# Frequency of Subacute Stent Thrombosis (SAT) in Patients Presenting with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention (PCI)

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## ABSTRACT

*Objective:* To assess the rate of occurrence of sub-acute Stent Thrombosis (SAT) after primary PCI in the patients presented with the acute coronary syndrome.

*Study Design:* Retrospective cross-sectional study.

*Place and Duration of Study:* Tertiary Cardiac Care Center of Lahore Pakistan, from Jul 2019 to Jun 2021.

*Methodology:* The retrospective demographical and angiographic data of the admitted patients who underwent PCI for ACS, was gathered from the Hospital Registry of a tertiary cardiac care center of Lahore. The sampling technique was non-probability consecutive sampling, and all the data was analyzed using SPSS-20.0 and continuous data was presented as Mean±SD and frequencies & percentages for categorical variables. Chi square test (CI=95%, α=5%) was used to find the association of SAT with predisposing factors. *p*-value <0.05 was taken as statistically significant.

*Results:* Out of (n=551) patient underwent PPCI, the stent thrombosis was observed to occur in 29(5.2 %), among which 4.9 % were subacute stent thrombosis. The predisposing factors of sub-acute stent thrombosis were Diabetes Mellitus, ACS, smaller vessel size, presence of bifurcation lesion, under sizing of the stent and edge dissection and were in significant association with SAT (*p*<0.05).

*Conclusion:* Our study reveals that subacute stent thrombosis is an event with a comparatively higher frequency in patients who go through primary PCI for acute coronary syndrome, demonstrating a frequency of 4.9% and a mortality rate of 74% within 30 days of the procedure.

**Keywords:** Acute coronary syndrome, Percutaneous coronary intervention, ST elevated myocardial infarction, Subacute stent thrombosis.

## INTRODUCTION

Stent thrombosis had been the major shortcoming in the stenting of coronary arteries for several years as it limits the long-term efficacy of the procedure.[1] The employment of Drug-Eluting Stents (DES) has drasti-cally aided to counter this issue. Several studies have recently indicated that countering the problem of res-tenosis, however, might accompany the drawback of a higher occurrence of stent thrombosis. Stent throm-bosis is not a common phenomenon comparatively,[2] but is a critical complication that often results in ST-segment Elevation Myocardial Infarction (STEMI) and /or sudden heart failure causing death.[3] In comparison to instent restenosis, which is associated with anginal sort of symptoms, stent thrombosis is a process that occurs acutely and results in Acute Coronary Syndrome (ACS).

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Nevertheless, lower incidence rates of stent thrombosis are indicated in recent large-scale registries which are associated with the use of present-day antithrombotic therapies and contemporary Drug-Eluting Stents (DES).[4] The deployment of the stent with high-pressure along with IVUS guidance cont-ributes to lower occurrences of subacute thrombosis with the use of only aspirin and ticlopidine (antipla-telet therapy).[5-6] The advantage of this antiplatelet therapy after optimal expansion of the stent with high-pressure post-dilation routinely implemented, in com-parison with other antithrombotic regimens has been confirmed by several randomized trials.[6] However, the stent thrombosis persists to be a drastic complication of PCI, the overall incidence of <1% is reported and can be higher in high-risk patients and multivessel procedures.[7] Nonetheless, the incidence of stent throm-bosis is higher in the case of Acute Myocardial Infarc-tion (AMI). The HORIZONS-AMI trial reported the incidence rate as 0.8% and 1.2% within 24 hours (acute ST) and 30 days (sub-acute ST), respectively in the

patients who undergo PCI for AMI. Some other studies have reported the rate of acute ST and sub-acute ST to be around 2.5% in AMI patients. The occurrence of early ST (in the period of 30 days) in patients with AMI and cardiac arrest might be even higher as some studies demonstrate the incidence rate of around 2-5%.[8]

Although the stent thrombosis occurrence is relatively reduced, the absolute rate of stent thrombosis is increasing side by side with the increased stents usage as a broad-spectrum intervention for complex lesions.[9] Patient with stent thrombosis generally suffer devastating clinical outcomes such as death, the rate of which may be as high as 20-40% and the majority of the patients suffer myocardial infarction.[10] In consideration of these facts, there is a need for the development of appropriate strategies to prevent this crucial complication.

