Clinic Presentation, treatment and outcomes of coronary stent thrombosis

Présentation clinique, traitement et pronostic de la thrombose de stent coronaire

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SUMMARY

Introduction: Stent thrombosis is a recognized as a dreadful complication of PCI yet our local knowledge of this disease is limited, as no registry addresses this complication.

Objective: The aim of our study is to review and compare the presentation of this pathology in our local environment, its therapeutic approach and prognosis.

Methods: Retrospective, descriptive, monocentric study in Sahloul hospital. We collected data about all stent thrombosis treated in our center between 2007 and 2017 and studied the context, treatment and outcome of stent thrombosis.

Results: 63 stent thrombosis files were exploitable. 24.2% of our patients had stopped their antiplatelet treatment before the occurrence of stent thrombosis. 87.3% of them presented with an ST segment elevation myocardial infarction most of it in the territory of the left anterior descending artery, 40% experienced a severe complication such as pulmonary edema, significant bleeding or cardiogenic shock. 85.7% underwent percutaneous revascularization with a success rate of 81.3%. The use of anti GP2B3A was routine. In hospital mortality reached 9.5% and rose to 18% one year after the episode. 8 % of these patients had redo stent thrombosis and 29.5% were hospitalized mostly for ischemic symptoms.

Conclusion: We found high rates of noncompliance to medical treatment. Whilst there is no optimal interventional strategy, adding GP2B3A inhibitors might be useful in the context of stent thrombosis. Despite all efforts, we witness the severe course of this disease.

RÉSUMÉ

Introduction: La thrombose de stent est reconnue comme une complication redoutable de l'angioplastie. Peu de données épidémiologiques sont disponibles en Tunisie.

Objectif: Le but de notre étude était de faire le point sur cette pathologie dans notre centre, ainsi que d'étudier ses modalités thérapeutiques et son pronostic.

Méthodes : Il s'agissait d'une étude rétrospective, descriptive, monocentrique à l'hôpital de Sahloul. Nous avons collecté les données sur toutes les thromboses de stent traitées dans notre centre entre 2007 et 2017 et nous avons étudié les données cliniques, le traitement reçu et les modalités évolutives de la thrombose de stent.

Résultats: 63 dossiers de thrombose de stent étaient exploitables. 24,2% de nos patients avaient arrêté leur traitement antiagrégant plaquettaire avant la survenue d'une thrombose de stent. 87,3% d'entre eux ont présenté un infarctus du myocarde avec sus-décalage du segment ST dont la plupart dans le territoire de l'artère interventriculaire antérieure, 40% ont présenté une complication sévère telle qu'un œdème pulmonaire, une hémorragie importante ou un choc cardiogénique. 85,7% ont eu une revascularisation percutanée avec un taux de réussite de 81,3%. L'utilisation d'anti GP2B3A était systématique. La mortalité hospitalière a atteint 9,5 % et est devenu à 18 % un an après l'épisode. 8 % de ces patients avaient refait une thrombose de stent et 29,5 % ont été hospitalisés majoritairement pour des symptômes ischémiques.

Conclusion: Nous avons constaté des taux élevés de non-observance du traitement médical. Bien qu'il n'y ait pas de stratégie interventionnelle optimale, l'ajout d'inhibiteurs de GP2B3A pourrait être utile dans le cadre de la thrombose de stent.

KEYWORDS
thrombose de stent, présentation clinique, pronostic

MOTS-CLÉS
stent thrombosis, clinic presentation, outcomes.

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INTRODUCTION

Stent thrombosis, clinic presentation, outcomes.

METHODS

Retrospective, descriptive, monocentric study in Sahloul hospital. We collected data about all stent thrombosis treated in our center between 2007 and 2017 and studied the context, treatment and outcomes of stent thrombosis. We included all patients with a definite diagnosis of stent thrombosis as stated by The Academic Research Consortium [2]. All information were collected based on patients files and we investigated the type, clinical presentation and context of stent thrombosis as well as the therapeutic strategies, in hospital course of the disease and 1-year survival.

RESULTS

Our population was mainly masculine with 58 men for a population of 63 individuals. The mean age was 62 years. A quarter of these patients interrupted their antiplatelet treatment without medical advice and 12.9% experienced ST in the context of systemic inflammation based on elevated CRP (Table 1).

Table 1. Context of stent thrombosis

Context of stent thrombosis	Percentage of patients
Poor therapeutic adherence	24.2%
Dependent individuals	3.2%
Biological inflammatory syndrome	12.9%
Resistance to Clopidogrel	3.2%
Urgent surgery	1.6%

Very late stent thrombosis was the commonest presentation, followed by subacute onset. Most cases showed as STEMI with 40% of patients presenting with various degrees of heart failure. The LAD was frequently the culprit artery and a third of the angiograms revealed associated stent restenosis (Table 2).

