Frequency, Risk Factors and Management of Definite Stent Thrombosis in a Tertiary Care Teaching Hospital in Central India: An Observational Study

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Abstract: <u>*Background and objectives*</u>*: Stent thrombosis is a rare but dreaded complication of coronary intervention. The present study was carried out to investigate the clinical, procedural and lesion factors related to early and late/very late stent thrombosis in patients with stent thrombosis.* <u>*Methodology:*</u> *This was a single-centred observational study conducted in central India, among 34 patients with stent thrombosis post percutaneous coronary intervention with drug eluting stent during September 2022 to April 2024. Relevant data were collected through structured questionnaires, hospital records, clinical examination and lab investigations. Frequencies and percentages were calculated. The chi-square test was used to compare the categorical variables and the unpaired t-test for continuous variables, and a p-value of 0.05 was taken as statistically significant.* <u>*Results:*</u> *Out of 34 cases, early ST was observed in 20 (58.82%) cases, late in 9 (26.47%) cases, and very late in 5 (14.71%) cases respectively, 21 cases (61.76 %) were male, 28 (82.35 %) were diabetic and 24 (70.58 %) were hypertensive. and 12 (35.29 %) patients reported anti-platelet withdrawal. The mean age of the study participants was 52.4 ±4.2 years. Age of the patients, past history of diabetes mellitus, past history of hypertension, and anti-platelet withdrawal were significantly associated with the timing of ST(p<0.05).* <u>*Conclusion:*</u> *The current study concluded that patient age, diabetic status, hypertensive status and antiplatelet withdrawal as factors significantly associated with the timing of stent thrombosis.*

Keywords: Stent Thrombosis, Coronary Intervention, Percutaneous Coronary Intervention, Cardiovascular Diseases

1. Introduction

Cardiovascular diseases (CVDs) are one of the leading causes of death worldwide. Approximately 17.9 million people died from CVDs in 2019, which represents around 32% of all worldwide deaths. Of these deaths, 85% were due to Myocardial Infarction (MI) and Stroke. Most of CVD deaths take place in low- and middle-income countries.[1]

In 21st century, cardiovascular diseases (CVDs) became the leading cause of mortality and morbidity in India. This epidemiological transition is largely attributed to the increase in the prevalence of CVDs and CVD risk factors in India. In 2016, the estimated prevalence of CVDs in India was estimated to be 54.5 million. Ischemic heart disease (IHD) and stroke are responsible for >80% of mortality related to CVDs. [2]

The CVD epidemic in Indians is characterized by a higher relative risk burden, an earlier age of onset, higher case fatality including higher premature deaths. [3] According to the World Health Organization report, India accounts for one-fifth of these deaths worldwide especially in younger population. The Global Burden of Disease study result showed that age-standardized CVD death rate of 272 per 1 lac population in India which is higher than that of worldwide estimated average of 235. CVDs affects Indians a decade earlier than the western population. [4] The INTERHEART study showed that CVD risk factors such as abdominal obesity, hypertension, and diabetes are higher among Indians, even at young ages compared to other ethnic groups.[5]

Percutaneous coronary intervention (PCI) is an invasive procedure designed to alleviate the obstruction to blood flow in coronary artery, thus enhancing blood flow to the heart musculature. PCI is essential in managing a primary cause of mortality globally which is coronary artery disease (CAD). [6] However, PCI has its own complications including restenosis (reocclusion of the vessel), stent thrombosis (blood clot within the stent), bleeding manifestations and radiation hazard. As compared to bare metal stents (BMS), drug-eluting stents (DES) have shown to reduce restenosis rates and target lesion revascularization in patients with IHD. [7]

However, the available current literature regarding the timing of stent thrombosis post PCI and its management strategies varies with respect to population characteristics, patient and other procedural factors. There is insufficient evidence about the likely causes of stent thrombosis in low and middle-income countries. Hence the present study was carried out to investigate the clinical, procedural and lesion factors related to early and late/very late stent thrombosis in patients with stent thrombosis and to study their management strategy.

