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STENT THROMBOSIS IN REAL WORLD REGISTRY PATIENTS

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Abstract

Many risk factors for stent thrombosis (ST) have been identified, some modifiable and some not. Adequate patient, lesion, and stent selection; a good technical result; and effective treatment are critical in minimizing the risk of ST. In this observational clinical study we tried to elucidate the predictors of ST in real world percutaneous coronary intervention (PCI) patients.

Patients who underwent percutaneous coronary interventions with stent implantation were included in a prospective study for 9 months. ST was defined according to Academic Research Consortium for definitive ST. Conditional logistic regression analysis was performed to determine independent predictors.

A total of 194 consecutive PCI patients were included in the study. The mean age was 59.37±11.04 years. After 9 months, the total number of definitive stent thrombosis was 7 (3.6%). In the last model of the multivariate analysis two most powerful predictors of stent thrombosis emerged. In patients who had interrupted DAPT therapy, the risk for stent thrombosis was 4.6 times higher than in the rest of the PCI population and long lesions elevated the risk by 1.28 times (HR: 4.63, 95% CI: 2.64 to 17.63, p= 0.0007); (HR: 1.28, 95% CI: 1.14 to 1.56, p= 0.0003), respectively.

Stent thrombosis is a multifactorial disease. There is interaction of clinical, angiographic characteristics and also patient's adherence to treatment. Risk factors identification obtains possibility to identify patients who would benefit from alternative therapy.

Key words: stent thrombosis, percutaneous coronary interventions, therapy, predictors

Introduction

Stent thrombosis (ST) with either drug eluting stents (DES) or bear metal stents (BMS) remains catastrophic and, although infrequent, occupies a central place in the risk-benefit equation of percutaneous interventions (PCI). The estimated incidence occurs in varying percentage, between 1 – 5% [1]. Factors associated with ST may be categorized into several groups: 1) the stent, including its geometry, polymer, and drug; 2) the patient, including clinical presentation and comorbid conditions; 3) the procedure, including residual dissection or incomplete expansion; and 4) the extent and duration of antiplatelet therapy and the patient-specific response to this therapy. Improved understanding of these factors will facilitate identification of optimal preventive strategies [2]. The incidence of early and late ST is similar in BMS and DES, but very late ST, although uncommon, occurs more frequently in first-generation DES. Many risk factors for ST have been identified by intravascular imaging and pathology, some modifiable and some not. Adequate patient, lesion, and stent selection; a good technical result; and effective DAPT are critical in minimizing the risk of ST [3]. Discontinuation of clopidogrel, undersizing of the coronary stent, present malignancy, and intermediate stenosis coronary artery disease proximal to the culprit lesion were the strongest predictors of ST [4]. In this observational clinical study we tried to elucidate the predictors of stent thrombosis in real world PCI patients.

Material and methods

Patients who underwent percutaneous coronary interventions with stent implantation were included in a prospective observational study for 9 months. Patients with malignancy and susceptibility to hemorrhage were excluded from the study. Stent thrombosis was defined according to Academic Research Consortium for definitive stent thrombosis [5]. Clinical criteria consisted of a

new episode of chest pain and/or ischemic electrocardiographic changes and/or increase of cardiac biomarkers release. Angiographic criteria consisted of partial or complete occlusion within the previously implanted stent with evidence of fresh thrombus. On the basis of the elapsed time since stent implantation, ST was classified as acute (intraprocedural or within 24 h of the procedure), subacute (from 24 h to 30 days), and late (30 days to 9 months). PCI was performed by standard techniques via radial approach in most cases. During PCI patients were anticoagulated with 70 IU/Kg of unfractionated heparin. All patients were treated with aspirin (100 mg) before PCI and were loaded with clopidogrel (300-600 mg). Aspirin was continued permanently and in patients with acute coronary syndrome 12 months clopidogrel was recommended 75 mg per day. Data on patient demographics, clinical and angiographic characteristics were collected. Statistical analysis: Continuous variables were presented as mean SD and were compared with the Student's t-test or Mann-Whitney U test. The chi-square or Fisher exact test was used to analyze differences in categorical variables. Conditional logistic regression analysis was performed to determine independent predictors of ST. Selected variables were first entered into the univariate analysis. Variables with $p < 0.05$ by univariate analysis were then entered in the conditional logistic regression analysis for identification of predictors of ST.

Results

A total of 194 consecutive PCI patients were included in this study. The mean age of study participants was 59.37±11.04 years; there were 35 (18%) women, and 64 (33%) were diabetics. Active smokers were 130 (67%). From angiographic characteristics, multivessel disease was noted in 41 (21%), long lesions >18 mm in 89 (46%) and small diameter <2.75 mm in 30 (15%) patients.

