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Case Report

Intraprocedural Stent Thrombosis During Percutaneous Coronary Intervention: How to Predict

Bayu Aji[1*], Mohammad Saifur Rohman[2], Budi Satrijo[2], Arief Wibisono[3]

[1] *Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*
[2] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*
[3] *Department of Cardiology and Vascular Medicine, dr. Iskak General Hospital, Tulungagung, Indonesia.*

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ABSTRACT

Background: Intraprocedural stent thrombosis (IPST) during percutaneous coronary intervention (PCI) is an uncommon event that results in a poor outcome including STEMI and sudden cardiac death. Concerns about an increased risk of stent thrombosis with drug-eluting stents (DES) continue, even though the incidence, timing, and predictors of stent thrombosis with DES have not been identified.
Objective: This study aimed to describe the diagnosis and management of Intraprocedural Stent Thrombosis.
Case presentation: We will discuss a 49 year-old male brought to our hospital because of chest pain while doing moderate activity. One month prior to admission, he had history of acute coronary syndrome and 1 DES on right coronary artery was placed. Ticagrelor and aspirin were routinely consumed as dual antiplatelet therapy. The patient was diagnosed with intraprocedural stent thrombosis during PCI with the evidence of intra-catheter thrombosis and ST segment elevations seen in the ECG monitor. We treat the patient with Ticagrelor 180 mg loading dose and intracoronary unfractionated heparin (UFH) during procedure continued with continuous infusion until 24 hours. No event of subsequent acute coronary syndrome was observed.
Conclusion: Intraprocedural Stent Thrombosis was a strong predictor of mortality in STEMI patients. This case showed that the present widespread use of DES instead of BMS for coronary implantation although decreased the future risk of repeat revascularization, increased the risk of thrombosis. Prior risk stratification, potent early antiplatelet treatment and anticoagulant of choice with UFH might be used to reduce the risk of thrombosis in STEMI patients undergoing stent implantation.

1. Introduction

Intra-procedural stent thrombosis (IPST) is an angiographically confirmed occlusive or non-occlusive intraluminal filling defect within the stent, due to the creation of new or expanding thrombus within or next to a freshly implanted stent, occurring during the index procedure or before the completion of percutaneous coronary intervention (PCI) which resulted in thrombolysis in myocardial infarction (TIMI) grade 0 or 1 anterograde flow.[7,9]

IPST is strongly associated with mortality albeit a rare complication. IPST was strongly predictive of subsequent adverse cardiovascular events. In patients without dissections, thrombus-containing lesions, or acute myocardial infarction (AMI), IPST occurs at a rate of 0.7% and 0.01% following drug-eluting stent (DES) and bare metal stent (BMS) implantation, respectively. Approximately 1% of people with ST-segment elevation myocardial infarction (STEMI) is affected with this complication.[9]

2. Case Illustration

A 49-year-old male, Javanese, brought to our hospital (October 17, 2021) because of chest pain while doing moderate activity. He had history severe chest pain (September 18, 2021) that was not relieved by rest and felt like heaviness sensation on her left chest radiated to the back accompanied with diaphoresis (Visual Analogue Scale/VAS: 9/10). He was diagnosed with acute coronary syndrome and underwent PCI with 1 DES implantation on right coronary artery 2 weeks later (October 7, 2021).

The patient was physically active and works as a firefighter. He initially complained chest pain related with activity since 4 months prior admission. The chest pain was increased in frequency and intensity since 1 month prior admission. He refused to seek medical consultation because he felt the chest pain was relieved by rest.

*Corresponding author at: Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.
E-mail address: bayulaut20@gmail.com (B. Aji).

