, that was tested by applying Chi square test as these variables are qualitative in nature. A p-value of < 0.05 was considered significant.

## RESULTS

The study comprising of 300 patients out of which 254 (85%) were male and 46 (15%) were female (Figure I). Out of 254 males, 22 (8.7%) patients were less than 40 years of age, 94 (37%) patients were between 40 - 49

years of age, 87 (34.3%) patients were between 50 – 59 years of age and 51 (20.1%) patients were more than 60 years of age while out of 46 females, 11 (23.9%) patients were between 40 – 49 years of age, 17 (37%) patients were between 50 – 59 years of age and 18 (39.1%) patients were more than 60 years of age (Table 1). The mean age of male patients was 51 + 9.814 years while of female patients was

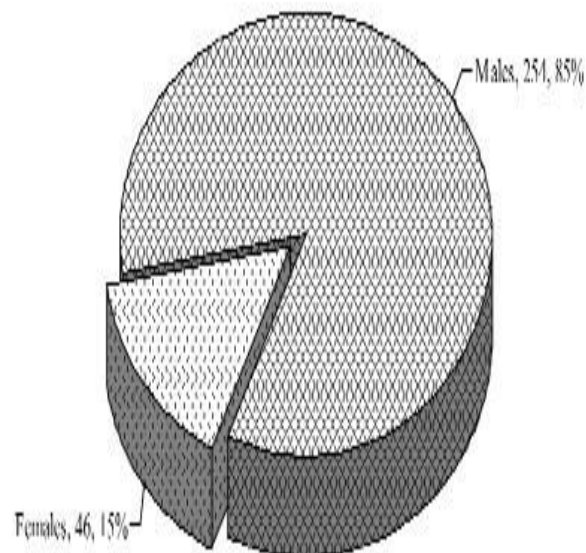


Figure I: Distribution of Patients According to Sex.

Table 1: Distribution of Patients According to Age and Sex.

Patient Age	Patient Sex		Total			
	Males	Females				
	Freq.	Percent.	Freq.	Percent.	Freq.	Percent.
< 40 Years	22	8.7%	-	-	22	7.3%
40-49 years	94	37.0%	11	23.9%	105	35.0%
50-59 years	87	34.3%	17	37.0%	104	34.7%
> 60 years	51	20.1%	18	39.1%	69	23.0%
<b>Total</b>	<b>254</b>	<b>100.0%</b>	<b>46</b>	<b>100.0%</b>	<b>300</b>	<b>100.0%</b>

55.83 + 9.518 years. Comparison of mean age with Out of 300 patients, 154 (52%) patients were patient’s sex showed p-value < 0.01 which is admitted as a diagnosis of unstable angina, 133 significant. (44%) patients as a case of acute myocardial infarction while 13 (4%) patients were diagnosed.

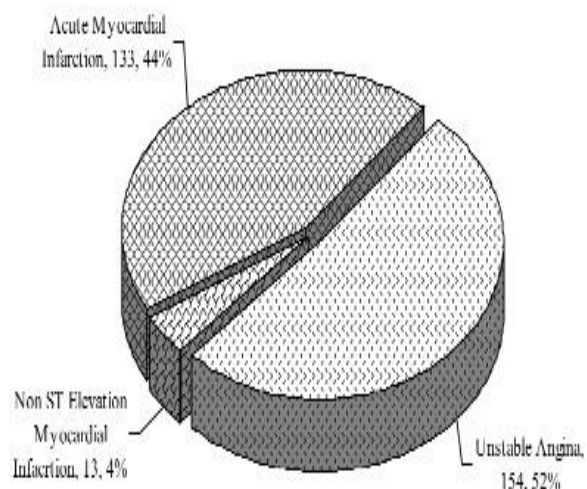


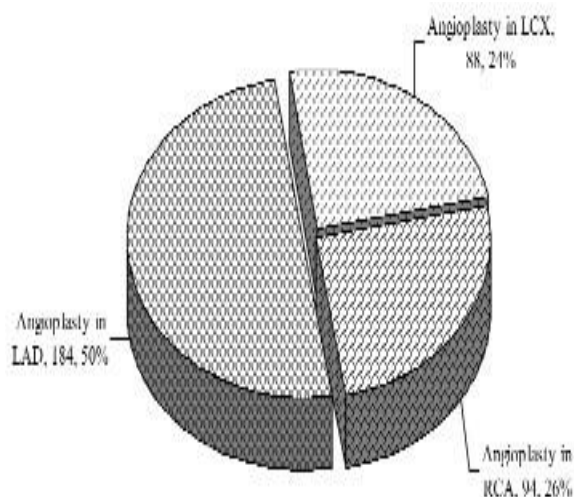
Figure II: Distribution of Patients According to Initial Diagnosis before Aangiography and PCI.