Table 2. Clinical presentation and angiographic findings of stent thrombosis

Variable	Percentage of patients
Timing of stent thrombosis according to the ARC definition	
Acute	18%
Subacute	24%
Late	14%
Very late	44%
Clinical presentation	
ST segment elevation myocardial infarction	87%
Non ST segment elevation myocardial infarction	8%
Unstable angina	5%
Uncomplicated coronary syndrome	60%
Cardiogenic shock	27%
Pulmonary edema	8%
Moderate manifestations of heart failure	7%
Angiographic presentation	
Left main thrombosis	1%
LAD thrombosis	59%
Circumflex thrombosis	13%
Right coronary thrombosis	27%
Associated stent restenosis	33%

There was no uniform therapeutic strategy and both balloon and stent angioplasty were performed according to patients characteristics. The Average time to coronary angioplasty was 147 minutes. Thromboaspiration was used in 41.3% of procedures and administration of GP2B3A was the common denominator of 69.4% of angioplasties. Angiographic success reached 86.7% but TIMI flow was optimal in only 75% of cases. After PCI, heart failure was the most common complication. Major bleeding occurred in 3% of cases, therefore the use of anti GP2B3A treatment did not seem to significantly increase the risk of life threatening hemorrhage. 9.5% of our patients died in hospital following their stent thrombosis, this percentage rose to 18% after a year of follow-up. Amongst the survivors, 29.5% were re-hospitalized mostly for ischemic heart disease symptoms and 8% of them had redo stent thrombosis (Table 3).

Table 3. Treatment and outcomes of stent thrombosis

Variable	Percentage of patients
Therapeutic strategy	
Thromboaspiration	41.3%
Ballon angioplasty	45.9%
Stent angioplasty	34.4%
Use of GP2B3A inhibitors	69.4%
Result	
Clinical improvement	77.4%
Angiographic success	86.8%
TIMI flow = 0	10%
TIMI flow = 1	3%
TIMI flow = 2	12%
TIMI flow = 3	75%
In hospital morbidity	
Major bleeding	3%
Minor bleeding	9%
Heart failure symptoms	39.6%
Deterioration of ejection fraction	35%
Short and long term prognosis	
In hospital mortality	9.5%
One year mortality	18%
Rehospitalization and stent thrombosis recurrence	
Rehospitalization	29.5%
Recurrence of stent thrombosis	8%

DISCUSSION

Distribution of stent thrombosis

Stent thrombosis is often described as an early complication of angioplasty, yet we found a bigger proportion of very late stent thrombosis in our study. We confront our results with the German [3] and Spanish [4] registries (Figure 1).
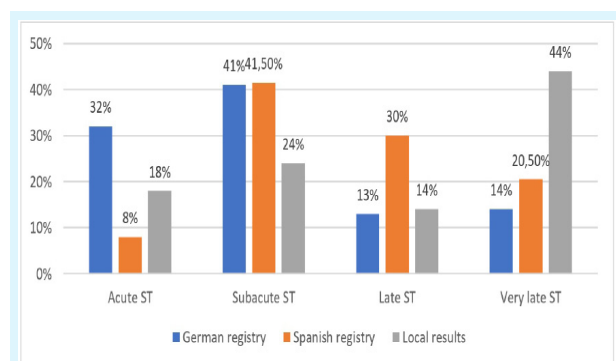
Figure 1. Timing of stent thrombosis (ST).

Factors favoring ST development

Biological inflammatory response

Duk-Woo Park et al examined the CRP of 2691 patients undergoing PCI with DES, they found that elevated preoperative CRP determines a higher rate of ST, curiously this effect was long standing [5]. Another study enrolled 1859 patients for a 27-month follow up and found elevated CRP to be an independent predictive factor of MACCE and ST [6].

In our series, 12.9% of patients had elevated CRP thus reminding us of avoiding angioplasty when biological markers of inflammation are elevated.

Infirmity and dependence

Older patients often suffer from frailty and cognitive impairment. Concerns are raised about medical observance in this population. An American report studying 15996 patients undergoing angioplasty between 2006 and 2007 states that one in five patients did not respect his Clopidogrel prescription in the 7 days following intervention and one in seven stopped the treatment in the first three months. The report indicates that an age > 84 years, dementia and depression favored this behavior [7].

Unplanned surgery

Urgent surgeries raise the issue of antiplatelet treatment interruption. Maintaining Aspirin could result in 2.5 to 20% incremental blood loss, this percentage reaches 30 to 50% when Aspirin and Clopidogrel are combined [8], in the other hand, treatment interruption might lead to rebound aggregation activity thus raising concerns about thrombotic events such as ST especially in recently implanted stents. Several studies showed that, despite the bleeding risk, operating under antiplatelet agents did not increase mortality or procedural failure in the exception of interventions on the cranial cavity [9],[10],[11] whilst some trials reported a very high mortality ranging from 20 to 80% for postoperative stent thrombosis [12],[13]. In the light of this information, ST prevention would prevail on the bleeding risk in a majority of patients.

Poor therapeutic adherence

Interruption of antiplatelet treatment without medical advice was seen in 24.2% of our ST patients. The J-Cypher registry showed that interruption of antiplatelet therapy was

consistently associated with ST through a 5-year follow-up period [14]. An article of Hirotoshi Watanabe showed that among 15939 patients treated with angioplasty, antiplatelet interruption could raise ST rates up to 4 times [15].