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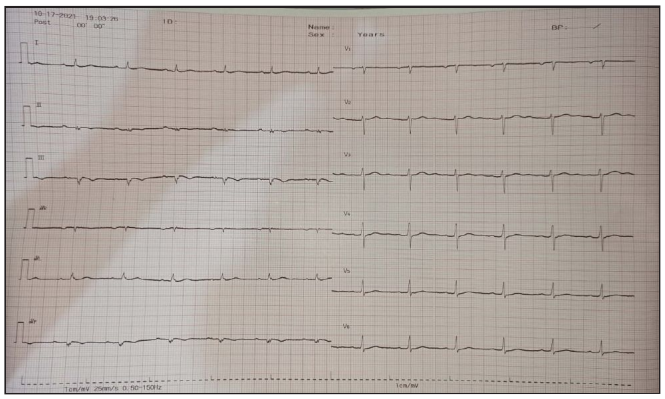

Figure 1. ECG performed at our hospital showed normal sinus rhythm with pathological Q wave at II, III and aVF

He was newly diagnosed with diabetes mellitus from prior hospital, and treated with bed time long acting insulin qDay and pre meal short acting insulin TID. He was an active smoker, 1 pack a day, and quit smoking since prior hospitalization.

On physical examination, it was found that blood pressure (BP) 118/76 mmHg, HR 69 bpm, RR 18 tpm, T 38 C, saturation (SpO2) 99% on nasal canule 4 liter per minute (lpm), with appropriate urination.

Anemia was not found. Jugular venous pressure (JVP) was R + 3cmH20. There was heart enlargement finding from auscultation with palpable apex cordis at intercostalis (ICS) VI and left anterior axillary line (AAL). Abnormal lung sound was not heard from auscultation. Cold acrals were not found in extremities. The electrocardiography (ECG) examination showed a sinus rhythm with pathological Q waves at II III aVF, as seen in Figure 1(A). X-ray examination revealed cardiomegaly (Figure 2).

Laboratory examination at our ER showed normal leucocyte (4,540/μL), haemoglobin (13.6 g/dL), platelets (247,000/uL), ureum (28.2), creatinine (1.0), sodium (138), potassium (3.78), chloride (99), partial prothrombin time (9.80) and activated partial thromboplastin time (21.2). The HbA1C was high (9.7%) despite insulin treatment. The patient received dual antiplatelet therapy with aspirin 80 mg qDay and ticagrelor 90 mg bid.

Diagnostic coronary angiography showed diffuse stenosis from proximal to distal LAD with critical stenosis 99% on distal LAD, the septal branch gave collateral to RCA and wide diameter of intermediate coronary artery with diffuse stenosis 95%. The Intermediate Coronary Artery was large, with diffuse stenosis 80%. We decided the LAD and intermediate corornary artery as the target vessel.

After the DES implantation on mid-distal LAD, the monitor ECG showed ST segment elevation at lead aVR accompanied with ST segment depression at leads II, III, aVF, I and aVL. During observation, the ECG back to baseline within a minute. The chest pain was not complained by the patient during this procedure.

We continued the procedure to the intermediate coronary artery. After balloon inflation, we found thrombus on target vessel. We gave statin 40 mg before we continued stenting procedure. After the DES implantation on intermediate coronary artery , the monitor ECG showed ST segment elevation at lead aVR accompanied with ST segment depression at leads II, III, aVF, I and aVL. We gave Ticagrelor 180 mg and Heparin 1000 iu intracoronary. During observation, the ECG back to normal within a minute. The chest pain was not complained by the patient during this procedure.