Data regarding the rate of incidence of early ST within 30 days of primary PCI, is inadequate, particularly regarding the population of Pakistan. Thus, this study was aimed toward the assessment of the rate of occurrence of sub-acute Stent Thrombosis (ST) after primary percutaneous coronary intervention in patients presenting with Acute Coronary Syndrome (ACS).

## METHODOLOGY

The retrospective hospital records of all the admitted patients at a Tertiary Cardiac Care Center of Lahore Pakistan between July 2019 to June 2021 (IERB Letter number RTPGME/RESEARCH-222) who presented with ACS and had undergone PCI were obtained from the hospital data repository. The implemented sampling technique was non-probability consecutive sampling.

**Sample Size:** With reference to 2.5% prevalence of subacute stent thrombosis (SAT)[8], the sample size calculated was n=37 at 95% CI and 5% margin of error by using WHO calculator.

**Inclusion Criteria:** The patients with at least one-month follow-up records available were included in the research study and the subjects with adverse outcomes within 24 hours after PCI (acute stent thrombosis).

**Exclusion Criteri**a: Those with major or minor periprocedural bleeding events were excluded from the study. The study was carried out after thorough approval from the Ethical Review Committee along with all the concerned authorities and departments.

All the selected patients were put on the guideline-recommended medication regimen, during the procedure, soluble aspirin 300 mg/day, clopidogrel 600 mg, and heparin bolus unfractionated (70-100 units/kg dose adjusted to body weight) proceeded by bolus glycoprotein IIb/IIIa inhibitor. Moreover, starting on the day of the procedure, all patients received 300 mg soluble aspirin once a day and 75 mg clopidogrel daily twice as Dual Anti-Platelet Therapy (DAPT) for the one-month duration, which was followed by 75mg aspirin indefinitely and 75mg clopidogrel once in a day for a duration of 12 months.

Data concerning demographics and the procedural outcome was collected from the hospital registry in a personalized database. For the assessment of subacute stent thrombosis, records of out-patient visits on the 30th day were also obtained. For the few patients with missing follow-up records who underwent primary PCI during the period of study, the outcome details were obtained through telephonic calls. The follow-up outcomes comprised unexplained all-cause death in a period of 30 days, recurrent MI, re-hospitalization, and procedure repetition.

In the present study, patients with subacute stent thrombosis were identified. Subacute stent thrombosis was illustrated as recurrent MI and occlusion at the site of the implanted stent of the treated vessel after 24 hours to 30 days of the successful angioplasty. Successful angioplasty was considered as the patency of TIMI flow Grade-3 in the treated vessel and angio-graphic residual stenosis <50%. Stent thrombosis was classified as definite or probable as per the definition of the Academic Research Consortium.[11]

IBM SPSS Statistics version 20.0 was used to analyze the gathered data. Mean±SD were calculated to express the continuous variable data and the categorical data was expressed in the form of frequencies and percentages.

## RESULTS

Total (n=551) patients who underwent PCI at our institution were included in the study, out of which, 445(80.7%) patients were male and the remaining 106(19.2%) were females. The mean age was observed as 55.86±11.12 years. The patients that developed stent thrombosis were 27(4.9%), amongst which 3(11.1%) were of definite stent thrombosis and the rest of 24 (88.8%) had probable stent thrombosis. The incidence rate of subacute stent thrombosis was 4.9% (27) taken out of the total number of study participants.

The stented arteries included LAD in 13 (48.1 %), RCA in 10 (37%) and LCX in 3 (11.1%) study participants. The demographics and angiographical characteristics of the patients of subacute thrombosis are summarized in Table-I.