Our study showed that out of 254 males, 68 as a case of non ST elevation myocardial infarction (26.8%) patients were diabetic, 89 (35%) were (NSTEMI) (Figure II). Out of the total study hypertensive, 149 (58.7%) were smoker, 96 population, 240 (80%) patients had single vessel (37.8%) patients had family history of ischemic coronary artery disease, 54 (18%) patients had two heart disease (IHD), 38 (15%) patients had hyperlipidemia and 23 (9.1%) patients had no risk factor. Smoking was the commonest risk factor in male group (58.7%). While out of 46 females 21 (45.7%) patients were diabetic, 34 (73.9%) patients were hypertensive, while no single female patient was smoker, 24 (52.2%) patients had family history of IHD, 10 (21.7%) patients had hyperlipidemia and 3 (6.5%) patients had no risk factor. Hypertension was the commonest risk factor in female group (73.9%) (Table 2). vessel coronary artery disease while 6 (2%) patients had three vessel coronary artery disease.

**Table 2: Distribution of Patients According to Sex and Presence of Risk Factors.**

Risk factors	Patient Sex				Total (n=300)	
	Males (n=254)		Females (n=46)		Freq.	Percent.
	Freq.	Percent.	Freq.	Percent.		
Diabetes Mellitus	68	26.8%	21	45.7%	89	29.7%
Hypertension	89	35.0%	34	73.9%	123	41.0%
Smoking	149	58.7%	-	-	149	49.7%
Family History	96	37.8%	24	52.2%	120	40.0%
Hyperlipedemia	38	15.0%	10	21.7%	48	16.0%
No Risk factors	23	9.1%	3	6.5%	26	8.7%

The distribution of the patients according to angioplasty in coronary arteries showed that PCI to left anterior descending artery (LAD) was done in 184 (50%) patients and in 88 (24%) patients PCI to left circumflex (LCX) was done while in 94 (26%) patients PCI to right coronary artery (RCA) was done (Figure III). Out of the study were implanted drug eluting stents.

**Figure III: Distribution of Patients According to Angioplasty in Coronary Arteries.**

All the patients took antiplatelet therapy (aspirin 150mg and 600mg clopidogrel) 2–4 hours before angioplasty as

loading dose. Following PCI, all patients took antiplatelet therapy (aspirin 150mg once daily and clopidogrel 75mg twice daily) regularly and all patients were admitted for 24 hours in the hospital so that patients developing ischemic chest pain within 24 hours (acute stent thrombosis) should be collected for the study. Not a single case of acute stent thrombosis was documented in our study. All other patients who remained asymptomatic for 24 hours during the hospital stay following PCI, were discharged on the same antiplatelet therapy and advised to follow after every two weeks for one month to collect cases of subacute stent thrombosis. So, all the patients were followed for one month following percutaneous coronary intervention to collect the information about ischemic chest pain and survival.

These 3 patients were admitted as initial diagnosis of unstable angina for coronary angiography and PCI. Out of 3 patients of subacute stent thrombosis, 2 patients were presented as a case of acute ST elevation myocardial infarction while 1 patient was presented as a case of unstable angina (Table 3). Risk factors of the patients of subacute stent thrombosis was described in Table 4. All the three patients showed single vessel coronary artery disease (LAD) and PCI to LAD was done in these 3 patients. 2 patients were deployed BMS while one patient was deployed DES.

**Table 3: Distribution of Patients According to Presentation of Patients with Stent Thrombosis.**

Presentation	Patient Sex				Total	
	Males		Females		Freq.	Percent.
	Freq.	Percent.	Freq.	Percent.		
ST Elevation	1	50.0%	1	100.0%	2	75%
Unstable angina	1	50.0%	-	-	1	25%
Total	2	100.0%	1	100.0%	3	100.0%

**Table 4: Distribution of Patients According Stent Thrombosis and Presence of Risk Factors.**

Risk factors	Stent thrombosis				Total (n=300)	
	Yes (n=3)		No (n=297)		Freq.	Percent.
	Freq.	Percent.	Freq.	Percent.		
Diabetes Mellitus	1	33.3%	88	29.6%	89	29.7%
Hypertension	2	66.7%	121	40.7%	123	41.0%
Smoking	1	33.3%	148	49.8%	149	49.7%
Family History	1	33.3%	119	40.1%	120	40.0%
Hyperlipidemia	1	33.3%	47	15.8%	48	16.0%
No Risk factors	-	-	26	8.8%	26	8.7%