Clinical presentation of stent thrombosis

A paper published in the JACC encompassed 7315 ST and categorized their clinical presentation as follows [16] (Table 4).

Angiographic data
Culprit lesions

The left anterior descending artery tends to be the culprit lesion in ST. 58.7% of ST occured in the LAD in our population whilst the Spanish registry of stent thrombosis concludes that the presence of a stent in the LAD is an independent predictor of all type of ST with a hazard ratio of 3.03 – p <0.0001 [4].

Intrastent restenosis

In their article Juan Torrado et al emphasize the role of intrastent restenosis in the genesis of ST, they also argue that neoatherosclerosis is a greater concern than intimal hyperplasia because of the presence of lipoid and necrotic corps [17]. In our work, 57% of patients presenting with late or very late ST had intrastent restenosis.

Therapeutic considerations
Fibrinolysis

Overall, rates of success for fibrinolysis in STEMI are near 80% [18]. A small study found 100% success in a population of 4 individuals with ST. 5 of our patients had fibrinolysis prior to admission but only two achieved success criteria. There is insufficient data to draw conclusions towards fibrinolysis efficacy in this setting.

Thromboaspiration

Gilles Lemesle et al treated 24 ST with thromboaspiration, procedural success reached 95.8% and they did not notice any increase in complications [19]. Stephen W. Waldo compared two strategies of treating ST with or without aspiration and found better improvement of coronary flow in the aspiration group 96% vs 83%

(p<0.001) [20]. 41.3% of our patients were treated using thromboaspiration, and we could rechannel 88.4% of culprit lesions, thus thromboaspiration appears a viable option for ST treatment.

Angioplasty

There seem to be no consensus for angioplasty in ST. The CathPCI registry indicates 69.9% of coronary stenting in the context of late ST and this percentage falls to 51.2% in the acute setting [16]. A Japanese registry mentions thromboaspiration in 77% of the procedures and stenting in 36% of cases [21]. 45.9% of our patients had balloon angioplasty and 34.4% had stents implanted, stenting was more frequent in very late ST (46.1%). No empirical strategy appears to be the best and we think that intracoronary imaging could play a central role in decision-making.

GP2B3A inhibitors

A meta-analysis of 10123 patients having primary angioplasty shows a reduction of 3.2% redo myocardial infarction in patients receiving GP2B3A inhibitors (p<0.001) at the expense of a 1.3% increment in minor bleeding and thrombocytopenia with no major hemorrhage or impact on mortality at a month and a year of follow-up, this profit was independent of P2Y12 administration [22]. These pharmacological agents have been used in 69.4% of our ST patient who presented with STEMI. Bleeding occurred in 14.3% of GP2B3A arm against 11.7% for the rest of our patients, however we observed only 2 major bleedings in the first group with no impact on mortality. Overall data seem to favor the use of GP2B3A inhibitors in patients with ST.

Immediate results

A publication in the Indian heart journal displays a 96.4% success rate in the percutaneous treatment of patients presenting with myocardial infarction [23]. This percentage falls to 91% in a series of 200 Americans treated for definite stent thrombosis and tumbles to 84% in the subset of patients presenting with MACCE [24]. We met success in 86.8% of our procedures. These numbers highlight the challenge encountered in the treatment of stent thrombosis.

Morbidity and mortality of stent thrombosis

Heart failure

A study by Pullara et al compared the complications of STEMI and ST and found 4.8% MACCE in the first setting versus 40% in the second (p<0.001) [25]. 39.6% of our patients experienced symptoms of heart failure and 35% had a deterioration of their left ventricular ejection fraction.

Rehospitalization

Depending on the survey, patients hospitalized for STEMI have different readmission rates. In one study this percentage reached 11.3% in one month after discharge [26], in another, 21.65% rehospitalization were noted during an 8-year follow-up period [27]. In our ST population, 29.5% of total individuals were readmitted to hospital mostly for ischemic symptoms and almost one third of them had redo stent thrombosis. Our findings suggest that ST is associated with a higher risk profile than classic myocardial infarction.

Recidivism and mortality

Recidivism of ST affected 8% of our population. Individuals with stent thrombosis seem to be prone to redevelop one with reports ranging between 5.9% and 18.8%. [28]

Mortality rate vary, a Californian registry displays a 5% in-hospital mortality [24]. Ehrin J Armstrong et al suggests that early stent thrombosis has the worst outcome with a mortality rate of 7.8% versus 3.8% for late thrombosis and 3.6% for very late ones in their study population [29]. We found a mortality of 9.5% in our group, escalating to 18% at one year; early stent thrombosis was also deadliest in our results.

CONCLUSION

Noncompliance to medical treatment seem to be a leading cause of ST in our population. Therapeutic strategies are heterogeneous with arguments favoring the use of thromboaspiration and GP2B3A inhibitors. Prognosis seem worse than in other forms of myocardial infarction with greater complications and less procedural success.

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