**Table-I: Demographic and Angiographic Characteristics of the patients with Subacute Stent Thrombosis (n=27)**

| Variable | | n (%), Mean±SD |
|---|---|---|
| **Gender** | Male | 22 (81.4 %) |
| | Female | 5 (18.5 %) |
| Age | | 59.15 ± 4.3 |
| BMI | | 25.08 ± 2.19 |
| **Culprit Artery** | LAD | 13 (48.1 %) |
| | RCA | 10 (37 %) |
| | LCX | 3 (11.1 %) |

Among the patients of subacute thrombosis, the mortality rate within 30 days of the primary PCI was observed to be 7% (2 patients). The rate of re-admission within 30 days of the procedure was 5 (18.5%), re-infarction rate was observed as 12 (44.4%) and the rate of re-intervention was 8 (29.6%). Definite stent thrombosis was seen in 3 (11.1%) patients while probable stent thrombosis was reported in 24 (88.8%) of the patients (Table-II).

**Table-II: Follow-up Outcome of the patients with Subacute Stent Thrombosis (n=27)**

| Variable | n (%) |
|---|---|
| **Outcome variables** | |
| Subacute Stent Thrombosis (ST) | 27 (100%) |
| Definite | 3 (11.2%) |
| Probable | 24 (88.8%) |
| Death within 30 days | 2 (7%) |
| Re-admission within 30 days | 5 (18.5%) |
| Recurrent MI | 12 (44.4%) |
| Repeated PCI | 8 (29.6%) |

Table-III depicts the post chi-square test analysis results showing association of predisposing factors of sub-acute stent thrombosis. Among the patients related factors, Diabetes Mellitus is observed to be related to higher rates of subacute stent thrombosis ($p$=0.04).

Smaller size of the vessel and presence of bifurcation lesion was significantly higher in patients with sub-acute stent thrombosis among the lesion related factors with a $p$-value of 0.002 and 0.05, respectively. The stent related predisposing factors of subacute stent thrombosis were due to under sizing of the stent ($p$ <0.0001) and edge dissection ($p$=0.012).

**Table-III: Association of SAT with predisposing factors**

| Variable | With SAT n=27 | $p$-value |
|---|---|---|
| **Patient Related** | | |
| DM | 6(22.2%) | 0.04 |
| Hypertension | 13(48.1%) | 0.51 |
| Smoking | 18(66.6%) | 0.49 |
| Heart failure | 1(3.7%) | 0.69 |
| ACS | 21(77.7%) | 0.03 |
| CKD | 1(3.7%) | 0.63 |
| Poor or non-compliance to medication | 3(11.1%) | 0.004 |
| **Lesion Related** | | |
| Long lesion | 23(85.1%) | 0.50 |
| Diffuse dissection | 1(3.7%) | 0.98 |
| Small vessel | 11(40.7%) | 0.002 |
| Bifurcation lesion | 11(40.7%) | 0.05 |
| Thrombus | 17(62.9%) | 0.69 |
| **Stent Related** | | |
| Under sizing | 5(18.5%) | <0.0001 |
| Under expansion | 1 (3.7%) | 0.98 |
| Edge dissection | 5 (18.5%) | 0.012 |

## DISCUSSION

The preferable treatment choice in most of the patients with STEMI has greatly emerged to be the PCI with the implantation of stent.[12-14] Drug-eluting stents (DES), in comparison with Bare-Metal Stents (BMS), are known to be associated with reduced stent thrombosis and improved revascularization of the target lesion in the patients with stable coronary artery disease and acute coronary syndromes also including STEMI.[4,15,16]

However, there is persistence of safety concerns related to greater risk of late and very late stent thrombosis specially with drug-eluting stents 40-42 and in off-label use, for example in STEMI patients.[17,18]

In the current study involving the (n=551) participants, the primary objective was to identify the stent thrombosis rate within thirty days of the procedure. As per our results, the subacute stent thrombosis is not a very rare event with a incidence rate of 4.9%, which is nearly the 5.3% subacute stent thrombosis rates reported by a recent retrospective study.[10]

