# Predictors and Outcomes of Recurrent Stent Thrombosis

## Results From a Multicenter Registry

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## ABSTRACT

**OBJECTIVES** The aim of this study was to determine the incidence, predictors, and outcomes of recurrent stent thrombosis (rST).

**BACKGROUND** Patients who had an initial stent thrombosis (ST) develop may be at high risk of rST.

**METHODS** We analyzed a multicenter California registry of angiographic definite ST at 5 academic hospitals from 2005 to 2013. A detailed review of the angiogram and procedure was performed of patients with and without rST.

**RESULTS** Among 221 patients with a median follow-up of 3.3 years, definite or probable rST developed in 29, including 19 with angiographic definite rST. The cumulative hazard ratio (HR) of definite or probable rST was 16% at 1 year and 24% at 5 years, whereas the cumulative HR of angiographic definite rST was 11% at 1 year and 20% at 5 years. Despite similar angiographic results, patients who had rST develop had significantly greater peak creatine kinase at the time of initial ST (mean, 2,655 mg/dl vs. 1,654 mg/dl; p = 0.05) than those without rST. The 3-year rate of major adverse cardiovascular events was 50% for patients with rST compared with 22% for patients with a single ST (p = 0.01). After multivariable adjustment, independent predictors of definite/probable rST were age (HR: 1.4; 95 confidence interval [CI]: 1.1 to 1.8 per 10 years), bifurcation ST (HR: 4.4; 95% CI: 1.8 to 10.9), and proximal vessel diameter (HR: 1.8; 95% CI: 1.1 to 3.2 per millimeter).

**CONCLUSIONS** rST represents an important cause of long-term morbidity and mortality after an initial ST. Bifurcation ST and a larger proximal reference vessel diameter are independently associated with an increased risk of rST. (J Am Coll Cardiol Intv 2014;7:1105–13) © 2014 by the American College of Cardiology Foundation.

Stent thrombosis (ST) is a rare complication of coronary intervention with a high morbidity and mortality. First-time ST has an in-hospital mortality rate of 5% to 10% and a 30-day mortality rate of 10% to 25% (1–6). Among patients who survive the initial episode of ST, recurrent ST (rST) is a not uncommon cause of continued adverse cardiovascular events.

## ABBREVIATIONS AND ACRONYMS

**CI** = confidence interval

**HR** = hazard ratio

**LAD** = left anterior descending artery

**MACE** = major adverse cardiovascular event(s)

**PCI** = percutaneous coronary intervention

**rST** = recurrent stent thrombosis

**ST** = stent thrombosis

**TIMI** = Thrombolysis In Myocardial Infarction

Although there are many biological, clinical, and angiographic features that contribute to initial ST, there are limited data on the incidence, clinical presentation, and outcomes of rST (7). Previous studies have reported incidence rates of rST of 10% to 20% during long-term follow-up (1-5,8). Two smaller studies with detailed angiographic analysis have also reported predictors of rST, including residual thrombus burden after the first ST event, a larger vessel diameter, residual dissection, and the presence of underlying malignancy (9,10). However, each of these studies was limited by a small number of events and differences in practice patterns. A larger, multicenter study may therefore better reflect real-world outcomes of rST.

In this study, we used a multicenter ST registry to analyze the incidence and outcomes of subjects with rST. We hypothesized that angiographic findings at the time of treatment for ST would be associated with subsequent risk of rST.

## METHODS

The University of California ST registry comprises all cases of angiographic definite ST at 5 academic medical centers (University of California, Davis; University of California, San Diego; San Francisco Veteran's Administration Hospital; San Francisco General Hospital; and University of California, San Francisco Moffitt-Long Hospital) from 2005 to 2013. Cases were identified using cardiac catheterization laboratory records and, from 2008 onward, prospective enrollment of subjects. After identification of a potential ST, each case was reviewed for clinical and angiographic characteristics by 2 interventional cardiologists using the Academic Research Consortium criteria for definite ST (11). Only cases of angiographic definite ST were included in the registry. For this analysis, the first presentation of ST was used as the entry criteria.

Once identified, cases were reviewed for demographic, procedural, angiographic, and in-hospital outcomes (12). Briefly, trained abstractors and physicians reviewed each medical chart for details of presentation, medications before admission, medication compliance, procedural details of coronary angiography and intervention, and in-hospital outcomes (death, stroke, or repeat myocardial infarction). Discharge medications were assessed for all surviving patients. ST was defined as occurring early if the event occurred ≤30 days after the index percutaneous coronary intervention (PCI), late if it occurred >30 days and <1 year after the index PCI, and very late if it occurred ≥1 year after index PCI as according to the Academic Research Consortium criteria (11). Long-term mortality was assessed using hospital records, patient follow-up, and the Social Security Death Index. Patients who died within 30 days after initial ST without a definite etiology were categorized as having probable rST, whereas patients who presented with recurrent acute coronary syndrome and angiographic evidence of thrombus in the same stent were categorized as have definite rST. These definitions were on the basis of extension of the Academic Research Consortium criteria to recurrent events of ST.

Angiographic analysis was performed by 2 interventional cardiologists blinded to outcomes. Quantitative coronary analysis was performed using Xcelera software (Philips Healthcare, Best, the Netherlands). Thrombus grading was angiographically scored into 5 grades: 0 if there was no apparent thrombus; 1 if possible thrombus was seen; 2 if definite thrombus was one-half or less of the vessel diameter; 3 if definite thrombus was more than one-half but <2 vessel diameters; 4 if definite thrombus was ≥2 vessel diameters; and 5 if there was complete vessel occlusion from thrombus (13). All patients in the study had grade 2 or higher thrombus to meet the definition of definite ST. In cases in which there was complete stent occlusion by thrombus, thrombus grading was also recorded after initial lesion crossing with a wire but before balloon inflation. Myocardial perfusion was scored before and after intervention from 0 to 3, as previously described (14). Corrected Thrombolysis In Myocardial Infarction (TIMI) frame counts were also scored for each infarct-related artery (15). A stent was defined as occurring at a bifurcation if the main vessel stent crossed a side branch ≥2.0 mm in diameter (provisional single stent), or if there were 2 stents present, with 1 originating in a main vessel and the second in a side branch (2-stent bifurcation). SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery Study) and residual SYNTAX scores were calculated as previously described (16). All angiograms were also scored for lesion calcification, lesion severity, moderate/severe tortuosity, aneurysm, ectasia, and ulceration. A previously published risk scoring system for the prediction of ST after initial angioplasty was also calculated for patients with and without rST (17).

The primary outcome of the study was definite/probable rST. Secondary endpoints included angiographic definite rST, mortality, and major adverse cardiovascular events (MACE), defined as death, myocardial infarction, or stroke.