

Stent Thrombosis after Rescue Percutaneous Coronary Intervention in Acute ST-Segment Elevation Myocardial Infarction

Khalid Bin Thani^{1,*}, Fajer Al-Moosa¹, Eman Murad¹, Aisha Al-Moosa¹, Mohamed E. Alalawi¹ and Hind Al-Sindi²

¹Salmaniya Medical Complex, Division of Cardiology, Department of Internal Medicine, Manama, Kingdom of Bahrain

²Primary Care and Family Physician Program, Ministry of Health, Manama, Kingdom of Bahrain

Abstract: *Main Problem:* To determine the incidence of coronary stent thrombosis (ST) in patients with acute ST segment elevation myocardial infarction (STEMI) after rescue percutaneous coronary intervention (PCI).

Methods: An observational study looking at the incidence of ST in a middle-eastern population. A total of 510 consecutive patients presented with ST-segment elevation myocardial infarction (STEMI) were enrolled and underwent thrombolytic therapy with a total follow-up period of 2 years. Study outcomes were ST, death, re-infarction or acute coronary syndrome requiring coronary angiography and PCI.

Results: A total of 510 patients enrolled, all diagnosed with STEMI and underwent thrombolytic therapy. Only 100 subjects underwent rescue PCI with intra-coronary stenting, including 54 patients with drug-eluting stent (DES) and 46 patients with bare metal stent (BMS). During the study period and follow-up, the overall rate of ST was 13.7%, definite ST occurred in 6 patients (5.5%), probable ST in 8 patients (7.3%), and possible ST in one patient (0.9%), including 0.9% acute ST, 0.9% sub-acute ST, 2.8% late ST and 8.3% very late ST. Patients with ST were likely to have prior PCI ($p=0.001$), prior coronary artery bypass grafting (CABG) ($p=0.002$) and history of heart failure ($p=0.04$).

Conclusion: ST is infrequent event with major consequences in patients presenting with STEMI in the first 2 years after stent implantation.

Keywords: Acute myocardial Infarction, Arab, Bahrain, Gulf States, Middle East, Stent Thrombosis, STEMI.

INTRODUCTION

Percutaneous coronary intervention (PCI), if performed in a timely fashion, is the recommended reperfusion strategy for most patients with acute ST elevation myocardial infarction (STEMI) [1]. Intracoronary stenting became the standard of care as it has been associated with greater efficacy and lower rate of early re-occlusion and late restenosis significantly reducing the need for repeat target vessel revascularization compared to balloon angioplasty [2, 3]. Compared with bare metal stents (BMS), drug-eluting stents further reduce these complications [4, 5]. However, although uncommon, intracoronary stenting has been associated with an increased risk of stent thrombosis (ST). ST is a potentially life-threatening complication presenting either as myocardial infarction (MI) or death. Moreover, the emergence of drug-eluting stents (DES) has raised concerns regarding an increased rate of late and very late stent thrombosis [6, 7].

Since there has been a paucity of articles on ST in the Middle East region, the aim of our study was to determine the incidence of ST in patients with acute STEMI focusing on the timing and predictors of ST in Middle Eastern.

METHODS

This is an observational study which was conducted in Salmaniya Medical Complex; the largest multi-specialty secondary and tertiary hospital in the Kingdom of Bahrain. The hospital covers the whole Kingdom with a catchment area of 800,000 of the population. In our study we have included all consecutive patients who presented with STEMI and underwent thrombolytic therapy (TT), from May 2009 until December 2011. Patients were followed up for two years until May 2013. A total of 510 patients were enrolled with (109 subjects underwent coronary angiography and only 100 had rescue PCI with intracoronary stent placement out of the 510 thrombolysis patients). The study was approved by the Secondary Care Medical Research Subcommittee in the Ministry of Health at the Kingdom Of Bahrain. The data were extracted from our ST-segment elevation myocardial infarction registry data. All patients presented with STEMI and received TT, all patients went for rescue PCI were included and followed up. All information of the incident admission were collected including, patient