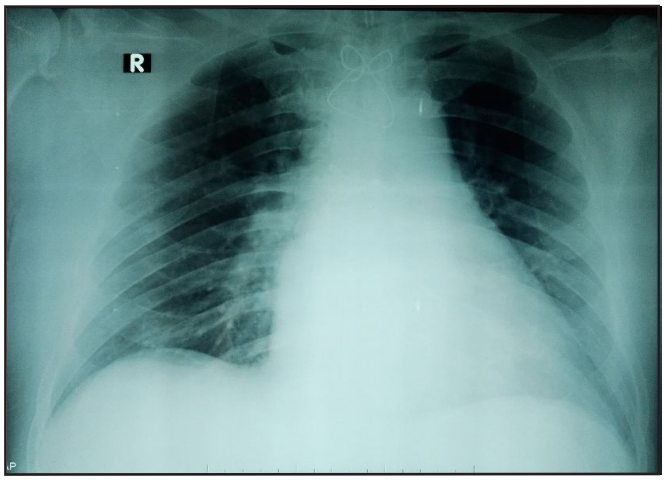

Figure 2. Thoracic antero-posterior (AP) X-ray imaging showed cardiomegaly.

After the DES implantation on intermediate coronary artery, the monitor ECG showed ST segment elevation at lead aVR accompanied with ST segment depression at leads II, III, aVF, I and aVL. During observation, the ECG back to normal within a minute. The chest pain was not also complained by the patient during this procedure.

Cineangiography was then perform with the results TIMI flow 3 and residual stenosis 0%. After the procedure we found thrombosis intracatheter and we decided to continue UFH 12 iu/kgBW/h for 24 hours. No event of subsequent acute coronary syndrome was observed.

3. Discussion

The Academic Research Consortium (ARC) has standardized ST definitions by classifying the adjudicated event's specificity (definite, likely, or potential) as well as its time in relation to PCI (acute, subacute, late, and very late). Intra-procedural stent thrombosis (IPST) is defined as the formation of occlusive or non-occlusive new thrombus in or close to a newly implanted stent before the PCI process is done.[3,9]

The most important aspect for the diagnosis and treatment of IPST is clinical suspicion of early stent thrombosis. Chest discomfort and ischemic electrocardiographic alterations in the target vascular region are the most common symptoms of stent thrombosis. ST, on the other hand, might show as abrupt death or be asymptomatic in the presence of collateral vessels. Patients with acute coronary syndrome, renal failure, low ejection fraction, smoke, decreased TIMI flow or diabetes mellitus has been known to increase the risk of Stent Thrombosis.[1,7]

An increase of cTn values greater than five times the 99th percentile URL in patients with normal baseline values is arbitrarily characterized as coronary intervention-related MI. In addition, one of the following elements is required:

1. New ischemic ECG changes
2. Newly developed pathological Q waves
3. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology
4. Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or a side branch occlusion/thrombus, disruption of collateral flow, or distal embolization.[12]

Table 1. Academic Research Consortium Definition of Stent Thrombosis[2]

Classification	Criteria
Definite	Acute coronary syndrome with angiographic or pathologic confirmation of thrombus
Probable	unexplained death eithin 30 d or MI involving target vessel territory without angiographic confirmation
Possible	Any unexplained death beyond 30 d
Timing*	
Early	0 - 30 d • 0 - 24 h = acute • > 24 h - 30 d = subacute
Late	31 d - 1 y
Very Late	> 1 y

*timing begin after completion of the procedure.
intraprocedural thrombotic events are not condsidered ST.

Intravascular ultrasonography (IVUS) can be utilized to diagnose the underlying mechanism of ST when a filling defect is discovered angiographically (underexpansion, malapposition, edge dissection). Because of its better resolution (10 mm), optical coherence tomography (OCT) is ideal for visualizing the stent surface, and its capacity to identify the presence of (sub)clinical thrombus has been experimentally demonstrated.[1,5,10] In this patient, as soon as the action predilatation with balloon and stent, we found ischaemic ECG changes and thrombus intracatheter in the end of procedure. The ECG monitor back to the baseline soon after we gave loading Ticagrelor 180 mg, Atorvastatin 40 mg and intracoronary heparin 1000 mg.