2. Methodology

This was a single-centred observational study conducted in the Cardiology department of a tertiary care teaching hospital

in Maharashtra, India, among 34 patients presenting with stent thrombosis post percutaneous coronary intervention with drug eluting stent for coronary artery disease during September 2022 to April 2024.

The Institutional Ethics Committee approval was taken prior to the study. Written informed consent was obtained from all the study participants, and confidentiality of data was maintained. Both males and females patients aged ≥18, patients who had undergone Percutaneous Coronary Intervention with a Drug-Eluting stent for coronary artery disease and presented with suspected stent thrombosis were recruited in this study, including the patients who had undergone PCI in our institute as well as those who had been operated in other hospitals previously and referred to our institute for stent thrombosis. Patients who underwent Percutaneous old Balloon Angioplasty were excluded.

Stent thrombosis was defined by per Academic Research Consortium (ARC). The ARC categorises stent thrombosis according to the level of documentation and timing. Definite or confirmed event (symptoms suggestive of an acute coronary syndrome and angiographic or pathologic confirmation of stent thrombosis).

Based on the elapsed time since stent implantation, stent thrombosis can be classified as early (0-30 days post-stent implantation), late (>30 days- 1 year), and very late (>12 months). Often, early stent thrombosis is further subdivided into acute (<24 hours) and subacute (1-30 days) events. [8]

Patients details were obtained by the primary investigator with help of a structured proforma which contained socio demographic details, information regarding the presenting complains, past history of co-morbidities such as diabetes, systemic hypertension, chronic kidney disease, coronary artery disease or acute coronary syndrome, smoking habits, alcohol intake, past medication history, any family history of premature cardiac disease, coronary artery disease, or sudden death.

Details regarding the type of stent implanted procedural details including lesion type, evidence of thrombus containing lesion, inflation details, TIMI flow before and after the procedure were collected from the hospital records. All study participants were subjected to thorough clinical examination and routine blood investigations such as random blood sugar, Troponin, lipid profile, blood urea and serum creatinine. ECG and cardiac 2 D ECHO were done for all patients. Suspected stent thrombosis was confirmed with a coronary angiogram, and the patients have managed accordingly in the Dept. of Cardiology by senior consultants. Details regarding the procedural factors of the coronary stents were recorded for all study subjects.

The features accountable for ST were assessed based on patient, procedure related and lesion characteristics. The management strategy for stent thrombosis patients was assessed.

Statistical Analysis

The data collected and entered in MS Excel. The data was analysed with IBM SPSS trial version 23.0. Frequencies and percentages were calculated. Mean and standard deviations were calculated for continuous variables. The chi-square test was used to compare the categorical variables and the unpaired t-test for continuous variables, and a p-value of 0.05 was taken as statistically significant.

3. Results

This study was conducted among 34 patients presenting to the dept. of cardiology with stent thrombosis (ST) post PCI with drug eluting stent from September 2022 to April 2024.

Out of 34 cases, early ST was observed in 20 (58.82%) cases, late in 9 (26.47%) cases, and very late in 5 (14.71%) cases respectively. Table 1 shows the distribution of study subjects according the types of ST suffered. The figures in parenthesis denote row percentages.

Out of 34 study subjects. 21 (61.76 %) were male, 28 (82.35 %) were diabetic and 24 (70.58 %) were hypertensive. Thirteen ((38.23 %) patients were smokers, and 12 (35.29 %) patients reported anti-platelet withdrawal. Nine (26.70%) patients had ejection fraction of less than 40 %, 13 (38.23%) cases had a prior history of myocardial infarction, and only 4 (11.76%) had a prior history of PCI. Age of the patients, past history of diabetes mellitus, past history of hypertension, and non-compliance or poor compliance with anti-platelet drugs were found to vary significantly in cases with early ST and late/very late ST (p<0.05) (Table 2).

The most common mode of presentation was MI, seen in 14 (41.17%) cases. Mode of presentation was not found to be significantly associated with the timing of ST post PCI. (Table 2).