*Address correspondence to this author at the Division of Cardiology, Department of Internal Medicine, Salmaniya Medical Complex, P.O. Box 12, Manama, Kingdom of Bahrain; Tel: (+973) 17-279750; Fax: (+973) 17-279774; E-mail: genfith@hotmail.com

demographics (*i.e.* age, nationality, and gender), full cardiovascular history (past stable or unstable angina, heart failure, coronary artery bypass surgery and history of PCI), data related to prior stenting procedure, pre-admission medication history, blood chemistries (including renal function, cardiac enzymes, and lipid panel), cardiac markers of Troponin and CKMB, and transthoracic echocardiogram (TTE) if available (measuring left ventricular ejection fraction (LVEF%). Furthermore, the procedural and angiographic characteristics of the cardiac catheterization and intervention were reviewed by obtaining the full angiographic report and by reviewing the angiographic study, if available in the patient's charts. The study outcomes were re-infarction episode *i.e.* STEMI, non-STEMI and left bundle branch block myocardial infarction (LBBB-MI), death and documented stent thrombosis in any future coronary angiography and PCI for any ACS episode.

Definition of Stent Thrombosis: ST was categorized according to the timing after the initial PCI and to the evidence of ST based on the Academic Research Consortium (ARC) definition of ST [8]. Events occurring within the first 24 hours of stent implantation were considered to represent acute ST, with sub-acute occurring between 24 hours and 30 days, late between 30 days and one year and very late after one year.

The Definite ST was defined as the presence of angiographic confirmation of a thrombus that originates in the stent or in the segment 5 mm proximal or distal to the stent, with or without vessel occlusion, which is associated with acute onset of ischemic symptoms at rest or ECG signs of acute ischemia or typical rise and fall of in cardiac biomarkers within 48 hours of angiography or pathologic confirmation of ST determined at autopsy or from tissue obtained following thrombectomy. While probable was defined as unexplained death occurring within 30 days after the index procedure, or an MI occurring at any time after the index procedure that was documented by ECG or imaging to occur in an area supplied by the stented vessel in the absence of angiographic confirmation of stent thrombosis or other culprit lesion. Possible ST was defined as unexplained death occurring more than 30 days after the index procedure [8].

STATISTICAL ANALYSIS

The overall ST incidence was calculated from the total number of the screened patients who underwent PCI and stent placement. Demographic and other clinical characteristics of patients with and without ST were compared between patients. Categorical variables are presented as raw numbers and percentages and were compared with the χ^2 test or Fisher exact test. Continuous variables are presented as mean \pm SD and were compared with the Student *t* test. All statistical tests were 2-tailed with a P value <0.05 was considered statistically significant. All analyses were conducted using IBM[®] SPSS[®] Statistics 20 Software.

RESULTS

Characteristics of the Study Patients: Between May 2009, and December 2011 a total of 510 patients presenting

with STEMI and undergoing TT were enrolled. Out of the 510 patients, PTCA was performed in 109 subjects among whom intra-coronary stenting was performed in 100. Among those patients undergoing stenting, 54 patients received a DES and 46 patients had a BMS. The mean age of the patients was 51 years, and 91.6% were men. Hypertension and diabetes were present in approximately one third of the study population, 33.5% and 34.5% respectively, and nearly half of the patients (53.5%) were current smokers (Table 1).

Table 1. The total study population baseline clinical characteristics.