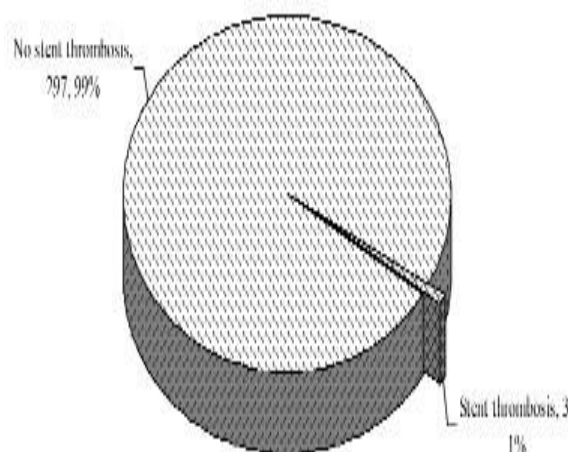
Out of 2 patients who were deployed BMS, first patient was 45 years old female who was hypertensive, with high cholesterol level and had family history of IHD. She was deployed 2.75 X population, half (50%) of the patients were In our study out of 300 patients, only 3 (1%) implanted bare metal stent while other half (50%) patients developed subacute stent thrombosis. 24 mm BMS in LAD at 18 atm. She took regular oral antiplatelet drug but after 8 days of PCI she developed acute anterolateral wall myocardial infarction with raised cardiac enzymes. Subacute stent thrombosis was confirmed on angiography and Plain Old Balloon Angioplasty (POBA) to LAD was done. Second patient was 73 years old male who was smoker. He was deployed 3 X 26 mm BMS in LAD at 14 atm, he took regular oral antiplatelet drug but after 2 days of PCI he developed acute coronary syndrome without raised cardiac enzymes (unstable angina). Subacute stent thrombosis was confirmed on angiography and POBA to LAD was done.

The third patient who developed subacute stent thrombosis was 58 years old male who was diabetic and hypertensive. He was deployed 2.5 X 23 mm DES in LAD at 16 atm, he took irregular oral antiplatelet drug due to some medical problem and after 29 days of PCI he developed acute anterior wall myocardial infarction with raised cardiac enzymes. Subacute stent thrombosis was confirmed on angiography and POBA to LAD was done.

The demographic features of the patients who developed subacute stent thrombosis showed that one (33%) patient was between 40-49 years of patient, one (33%) patient was between 50-59 years of patient and one (33%) patient was more than 60 years of patient. The mean age of the patients who developed subacute stent thrombosis in 3 patients was 58.7 + 14.01 years, while rest of the 297 patient who remained symptom less had mean age of 51.7 + 9.87 years, with t-value of 1.218 and p-value of 0.22. Although it is not significant but there is a trend of stent thrombosis in older age patients.

Distribution of presence of risk factors in patients developing stent thrombosis showed that 1 (33.3%) patient was diabetic, 2 (66.7%) patients were hypertensive, 1 (33.3%) patient was smoker, 1 (33.3%)

patient had family history of IHD and 1 (33.3%) patient had hyperlipidemia. So out of 3 patients, 1 patient had one risk factor, 1 patient had two risk factors and 1 patient had three risk factors. So out of 3 patients who developed sub acute stent thrombosis, 2 (66.7%) patients were implanted bare metal stent while 1 (33.3%) patient was implanted drug eluting stent, with fisher exact test p-value of 1.0 which is not significant. In our study population not a single death was documented. The frequency of stent thrombosis in our study is 1% (figure IV).

**Figure IV: Distribution of Patients According to Development of Stent Thrombosis**

## DISCUSSION

Evaluation of the frequency of stent thrombosis with DES versus BMS has been difficult.<sup>[10]</sup> Acute stent thrombosis may be the result of technical factors; the solution for this requires optimal deployment strategies. Late stent thrombosis appears to be multifactorial in its etiology and thus requires a multifaceted solution.