A stent is a foreign object inside the walls of blood vessels. Many factors are involved including procedural factors/stent, patient factors and lesion characteristics. Patients with acute coronary syndrome, inflammation and tissue necrosis were exposed to the circulation so as to strengthen the activity of platelets and easily formed thrombus.4,5 The material in the form of a polymer stent Cypher (sirolimus) and Taxus (paclitaxel) DES can cause infiltration of eosinophils suspected hypersensitivity reaction that can trigger platelet adhesion and activation cascade coagulant.[2,9]

The presence of vascular injury when stenting complications such as coronary dissection can lead to exposure of thrombogenic molecules of subintima and media (including plaque material) into the bloodstream.
There are two kinds of thrombus:
• White thrombus : a platelet-rich thrombus, usually only lead to partial occlusion
• Red thrombus : a rich thrombus fibrin and erythrocytes.

In a recent sample of patients from a high-volume referral hospital, white thrombi made up around one-third of the specimens collected after PCI. When compared to patients with red thrombi, white thrombi had a shorter ischemia duration and smaller vessels.[10]

Platelet activation was higher 30 days after implantation of an open-cell stent than a closed-cell stent, which might be due to the stents' distinct scaffolding qualities. The content of the drugs currently on the DES can be prothrombogenic. Rapamycin and Paclitaxel works by blocking the migration and proliferation of smooth muscle cells that plays a role in neointimal formation and restenosis. However, both drugs induce endothelial expression of tissue factor that will bind to the clotting factor so that the formation of fibrin.[2,9]

Acute coronary syndrome/unstable angina, vessel size, coronary blood flow , plaque features, left ventricular ejection fraction, and local platelet/coagulation activity are all patient or lesion specific variables. Platelet glycoprotein IIIa gene (PlA2) polymorphisms have also been linked to an increased risk of stent thrombosis. Other patient characteristics that favor the development of stent thrombosis include diabetes mellitus, chronic kidney disease, smoker, cancer, DAPT non-responsive, premature cessation of DAPT, advanced age and hypersensitivity to polymer or drug.[5,9]

Table 2. Predictors of Early vs Late Stent Thrombosis[2]

	Early Stent Thrombosis	(Very) late Stent Thrombosis
Patient	Malignancy, heart failure, peripheral artery disease, diabetes mellitus, acute coronary syyndromes, nonadherence to dual-antiplatelet therapy, genetic polymorphism, thrombocytosis	End-stage renal disease, smoking, STEMI, nonadherence, to dual-antiplatelet therapy (unknown for every late ST)
Lesion	Bifurcation lesion, LAD, vessel sixe, lesion length, thrombus, saphenous vein grafts	LAD, Incomplete endothelialzation, delayed healing, previous brachytherapy, vein graft stenting
Procedural	stent undersizing, stent underexpansion, stent malapposition, dissection, no pre-procedural thienopyridine administration, bivalirudin as anticoagulant in STEMI patients, stent length	DES (compared eith BMS), permanent polymer DES (compared eith bioresorble polymer DES), Overlapping DES
Post-Procedural	Discontinuation of antiplatelet theraphy	Discontinuation of antiplatelet theraphy (unknown for very late ST), late acquired stent malapposition

Many studies have looked at possible predictors of stent thrombosis, particularly in the acute and sub-acute categories, and have discovered a variety of angiographic, clinical, procedural, and post-procedural risk factors. A risk score has been developed to personalize risk assessment for the occurrence of ST, and it might be used to identify individuals who would benefit the most from more aggressive antiplatelet medication following stent placement.2 Baran et al. established a clinical risk score for predicting stent thrombosis and risk stratification. important predictors have been verified using 1-year data from 4,820 patients, with patients stratified into low, medium, and high risk categories.[6]

Early stent thrombosis (ST) following initial Percutaneous Coronary Intervention can be predicted using the Stent Thrombosis Risk Score (STRS) (PCI). There were 569 patients in all, with a median age of 56. Early ST was found in 33 (5.8%) of the patients. At STRS of 0-2, the early ST rate was 3.3 percent, rising to 5.0 percent at STRS of 3-4, and 17.2 percent at STRS of ≥5.[8]