Variable	Total=510 subjects n (%) or (mean \pm SD)
Age (Mean), Year	51.6 (\pm 11.2)
Male, %	467(91.6%)
Past Medical History	
Hypertension	171(33.5%)
Hyperlipidemia	107(21.0%)
Diabetes Mellitus	176(34.5%)
Current Smoking	273(53.5%)
Prior Myocardial Infarction	19(3.7%)
Prior PCI	19(3.7%)
Prior CABG	6(1.2%)
Renal Insufficiency	11(2.2%)
Peripheral Arterial Disease	6(1.2%)
History of Congestive Heart Failure	9(1.8%)
Left Ventricular Ejection Fraction (LVEF %)	49.9(\pm 14.4)
Door-to-Needle (Minutes)	66.9(\pm 80.7)
Hemoglobin (mg/dL)	14.9(\pm 7.1)
Platelet Count ($\times 10^9$ cells/mm ²)	237.9(\pm 60.2)
Creatinine (mmol/L)	95.6(\pm 32.6)
HbA1c%	7.3(\pm 2.5)
Fibrinogen (mg/dl)	272.5(\pm 170.3)

Stent Thrombosis: By using the ARC definition of stent thrombosis, we report an overall rate of ST of 13.7%. During the study period, 8 subjects presented to the emergency room at our centre with ST while 7 subjects had ST during the follow-up period. Among the 15 patients with ST, definite ST was present in 6 patients (5.5%), probable ST in 8 patients (7.3%), and possible ST in one patient (0.9%).

Acute ST occurred in one patient (0.9%); sub-acute ST occurred in one patient (0.9%); late ST occurred in 3 patients (2.8%); and very late ST occurred in 9 patients (8.3%).

Predictors of Stent Thrombosis: In Table 2 the clinical, angiographic and procedural correlates of ST are shown compared with patients without ST. Those with ST had a higher trend rate of prior MI ($P=0.08$), and a significant history of coronary artery disease with previous revascularization (i.e. PCI ($P=0.001$) or CABG ($P=0.002$)), and history of heart failure ($P=0.04$). Other baseline clinical characteristics and laboratory data were comparable between the two groups (Table 2). Pre- and Post-PCI angiographic data and Thrombolysis In Myocardial Infarction (TIMI) Flow Grade were comparable between the two groups. Neither glycoprotein IIb/IIIa Inhibitors nor Intra-aortic Balloon Pump usage had significant effect on the incidence of stent thrombosis.

DISCUSSION

To our knowledge, this is the first study on ST in the Gulf States region to date. We have included and analyzed a cohort of 510 patients who presented with STEMI and received initially TT with a follow-up period of 2 years. In our study the overall incidence of ST according to the ARC definitions was 13.7% and the very late ST was the commonest. We did encounter in the literature a case report from the region on very late ST, in a 41 years-old Arab male who underwent multivessel PCI with sirolimus-eluting stent (SES), the risk profile of the described case is not far from our cohort risk profile and clinical presentation [9].

The Gulf Registry of Acute Coronary Events (Gulf RACE); a prospective, multinational study of all consecutive patients hospitalized with a final diagnosis of ACS in 6 Arab countries, gave us an insight to our population in the Gulf region [10]. Some of the factors that may have played a major role in our patients presentation were delayed presentation and missed reperfusion therapy as nearly one-third of STEMI patients in the Arab Middle East presented to the hospital >12 hours after symptom onset which was associated with increased in-hospital mortality, cardiogenic shock, and new-onset heart failure [11]. Furthermore, in regard to the Emergency Medical Services (EMS) utilization by patients with ACS in the Arab Middle East, it has been shown that only 17% of hospitalized patients presented by EMS and those who presented by EMS were significantly less likely to exhibit major delay in presentation with a higher likelihood of receiving coronary reperfusion therapy in a timely fashion [12]. These factors may have played a role in our study population presentation and contribute to the likelihood of receiving appropriate therapy and treatment delivery. Hence, cardiac catheterization among patients with ACS in the Middle East is under utilized as compared with Western countries with an overall rate of 20% of all ACS presentations [13]. This underutilization of the cardiac catheterization facilities is another caveat in our data and this shown clearly from the total number of catheterized patients in our cohort.

In an attempt for a comparison between the in-hospital outcomes of primary PCI and the usage of TT in STEMI patients in the Middle East, we found that the overall rate of reperfusion therapy was 92%; (8 % PPCI and 84 % TT), and it showed clearly that the main reperfusion strategy for STEMI patients in the Arab Middle East region is TT [14]. By this means, re-infarction in previously stented patients may not undergo cardiac catheterization and to be given the benefit of early reperfusion by mechanical and endovascular means. By taking these regional medical health facts and the probable outcomes that may arise from them we still believe that our reported data in this study is a “real-world” and a reflection of the practice not only in our state level but regional level as well.