Similarly, vigilance in maintenance of dual antiplatelet therapy is mandatory. More data are required to determine the optimal duration of dual antiplatelet therapy, which may ultimately be determined to be individual patient specific.<sup>[11]</sup>

In the integrated TAXUS program involving over 3,400 patients, the total rate of stent thrombosis was 1.2% with DES versus 0.7% with BMS. After Taxus stent deployment 50% of stent thrombosis were observed within 30 days; the remainder occurred between 30 and 180 days.<sup>[12]</sup> Similarly in our study 3 patients are presented as a case of stent thrombosis within 30 days of stent implantation. Stent thrombosis may present as sudden death, cause of death was studied in 4 randomized Cypher stent trials involving 1,748 patients.<sup>[13]</sup> In that analysis, total mortality was slightly increased in patients who received the SES (vs. BMS), but that was the result of an increase in noncardiac mortality in the 2 smallest studies (RAVEL [Randomized Comparison of a Sirolimus Eluting Stent With a Standard Stent for Coronary Revascularization] and e-SIRIUS [Sirolimus Eluting Stent in Coronary Lesions]). When cardiac deaths alone were analyzed, no difference in frequency was seen in patients treated with DES or BMS. In our study population not a single death was documented.

Recently, the results of the Swedish Coronary Angiography and Angioplasty Registry have been published and included 6,033 patients with DES and 13,738 patients with BMS.<sup>[14]</sup> The primary outcome analysis was death and infarction. During 3 years of follow-up, there was no difference in the composite of death and infarction between the 2 groups. There was a bimodal distribution of events: at 6 months, the event rate was lower with DES. Similarly in our study it was observed that out of 3 patients developing stent thrombosis, 1 patient belonged to DES group. After 6 months, however, patients with DES had higher events. After 6 months, patients with DES experienced death and/or infarction at a rate of 0.5% to 1.0% higher per year.

In the French registry, thrombosis rates after deployment of stents using balloons 3.5mm or greater, 3.0 mm, or 2.5 mm or less in diameter were 1.0%, 2.3%, and 10%, respectively;<sup>[15]</sup> more recently, Cutlip and colleagues documented a twofold increase in thrombosis rates for stents placed with a final luminal diameter of less than 3.0 mm versus 3.0 mm or greater in their pooled clinical trial analysis.<sup>[16]</sup> Several studies have correlated stent thrombosis with greater stented lesion length and variably with the use of multiple stents.<sup>[16]</sup> Other studies showed the increase incidence of stent thrombosis associated with greater plaque volume and a stented vessel perfusing an area of poorly functional myocardium.<sup>[17]</sup>

Residual uncovered dissection following stenting conferred a fourfold increase in risk in the French registry,<sup>[15]</sup> and clinical trial pooled analysis.<sup>[16]</sup> Other procedural angiographic correlates of stent thrombosis have included slow flow, suboptimal postprocedural lumen, and poor distal runoff.<sup>[17]</sup>

The BASKET-LATE (Basel Stent Kosten Effektivitäts Trial-Late) study evaluated the issue in 826 patients randomized in a 2:1 fashion to receive DES or BMS,<sup>[18]</sup> which concluded that after clopidogrel discontinuation, the benefit of DES in reducing target vessel revascularization is maintained but has to be balanced against an increase in late cardiac death or nonfatal myocardial infarction, possibly related to late stent thrombosis. Between 7 and 18 months of followup, the rates of nonfatal infarction and death were increased in the DES group although the absolute frequency was low. Our study also highlighted that out of 3 patients who developed stent thrombosis, 1 patient was deployed DES who discontinued antiplatelet therapy (aspirin and clopidogrel) due to some medical problem.

The focus now is to minimize the risk of stent thrombosis with either BMS or DES. Should the incidence of late stent thrombosis be found to be small but continuous after DES, the challenge will be to mitigate this risk given the known benefits of these devices in terms of their efficacy in reducing clinical and angiographic restenosis.<sup>[19]</sup> Finally, advances in stent platforms for drug elution as well as adjunctive pharmacotherapy may be promising ways to enhance the long-term safety of DES. Longer-term studies of 5 years or even longer of large unselected patient populations are required to fully study the issues of this complex problem.

## CONCLUSION

Stent thrombosis is an infrequent but very severe complication of both BMS and DES. Our study revealed that stent thrombosis is more common in patients of unstable angina with long lesions in coronary artery and following PCI with bare metal stents. Patients with poor compliance to dual antiplatelet therapy following PCI have more risk of stent thrombosis. Commonest presentation of stent thrombosis is acute myocardial infarction. The frequency of acute and subacute stent thrombosis is 1% in one month follow up.

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