There is association of the CHA2DS2VASc Score with Acute Stent Thrombosis. 3,460 consecutive patients with STEMI who underwent a PPCI. Acute stent thrombosis was linked to CHA2DS2VASc scores of ≥4. When compared to those with a CHA2DS2VASc score of 1, patients with a CHA2DS2VASc score of 4 had a 4.3 times greater risk of acute stent thrombosis.[11]

In Patients with Acute Coronary Syndromes, an Integer-Based Risk Score predicts 1-Year Definite/Probable Stent Thrombosis. For ACS, 6,139 patients had PCI with stent placement. Low risk (1.36 percent), moderate risk (3.06 percent), and high risk (10 percent) were assigned to risk ratings 1 to 6. (9.18 percent).[1]

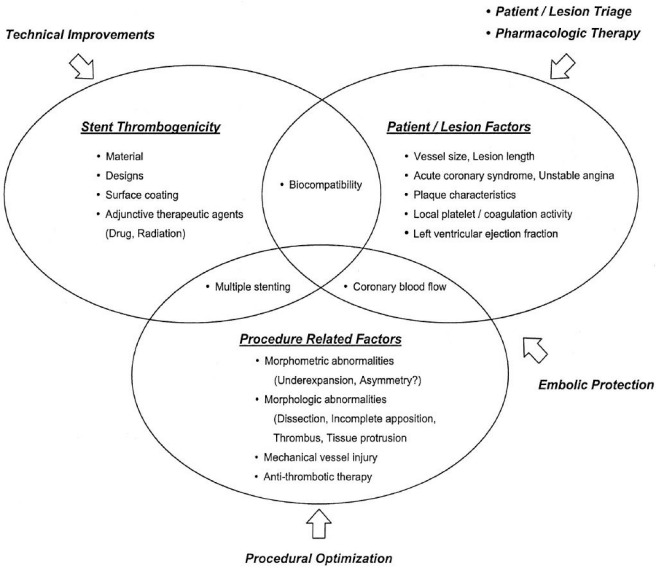

Figure 3. Factors Contribute to Stent Thrombosis[13]

If ST is the case then action targets PTCA for revascularization of blood vessels should be done immediately. Guidewire selected must be soft and floppy to ensure free through the lumen of the stent and not crossing through the strut stent .[9]

Table 3. Clinical Risk Factors for Prediction of Stent Thrombosis by Baran et al[14]

Clinical Factor	Hazard Ratio	Weight
Thienopyridine discontinuation <6 mo	5.28	5
insulin treated diabetes	4.74	5
Left main stenting	2.73	3
Smoking status	2.63	3
Lesion length .28 mm	2.35	2
Multiple stenting	2.25	2
Moderate to severe lesion calcification	2.25	2
Reference vessel diameter <3 mm	1.72	2
Total possible score		24
Risk stratification		
Low (ST rate%)		0–6 (0.8)
Moderate (ST rate%)		7–13 (3.6)
High (ST rate%)		14–24 (12.6)

Table 4. Stent Thrombosis Risk Score (STRS) in Predicting Early Stent Thrombosis[8]

Serial	Variable	Levels and scoring schema
1	Baseline platelet count, K/μl	<250 [+0]
		250 to 400 [+1]
		>400 [+4]
2	History of IDDM	Yes [+2]
		No [+0]
3	Baseline TIMI flow grade of 0-I	Yes [+2]
		No [+0]
4	Early anticoagulant therapy	Yes [+0]
		No [+1]
5	Aneurysm or ulceration	Yes [+2]
		No [+0]
6	Number of vessel treated	<2 [+0]
		2 [+1]
		3 [+2]
7	Final TIMI flow grade of 0-II	Yes [+2]
		No [+0]