According to our findings, the rate of early ST after primary PCI was found to be 5.2%, of which 4.9% were sub-acute stent thrombosis. Previously, the range of the reported rates of ST in STEMI patients based on 1-year data from various randomized trials of modest sample size comparing DES and BMS was approximately 1% 6 to as greater as 3-4%.[19] Our ST incidence

rates are found to be comparatively greater than the studies previously conducted, for example, a HORIZONS AMI trial reported the 2.5% rate of early stent thrombosis (acute and subacute).[20] Lastly, according to the Dutch registry of stent thrombosis, of the 5842 patients, 3.5% patients developed early ST after PCI categorized as definite stent thrombosis.[21] The rate of early acute or subacute ST for patients suffering from STEMI that were either observed in our studies or the later ones was found to be significantly higher as compared to the rates (0.1-1.4%) that were reported for medium- high risk non-STEMI patients and patients diagnosed with coronary artery disease (CAD).[22] Our study, unlike previous studies, reported rates of stent thrombosis by using initially treated population as a basis rather than only using subjects who attained optimal result of the angiographic findings.

The higher rates of stent thrombosis in STEMI patients might be associated with underlying plaque composition which is a cause of MI and the following vascular responses against stents. Inflammation, and deposition of fibrin might occur due to the penetration of stent strut in the underlying necrotic core which might lead to the inhibition of growth of neointima which results in exposed stent struts, particularly with DES.[23]

Our study revealed some patient-, lesion- and stent-related factors that predispose patients to subacute stent thrombosis. Among the patient related factors, Diabetes Mellitus and acute coronary syndrome were the predisposing factor of SAT, in line with other studies.[24] Among the lesion related characteristics, smaller size of the vessel and presence of bifurcation lesion are the observed predisposing factors as described by other trails.[25]

The most terrible complication that can arise after any successful PCI is stent thrombosis. A thorough examination of a patient's potential risk factors along with their ability to tolerate and stick to dual platelet therapy are crucial steps before deciding to proceed with PCI with stenting. Scrupulous care towards technical aspects and details is mandatory for the optimization of implanting and deployment of a stent especially in complex diseases and also to inherently lower the potential risk of ST, novel stents are being developed.

After the implantation of stent, any elective surgery should not be performed without discontinuing dual antiplatelet therapy (if possible). Lastly, anti-platelet agents with high potency such as,

ticagrelor in ACS patients with minimal risk of bleeding is preferred. Consequently, for the prevention or at least reducing the risk of catastrophic complication of stent implantation, evaluation of individual risk of the patients to develop ST is necessary.

## LIMITATIONS OF STUDY

Our study possessed some limitations being it a single-center retrospective study which lacked the data of late and very late stent thrombosis. Secondly, the predisposing factors that lead to subacute stent thrombosis were intro coronary stunt was not done due to cost constraints. Under sizing and edge was assessed by visual estimation which play a major role in causation of stent thrombosis.

## CONCLUSION

Conclusively, our study reveals that subacute stent thrombosis is an event with a comparatively higher frequency in patients who undergo Revascularization PCI for acute coronary syndrome, demonstrating a frequency of 4.9% and a mortality rate of 74% within 30 days of the procedure. Patient-associated, stent-associated and lesion-associated, pre disposing factors must be considered for the better outcome of the intervention

**Conflict of Interest:** None.

**Author's Contribution**

Following authors have made substantial contributions to the manuscript as under:

KA: Study design, concept & critical review

MAA: Manuscript writing, drafting and editing

KZ: Data collection, data entry and review of article

IA: Data collection, data entry and review of article

AI: Drafting the manuscript, proof reading & critical review

SG: Review of article, formatting and critical review

BA: Study design, concept and critical review

JK: Analysis, result interpretation and proof reading

NA: Review of article, formatting and critical review

AS: Review of article, formatting and critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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