The incidence of the early and late stent thrombosis is shown in Table 1. Early definitive stent thrombosis occurred in 6 patients (3%) with similar distribution of acute and subacute cases. After 9 months, the total number of definitive stent thrombosis was 7 (3.6%). In the first 30 days of follow-up, in 9 patients DPAT therapy was erroneously interrupted after discharge, and in 12 patients it was interrupted in the next eight months.

Table 1. Early stent thrombosis

Stent thrombosis N=194	n (%)
DST – from 0-30 day	6 (3)
Acute - on day 0	3 (1.5)
Subacute from 1-30 days	3 (1.5)
DST – 9 months	7 (3.6)

DST – definitive stent thrombosis. Acute thrombosis – in 24 hours, subacute thrombosis from day 2 until 30 days.

Predictive analysis

Table 2 illustrates the predictors of stent thrombosis after 9 months of follow- up. In the univariate analysis from the clinical factors heart failure and acute myocardial infarction were significantly associated with stent thrombosis, but this was not the case with advanced stage of angina pectoris (CCS angina III/IV). In regards of demographic data as risk factors, gender and age were not associated with stent thrombosis, but smoking was. Patients with smoking habits had significantly higher rates of stent thrombosis. Diabetes, previous PCI and AIM also did not predict thrombosis in our analysis. History of CABG enlarged risk of thrombosis. Among angiographic variables lesions on smaller vessels (diameter less than 2.75 mm) and long lesions were at higher risk of thrombosis. Multivessel disease was not predictive for stent thrombosis. The usage of rescue stent significantly worsened the incidence of stent thrombosis.

In patients who discontinued DAPT therapy in the first 30 days the analysis showed elevated risk for the adverse event and the presence of polymer did not aggravate the risk of thrombosis.

Table 2. Univariate ß – Coefficients of regression analysis on predictors of definitive stent thrombosis after 9 months of PCI

Predictor	Standardized Coeff. ß	p
Age > 65 years	0.117	ns
Female	0.014	ns
Active smoking	0.178	0.056
Diabetes	0.023	ns
Hypertension	0.078	ns
Hyperlipidemia	0.178	0.086
Heart failure	0.235	0.01
Previous CABG	0.209	ns
Previous PCI	0.009	ns
Previous AMI	0.014	ns
AMI	0.271	0.001
Rescue stent	0.199	0.05
Multivessel disease	0.332	0.002
Diameter < 2.75 mm	0.217	0.01
Long lesions > 18mm	0.198	0.059
DAPT interruption < 30 days	0.377	0.037
DAPT interruption > 30days	0.016	ns

Multivariate predictive analysis

In the last model of the multivariate analysis two most powerful predictors of stent thrombosis in 9 months emerged. In patients who had interrupted DAPT therapy, the risk of stent thrombosis was 4.6 times higher than in the rest of the PCI population and long lesions elevated the risk by 1.28 times (HR: 4.63, 95% CI: 2.64 to 17.63, p= 0.0007); (HR: 1.28, 95% CI: 1.14 to 1.56, p= 0.0003), respectively.

Discussion

Mass adoption of first generation stents was followed by impression of higher risk of late stent thrombosis [6, 7, 8], and this was confirmed in several randomized trials [9, 10, 11]. In our study stent thrombosis occurred in 3.6% and the incidence is comparable to current literature [1]. Most of the thrombosis happened in the early period of 30 days, as it was in the large clinical study from the Dutch registry [4]. The real performances in regard of stent thrombosis and major cardiac adverse events were seen in the large study of Naidu et al. on Xience V in 8061 patients followed for one year [12]. In this study 85.6% of patients did not discontinue antiplatelet therapy for one year. Our results showed a similar percentage of 89%.The most powerful predictors of ST were found in the early discontinuation of DAPT, renal failure and length of the stent. The late discontinuation of DAPT did not predict stent thrombosis. The late interruption of DAPT did not predict thrombosis (4). In our study we found similar predictors of stent thrombosis as in other studies [12, 13], except for the smoking habit. The explanation behind this is in the high prevalence of smoking among our study participants. Implanting stents in smaller vessels was associated with more cases of thrombosis. Both factors lost their predictive significance in the last multivariate model where the discontinuation of DAPT remained the best predictor. In the Swedish real-world registry on 73798 implanted stents, 882 ST (12%) were found. In the multivariate model acute coronary syndromes, insulin-treated diabetes mellitus, smoking, previous coronary interventions, warfarin treatment, small stent diameter and stent in restenotic, complex or by-pass graft lesions had the strongest association with ST [14]. Drug-eluting stents improved the principle of BMS by also delivering drugs locally to inhibit neo-intimal hyperplasia. DES greatly reduced the incidence of restenosis and resulted in a better safety profile as compared to radiation or systemic drug administration [15]. All these studies confirmed our results.

Conclusions

Stent thrombosis is a multifactorial disease. There is interaction of clinical, angiographic characteristics and patient's adherence to treatment. Risk factors identification gives possibility to recognize patients who would benefit from alternative therapy.

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