Characteristics and Outcome of Angiographically Confirmed Stent Thrombosis
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INTRODUCTION

The incidence of confirmed stent thrombosis (ST) is unclear since most of the studies performed to date have omitted angiographic confirmation of this complication as an inclusion criterion. Although it appears to be a rare problem, it is suspected of being associated with high morbidity/mortality.1 The idea that drug-eluting stents may provoke this complication is a focus of interest,2 although recent work suggests that the thrombosis rates in conventional and drug-eluting stents are similar.3 The best treatment for patients with confirmed ST remains known; neither is it known how such patients progress. The aim of the present work was to describe this complication and its prognosis.

METHODS

This retrospective work involved the examination of a single-center registry of angiographically-confirmed ST, using the data available from January 1998 until December 2007. The first angiographically-confirmed ST (presence of thrombotic-type material and TIMI 0-II; TIMI 0-I in patients implanted for >1 month) of each patient was included in analyses. Acute ST was defined as occurring in the first 24 h after implantation, subacute ST as occurring between 1 and 30 days post-implantation, late ST as occurring...
between 1 and 12 months post-implantation, and very late ST as occurring more than 12 months post-implantation. Proportions were compared using the $\chi^2$ test. The mean follow-up time was 2.7 years (median, 1.7 years).

RESULTS

During the study period, a total of 7121 conventional stents and 2390 drug-eluting stents were implanted. Although the present data do not allow the risk of thrombosis to be calculated, the estimated incidence of ST was 6/1000 implants for both type of stent.

The present criteria for ST were met by 58 patients, 43 implanted with conventional stents and 15 with drug-eluting stents. The mean age of the patients was 64.5 (12.9) years (range, 38-94 years); 48 (82.8%) were men. Nineteen (32.8%) patients had coronary artery disease involving 1 vessel, in 20 (34.5%) 2 vessels were affected, in 17 (29.3%) 3 vessels were affected, and 2 patients (3.4%) presented with disease of the trunk and 3 vessels.

Sixteen patients (27.6%) underwent emergency implantation of a stent (12 primary angioplasties and 4 rescue angioplasties). The arteries into which stents were implanted that later became thrombotic were the anterior descending artery (28 patients [48.3%]), the right coronary artery (in 19 patients [32.8%]), the circumflex artery (in 4 patients [6.9%]), and the coronary trunk (in 1 patient [1.7%]). Five patients (8.5%) suffered thrombosis in more than 1 artery. Thirty patients (51.7%) received more than 1 stent. Fourteen patients (24.1%) were administered glycoprotein IIb/IIIa inhibitors. The mean diameter of the implanted stents was 3.2 (0.5) (2-4) mm; the mean length was 18.7 (5.9) (9-32) mm. Twenty-five patients who were implanted with stents that later gave thrombosis problems suffered complications during the procedure; these complications included 14 dissections, 4 failures to restore blood flow, 3 occlusions/thromboses, 2 ventricular fibrillation problems, 1 coronary artery breakage, and 1 case of extreme bradycardia.

Patients most commonly presented with acute myocardial infarction with elevation of the ST segment (STEMI) (48 patients [82.8%]). Seven presented with acute coronary syndrome without elevation of the ST segment (4 with infarctions, 3 with unstable angina), 1 presented with acute pulmonary edema, and 2 presented with no symptoms. Three patients (5.2%) died in hospital and another 3 (5.2%) suffered ventricular fibrillation.

Fourteen patients (24.1%) experienced acute ST, 27 (46.6%) experienced subacute ST, 9 patients (15.5%) experienced late ST, and 8 (13.8%) experienced very late ST. Differences were seen in the number of ST—especially very late ST—associated with each type of stent (Figure 1). The estimated incidence of very late ST was greater for the drug-eluting stents (Figure 2). Even so, the 2 very latest ST (7 and 8.3 years post-implantation) were seen in patients who had received conventional stents.

Table 1 shows the anti-thrombotic treatment being received by the patients who experienced ST at the time when this occurred. In the month prior to the ST, 9 patients (15.5%) interrupted treatment with at least 1 antiaggregant; 3 patients interrupted treatment with 2. The latter 3 patients, plus 2 of those who interrupted treatment with at least
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Four (6.9%) underwent intravascular echography during the ST treatment procedure; all 4 had an occlusive thrombus and in 3 the stent showed signs of infra-expansion. Of the total 58 patients, TIMI III flow was achieved in 49 (86.2%), TIMI II in 4 (6.9%), and TIMI I or 0 in 5 (8.6%) (including the 4 patients who received no percutaneous treatment).

The 55 surviving patients were prescribed the following at release: dual antiplatelet treatment with aspirin (100 mg) and a thienopyridine (clopidogrel 75 mg once a day, or ticlopidine 250 mg/12 h), and were recommended to stay on thienopyridine therapy for 1 month (2 patients [38%]), 6 months (3 patients [5.7%]), 1 year (26 patients [49.1%]), or indefinitely (22 patients [41%]). Recurrences of angiographically-confirmed ST occurred at 5-166 days after the first thrombosis in 9 patients (16.4%), of whom 8 (88.9%) were receiving dual antiplatelet therapy. One patient suffered 2 recurrences. Only 1 of the recurring thromboses was in an artery different to that of the first ST. Four patients (7.3%) suffered sudden death during the follow-up period.