An overall 5.5% incidence of definite ST at two years is relatively higher than that reported in large registries and randomized trials. Both in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and in The Dutch stent thrombosis registry [15, 16], the rate of definite stent thrombosis was 1.2% while in The HORIZONS-AMI trial the incidence was 4.4% [17]. The higher rate of ST in our study could be related to the small study population compared with the above mentioned trials. Other plausible explanations are noncompliance with antiplatelet therapy and the higher prevalence of antiplatelet hyporesponsiveness or resistance in our populations as compared with western populations due to genetic polymorphisms [18]. Several studies have supported the clinical significance of antiplatelet resistance and in this regard a collaborative meta-analysis of 6 studies which included 3,059 patients with an objective of evaluating the impact of platelet reactivity on clinical outcomes after PCI concluded a significantly higher rate of ST in patients with higher on-treatment platelet reactivity [19]. A similar observation was made in The RECLOSE trial; a prospective study on the Incidence and Clinical Impact of Dual Nonresponsiveness to Aspirin and Clopidogrel in Patients With Drug-Eluting Stents; which concluded that dual nonresponsiveness was an independent predictor of DES thrombosis [20]. Again the data regarding the antiplatelet hyporesponsiveness, genetic polymorphisms, and the liberal use of proton-pump inhibitors are limited and warrant further investigation in our region. However, with the newer generation antiplatelet therapy, the hyporesponsiveness and genetic polymorphisms may not have a major contribution in the future.

STUDY LIMITATION

The study is an observational registry and only included patients who presented with STEMI and underwent TT which is the mainstay reperfusion modality in the Gulf region [14]. Patients who may presented for the first or initial evaluation with unstable angina, non-STEMI and late-presentation STEMI or the one who did not received thrombolysis were not included, this may have affected the overall incidence. Furthermore, although the study was conducted in the main governmental hospital, patients may have presented to other private sector or other local or regional hospitals. Moreover, some patients might have

Table 2. Baseline clinical and core angiographic laboratory characteristics of the lesion and procedural intervention in patients who underwent percutaneous coronary intervention.

Variables	Stent Thrombosis (n=15) n (%) or (mean \pm SD)	No Stent Thrombosis (n=102) n (%) or (mean \pm SD)	P value
Age (Mean), Year	54.6 (\pm 14.6)	53.8 (\pm 9.4)	0.77
Male, %	12(11.7%)	91(88.9%)	0.25
Past Medical History			
Hypertension	9(17.6)	42(82.4)	0.26
Hyperlipidemia	5(15.6)	27(84.4)	0.55
Diabetes Mellitus	71(14.6)	44(85.4)	0.78
Current Smoking	8(15.4)	44(84.6)	0.32
Prior MI	2(50.0)	2(50.0)	0.08
Prior PCI	8(66.6)	4(33.4)	0.001
Prior CABG	3(100)	0	0.002
Renal Insufficiency	1(33.3)	2(66.7)	0.34
Peripheral Arterial Disease	1(33.3)	2(66.7)	0.34
History of HF	2(66.7)	1(33.3)	0.04
Left Ventricular Ejection Fraction (LVEF %)	43.3 (\pm 12.2)	44.3(\pm 11.8)	0.76
Door-to-Needle (Minutes)	73.3(\pm 68.9)	78.6(\pm 100.3)	0.84
Hemoglobin (mg/dL)	13.9(\pm 1.9)	14.3(\pm 1.8)	0.45
Platelet Count ($\times 10^9$ cells/mm ²)	234.4(\pm 41.2)	236.6(\pm 60.2)	0.88
Creatinine (mmol/L)	98.5(\pm 23.1)	92.1(\pm 23.6)	0.32
HbA1c%	6.4(\pm 1.9)	7.4(\pm 2.4)	0.33
Fibrinogen (mg/dl)	257.5(\pm 156.7)	274.3(\pm 114.1)	0.63
Stent Type			
Bare-Metal Stent	6(11.1)	48(88.9)	0.21
Drug-Eluting Stent	2(4.3)	44(95.7)	
Lesion Target Vessel			
Left Anterior Descending Artery	3(5.1)	56(94.9)	0.68
Left Circumflex Artery	3(17.6)	14(82.4)	
Right Coronary Artery	2(6.3)	30(93.8)	
Number of Vessels Treated	8(7.3)	102(92.7)	0.83
Diameter Stenosis, mm (Pre-Procedure)	94.2(\pm 4.9)	87.8(\pm 10.4)	0.14