Aspiration thrombectomy intracoronary thrombus is effective for the treatment of ST especially on stents with a diameter of more than 2.5 mm, large blood vessels and large thrombus. Intracoronary thrombus aspiration can prevent distal embolization. The existence of intra coronary thrombus is also an indication of the provision of Glycoprotein IIb-IIIa inhibitors. The success of overcoming the acute thrombosis, characterized by normal blood flow (TIMI 3 flow) with stenosis <50%.[4,9]

Dual anti-platelet (DAPT) should be given as early as possible, especially in all patients with acute coronary syndrome patients. Acetylsalicylic acid (ASA) and the P2Y12 receptor antagonists such as clopidogrel, prasugrel and ticagrelor served to increase the effectiveness of treatment and preventison of stent thrombosis. PLATO Trial showed the effectiveness of ticagrelor compared with clopidogrel in preventing stent thrombosis. The incidence of stent thrombosis could still occur at 0.5-2% in the case of elective PCI and more than 6% in the case of PCI with acute coronary syndromes despite using dual antiplatelet.[9]

Unfractionated heparin (UFH) is the main option while undergoing PCI. From the research HORIZON-AMI, comparing UFH-Glycoprotein IIa/IIIb with direct thrombin inhibitors bivalirubin as monotherapy, showed a 0.3 vs 1.4%, P <0.001 in the incidence of Acute ST.[9]

Table 5. Integer-Based Risk Score for Prediction 1-Year Definite/Probable Stent Thrombosis in Patients With Acute Coronary Syndromes[2]

Variables	Integer Assigment for ST Risk Score Calculation			Add to Score
Type of ACS	NSTE-ACS	NSTE-ACS with ST-segment	STEMI +4	STEMI +4
Current smoking	w/o ST-segment	deviation: +2		
Insulin-treated diabetes mellitus	changes: +1	No: +0		
History of PCI	Yes: +1	No: +0		
Baseline platelet count, K/µl	Yes: +2	No: +0		
Absence of early (pre-PCI) heparin*	Yes: +1	250–400: +1	>400: +2	>400: +2
Aneurysm or ulceration	<250: +0	No: 0		
Baseline TIMI flow grade 0/1	Yes: +1	No: 0		
Final TIMI flow grade <3	Yes: +2	No: 0		
Number of vessels treated	Yes: +1	No: 0		
ST risk score:	Yes: +1	2: +1	3: +2	3: +2
	1: +0	ST risk score:		

Note; ACS = acute coronary syndrome (s); NSTE-ACS = Non–ST-segment elevation acute coronary syndrome; STEMI = ST-segment elevation myocardial infraction

It is important to choose the right size stents and perform high-pressure post-dilation effectively (> 14 atm). To further optimize the prevention of ST in calcified lesion, the use of rotational atherectomy can optimize stent expansion and better stent positioning. The use of intracoronary imaging modalities such as Optical Coherence Tomography (OCT) and Intra Vascular Ultrasound (IVUS) is very helpful as guiding the expansion and apposition of the stent to be more appropriate.[4,9]

4. Conclusion

Intraprocedural Stent Thrombosis was a strong predictor of mortality in STEMI patients. This case showed that the present widespread use of DES instead of BMS for coronary implantation although decreased the future risk of repeat revascularization, increased the risk of thrombosis. Prior risk stratification, potent early antiplatelet treatment and anticoagulant of choice with UFH might be used to reduce the risk of thrombosis in STEMI patients undergoing stent implantation.

5. Declarations

5.1. Ethics Approval and Consent to participate
Not applicable.

5.3. Availability of data and materials
Data used in our study were presented in the main text.

5.4. Competing interests
Not applicable.

5.5. Funding source
Not applicable.

5.6. Authors contributions
Idea/concept: BA. Design: BA. Control/supervision: MSR, BS, AW. Data collection/processing: BA. Analysis/interpretation: BA, MSR, BS. Literature review: MSR, BS, AW. Writing the article: BA. Critical review: MSR, BS, AW. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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