The most common type of lesion encountered in study subjects was thrombus containing lesion (13/34 cases, {38.23 %}), followed by B/C type lesion (7/34 cases, {20.58%}). The types of lesion did not vary significantly among cases with early and late/very late ST (p>0.05). However, there was a significant difference in the mean lesion lengths of cases with early ST and late/very late ST(p<0.05). (Table 3).

Table 1: Distribution of study subjects according to type of stent thrombosis (n=34)

Type of stent thrombosis		Frequency	Percentage
Early	Total	20	58.82%
	Acute	9	26.47%
	Sub-acute	11	32.35%
Late		9	26.47%
Very late		5	14.71%
Total ST		34	100%

Table 2: Association of Patient factors and mode of presentation with ST

Patient factors		Early ST, n=20	Late and very late ST, n=14	Total n=34	P
Age (Mean)		56.75 ± 8.76	48.32±6.42	34	**0.0028**
Gender	Male	12 (35.29)	9 (26.47)	21 (61.76)	0.800
	Female	8 (23.52)	5 (14.70)	13 (38.23)	
H/O DM	Present	19 (55.88)	6 (17.64)	28 (82.35)	**0.0006**
	Absent	1 (2.94)	5 (14.70)	6 (17.64)	
H/O HTN	Present	17 (50)	7 (20.58)	24 (70.58)	**0.0275**
	Absent	3(8.82)	7(20.58)	10 (29.41)	
H/O smoking	Present	8 (23.52)	5 (14.70)	13 (38.23)	0.800
	Absent	12 (35.29)	9(26.47)	11 (32.35)	
Anti platelet withdrawal	Present	2 (5.88)	10 (29.41)	12 (35.29)	**0.0002**
	Absent	18 (52.94)	4 (11.76)	22 (64.70)	
Ejection fraction <40%	Present	6 (17.64)	3 (8.82)	9 (26.70)	0.577
	Absent	14 (41.17)	11 (32.35)	25 (73.52)	
Prior H/O MI	Present	7 (20.58)	6 (17.64)	13 (38.23)	0.642
	Absent	13 (38.23)	8 (23.52)	21 (61.76)	
Prior H/O PCI	Present	2 (5.88)	2 (5.88)	4 (11.76)	0.702
	Absent	18 (52.94)	12 (35.29)	30 (88.23)	
Mode of presentation	STEMI	9 (26.47)	5 (14.70)	14 (41.17)	0.974
	NSTEMI	2 (5.88)	1 (2.94)	3 (8.82)	
	Unstable Angina	4 (11.76)	2 (5.88)	6 (17.64)	
	LV failure	3 (8.82)	3 (8.82)	6 (17.64)	
	AVRT/ Recurrent VT	3 (8.82)	2 (5.88)	5 (14.70)	

Table 3: Association of lesion factors with ST

Lesion factors	Early ST n=20	Late/ Very late ST, n=14	Total, n=34	p
Thrombus containing lesion	9 (26.47)	4 (11.76)	13 (38.23)	0.6847
Type B/C lesion	3 (8.82)	4 (11.76)	7 (20.58)	
Complete occlusion	2 (5.88)	3 (8.82)	5 (14.70)	
Bifurcation Lesion	2 (5.88)	1 (2.94)	3 (8.82)	
In-stent Restenosis	4 (11.76)	2 (5.88)	6 (17.64)	
Mean lesion length (mm)	21.4± 4.3	22.1± 3.9		0.63

Table 4 details the procedural details of the cases and their association with the timing of ST. There was no significant difference between the stent lengths and diameters used in cases with early and late/ very late ST. The Left anterior descending artery (LAD) was the most common vessel involved (25/34, 73.52%). Four (11.76%) patients developed dissection of the stented vessel. Lesion mismatch was seen in 3(8.82%) cases. Initial TIMI grade 3 flow was seen in only 2 (5.88%) cases, whereas the finial TIMI grade 3 flow was observed in 22 (64.7%) cases. There was no statistically significant difference in the vessel involvement, vessel dissection, lesion mismatch, initial and final TIMI grade flows in cases with early and late/very late ST ($p>0.05$).