Table 2. contd..

Variables	Stent Thrombosis (n=15) n (%) or (mean \pm SD)	No Stent Thrombosis (n=102) n (%) or (mean \pm SD)	P value
Lesion Length, mm	14.5(\pm 4.8)	20.9(\pm 8.8)	0.08
Stent Length, mm	18.8(\pm 5.1)	27.1(12.7)	0.11
Lesion Type			0.17
C Lesion	2(3.9)	49(96.1)	
Non-C Lesion	5(11.4)	39(88.6)	
Number of Stents Per Vessel (Culprit Lesion)	1.0(\pm 0.5)	1.5(\pm 0.7)	0.07
TIMI Flow Grade (Pre-PCI)			0.79
0/1	2(11.1)	21(88.9)	
2	0	5(100)	
3	4(5.9)	64(94.1)	
TIMI Flow Grade (Final or Post-PCI)			0.91
0/1	0	3(100)	
2	0	4(100)	
3	6(6.7)	83(93.3)	
Use of Glycoprotein IIb/IIIa Inhibitors	0	12(100)	0.59
Use of Intra-aortic Balloon Pump	0	4(100)	0.74
Final Target Lesion Findings			
Thrombus	0	2(100)	0.75
Distal Embolization	1(33.3)	2(66.7)	0.34
Abrupt Vessel Closure	0	1(100)	0.87
No Reflow	0	7(100)	0.36
Dissection	0	2(100)	0.75

SD: Standard Deviation; MI: Myocardial Infarction; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Graft Surgery; HF: Heart Failure; LVEF: Left Ventricular Ejection Fraction; HbA1C: Glycosylated Hemoglobin; TIMI: Thrombolysis In Myocardial Infarction.

missed follow up with our system. In addition, some of the predictor of ST may have been overcome in this study e.g. discontinuation of dual antiplatelet therapy at the follow up period and the non-responders to antiplatelet therapy.

CONCLUSION

ST is a detrimental complication in patients undergoing coronary intervention and is a major cause of mortality and morbidity. Additional studies are warranted to have a closer look at physician's experience and procedural characteristics and need to be confirmed in a trial adequately powered with a longer follow-up period in the Gulf region.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013; 127: e362-425.