DISCUSSION

Although the majority of studies appear to show no differences in the incidence of thrombosis in conventional and drug-eluting stents, some do report a greater incidence of this problem in drug-eluting stents after the first year.3 The registry associated with the present work shows that ST—and especially late ST—are rare with either type of stent. Certainly, given the very smaller number of late ST recorded—just 8—no conclusions can be drawn.

A risk factor for ST mentioned in all recently published studies is early clopidogrel withdrawal.4 In the present work, half of the patients who suffered

**TABLE 1. Anti-Thrombotic Treatment at the Time of Stent Thrombosis (All 58 Patients)**

<table>
<thead>
<tr>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Only aspirin</td>
<td>16 (27.6)</td>
</tr>
<tr>
<td>Only thienopyridine</td>
<td>4 (6.9)</td>
</tr>
<tr>
<td>Only acenocoumarol</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Aspirin and thienopyridine</td>
<td>26 (44.8)</td>
</tr>
<tr>
<td>Aspirin and acenocoumarol</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>Thienopyridine and acenocoumarol</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>Aspirin, thienopyridine, and acenocoumarol</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>None</td>
<td>3 (5.2)</td>
</tr>
</tbody>
</table>

1 agent, interrupted their treatment before 6 months had elapsed since implantation and before the date recommended at release for the interruption of thienopyridine treatment. The reasons for these interruptions were pancreatitis, peripheral vascular surgery, tooth extraction, digestive tract bleeding, and non-adherence to treatment. Finally, 4 patients interrupted their double antiaggregant treatment on medical recommendation since the time planned for the taking of clopidogrel (6 months in 1 patient, 9 months in another, and 12 months in 2 patients) had elapsed.

The most common treatment for ST was balloon angioplasty (25 patients [43.1%]), followed by thrombus extraction (15 patients [25.9%]), the latter with implantation of a conventional stent in 9 patients [15.5%]), implantation of a drug eluting-stent in 1 patient, or no further treatment in 5 patients (8.6%). Four patients (6.9%) received no percutaneous treatment: 1 received only a guidewire while the other 3 received conservative treatment. Glycoprotein IIb/IIIa inhibitors were administered to 20 patients (34.5%) as part of treatment for ST. Four (6.9%) underwent intravascular echography during the ST treatment procedure; all 4 had an occlusive thrombus and in 3 the stent showed signs of infra-expansion. Of the total 58 patients, TIMI III flow was achieved in 49 (86.2%), TIMI II in 4 (6.9%), and TIMI I or 0 in 5 (8.6%) (including the 4 patients who received no percutaneous treatment).

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A risk factor for ST mentioned in all recently published studies is early clopidogrel withdrawal.4 In the present work, half of the patients who suffered
ST were not following dual antiplatelet treatment, and in 16% the interruption of treatment occurred in the month prior to thrombosis, commonly for banal reasons such as tooth extraction or non-adherence.

With respect to the management of patients with ST, in the present work the most common course taken was balloon angioplasty with no stent implantation. The results of the Outcome of PCI for Stent Thrombosis Multicenter Study (OPTIMIST), presented at the penultimate European Congress of Cardiology, indicate that management should try to re-establish coronary flow, and that thrombectomy is recommendable (the second most common course of action in the present study) except in patients suffering cardiogenic shock.

In the present work, recurrences of ST were seen in 16% of the patients, always within 6 months of the first ST. One patient suffered 2 recurrences and 4 (7.3%) suffered sudden death. No other studies have focused on the recurrence of ST. However, in March 2008, van Werkum et al published preliminary data from the Dutch STent Thrombosis Study, and reported an 18.8% recurrence rate during the first 27 months of follow-up, along with a cardiac mortality rate of 12.3%. The ESTROFA (Estudio ESpanish sobre TROmbosis de stents FArmacoactivos; The Spanish Thrombosis in Drug-eluting Stents Study) registry recorded a recurrence of ST at 1 year of 4.6% and a mortality rate of 16%. This registry includes patients involved in the present study who met the required inclusion requirements (only those with drug-eluting stents).

The number of patients in the present study was small, hindering the drawing of conclusions. Neither was there a control group that might have allowed predictors of ST to be identified. Nor can it be ruled out that among the many patients implanted with a stent at our center, some who suffered ST may have sought treatment at another center; these would have been lost to the present registry. It is also possible that some ST events may have been inadequately recorded at the time of the event.

In conclusion, confirmed ST is rare, and very uncommon 1 year after stent implantation—although perhaps more common among drug-eluting stents. Patients most commonly present with STEMI. In the present work, this complication was non-fatal in 95% of cases. This risk of a recurrent ST would appear to be a high during the six months following an initial ST.

REFERENCES

6. van Werkum JW, DeKorte FI, Heestermans AA, Suttrop MJ, Kelder JC, Koolen JJ. High recurrence rates after a first episode of stent thrombosis: Results from the Dutch STent Thrombosis Study. American College of Cardiology Scientific Sessions/2 Summit-SCAI Annual Meeting; March 29, 2008; Chicago, IL.