Table 4: Association of procedural factors with ST

Procedural factors		Early ST n=20	Late/ Very late ST, n=14	Total, n=34	P
Mean stent length (mm)		27.2± 7.6	26.8± 6.3		0.87
Mean stent diameter (mm)		2.79± 2.5	2.9± 3.1		0.83
ST vessel	LAD	16 (47.05)	9 (26.47)	25 (73.52)	0.374
	RCA	2 (5.88)	1 (2.94)	3 (8.82)	
	LCX	2 (5.88)	4 (11.76)	6 (17.64)	
Dissection	Present	1 (2.94)	1 (2.94)	2 (11.76)	0.793
	Absent	19 (55.88)	13 (38.23)	32 (94.11)	
Lesion mismatch	Present	2 (5.88)	1 (2.94)	3 (8.82)	0.772
	Absent	18 (52.94)	13 (38.23)	31 (91.17)	
Initial TIMI grade flow	TIMI 0/1	17 (50)	12 (35.29)	29(85.29)	0.141
	TIMI 2	2 (5.88)	1 (2.94)	3 (8.82)	
	TIMI 3	1 (2.94)	1 (2.94)	2 (5.88)	
Final TIMI grade flow	TIMI 0/1	1 (2.94)	1 (2.94)	2 (5.88)	0.136
	TIMI 2	9 (26.47)	1 (2.94)	10 (29.41)	
	TIMI 3	12 (35.29)	10 (29.41)	22 (64.7)	

The management details of all cases are detailed in table 5. Cases were management by thrombus aspiration, thrombolysis, PCI, CABG, and POBA/Drug eluting balloon (DEB). The most common modality used for management was POBA/DEB. Plain old balloon angioplasty was performed in 13(38.23%) cases, followed by thrombolysis in 8(23.52%) cases, thrombus aspiration in 6(17.64 %), PCI in 4(11.76%) and CABG in 3(8.82%).

Table 5: Management details of study participants

Management	Early ST	Late/very late ST	Total

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PCI	1(2.94)	3(8.82)	4(11.76)
Thrombus Aspiration	6(17.64)	0	6(17.64)
POBA/DEB	7(20.58)	6(17.64)	13(38.23)
CABG	1(2.94)	2(5.88)	3(8.82)
Thrombolysis	5(14.70)	3(8.82)	8(23.52)
Total	20(58.82)	14 (41.17)	34 (100)

4. Discussion

The current study was conducted among 34 patients with stent thrombosis presenting to the cardiology department of a tertiary care teaching hospital in central India. Out of 34 patients, 20(58.82 %) presented with early ST, and 14 (41.17%) with late / very late ST. the mean age of patients varied significantly in cases with early and late/very late ST. similar findings were reported in a study by Forero MT et al, where late and very late ST was reported in older patients and age was found to be significantly associated with the timing of ST. [9]

In our study, diabetic and hypertensive status was found to be significantly associated with the timing of stent thrombosis. Early ST was more commonly observed among diabetic and hypertensive patients. There is abundant literature about diabetic and hypertensive status being associated with a significantly higher risk of definite stent thrombosis. [10-12] Armstrong, E, Feldman, D, Wang, T. et al. also reported similar findings. [13] Antiplatelet withdrawal was also found to be significantly associated with the timing of ST, and late/ very late ST was observed more frequently in cases with antiplatelet withdrawal. Multiple studies have identified that discontinuation of antiplatelet therapy is the dominant risk factor for the occurrence of late stent thrombosis (LST) and very late stent thrombosis (VLST) in patients with drug-eluting stents (DES).[14-16] Other patient factors, lesion factors, & procedural factors were not found to be statistically significant.

Cases were management by thrombus aspiration, thrombolysis, PCI, CABG, and POBA/DEB. The most common modality used for management was POBA/DEB which was performed in 13(38.23%) cases.

5. Conclusion

Stent thrombosis is a rare but dreaded complication of coronary intervention. The current study concluded that patient age, diabetic status, hypertensive status and antiplatelet withdrawal as factors significantly associated with the timing of stent thrombosis.

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