- [2] Nordmann AJ, Hengstler P, Harr T, Young J, Bucher HC. Clinical outcomes of primary stenting versus balloon angioplasty in patients with myocardial infarction: a meta-analysis of randomized controlled trials. *Am J Med* 2004; 116: 253-62.
- [3] Fischman DL, Leon MB, Baim DS, *et al.* A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study Investigators. *N Engl J Med* 1994; 331: 496-501
- [4] Weisz G, Leon MB, Holmes DR Jr, *et al.* Five-year follow-up after sirolimus-eluting stent implantation results of the SIRIUS (Sirolimus-Eluting Stent in De-Novo Native Coronary Lesions) Trial. *J Am Coll Cardiol* 2009; 53: 1488-97
- [5] Ellis SG, Stone GW, Cox DA, *et al.* Long-term safety and efficacy with paclitaxel-eluting stents: 5-year final results of the TAXUS IV clinical trial (TAXUS IV-SR: Treatment of De Novo Coronary Disease Using a Single Paclitaxel-Eluting Stent). *JACC Cardiovasc Interv* 2009; 2: 1248-59.
- [6] Finn AV, Joner M, Nakazawa G, *et al.* Pathological correlates of late drug-eluting stent thrombosis: strut coverage as a marker of endothelialization. *Circulation* 2007; 115: 2435-41
- [7] Joner M, Finn AV, Farb A, *et al.* Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 2006; 48: 193-202
- [8] Cutlip DE, Windecker S, Mehran R, *et al.* Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007; 115: 2344-51
- [9] Panduranga P, Al-Mukhaini M. Very late stent thrombosis of sirolimus-eluting stent 59 months after implantation: a first report from the middle-east and review of literature. *Heart Views* 2011; 12: 22-5.
- [10] Zubaid M, Rashed WA, Al-Khaja N, *et al.* Clinical presentation and outcomes of acute coronary syndromes in the gulf registry of acute coronary events (Gulf RACE). *Saudi Med J* 2008; 29: 251-5.
- [11] Al-Mallah M, Alsheikh-Ali A, Almahmeed W, *et al.* Missed opportunities in the management of st segment elevation myocardial infarction in the arab middle east: patient and physician impediments. *Clin Cardiol* 2010; 33: 565-71.
- [12] Fares S, Zubaid M, Al-Mahmeed W, *et al.* Utilization of emergency medical services by patients with acute coronary syndromes in the Arab Gulf States. *J Emerg Med* 2011; 41: 310-6
- [13] Panduranga P, Sulaiman K, Al-Zakwani I, *et al.* Utilization and determinants of in-hospital cardiac catheterization in patients with acute coronary syndrome from the Middle East. *Angiology* 2010; 61: 744-50.
- [14] Al-Zakwani I, Zubaid M, Al-Riyami A, *et al.* Primary coronary intervention versus thrombolytic therapy in myocardial infarction patients in the Middle East. *Int J Clin Pharm* 2012; 34: 445-51.
- [15] Lagerqvist B, Carlsson J, Fröbert O, *et al.* Stent thrombosis in sweden: a report from the swedish coronary angiography and angioplasty registry. Swedish coronary angiography and angioplasty registry study group. *Circ Cardiovasc Interv* 2009; 2: 401-8.
- [16] Van Werkum JW, Heestermans AA, Zomer AC, *et al.* Predictors of coronary stent thrombosis: the dutch stent thrombosis registry. *J Am Coll Cardiol* 2009; 53: 1399-409
- [17] Dargas GD, Caixeta A, Mehran R, *et al.* Harmonizing outcomes with revascularization and stents in acute myocardial infarction (horizons-ami) trial investigators. Frequency and predictors of stent thrombosis after percutaneous coronary intervention in acute myocardial infarction. *Circulation* 2011; 123: 1745-56.
- [18] Hasan MS, Basri HB, Hin LP, Stanslas J. Genetic polymorphisms and drug interactions leading to clopidogrel resistance: why the Asian population requires special attention. *Int J Neurosci* 2013; 123: 143-54.
- [19] Brar SS, ten Berg J, Marcucci R, *et al.* Impact of platelet reactivity on clinical outcomes after percutaneous coronary intervention. A collaborative meta-analysis of individual participant data. *J Am Coll Cardiol* 2011; 58: 1945-54
- [20] Gori AM, Marcucci R, Migliorini A, *et al.* Incidence and clinical impact of dual nonresponsiveness to aspirin and clopidogrel in patients with drug-eluting stents. *J Am Coll Cardiol* 2008; 52: 734-9.

Received: August 22, 2015

Revised: September 20, 2015

Accepted: October 22, 2015

© Thani *et al.*; Licensee *Bentham Open*.

This is an open access article licensed under the terms of the Creative Commons Attribution-Non-Commercial 4.0 International Public License (CC BY-NC 4.0) (<https://creativecommons.org/licenses/by-nc/4.0/legalcode>), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.