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EDITORIAL

Recurrent Stent Thrombosis: An Interventionalist's Nightmare

Sidakpal S. Panaich, MD; Saket Girotra, MD, SM

Advances in stent design, pharmacotherapy, and procedural techniques during the past decade have led to a remarkable reduction in the incidence of stent thrombosis (ST).[1] Nonetheless, ST remains a dreaded complication of percutaneous coronary intervention (PCI) that occurs in ≈1% of patients, typically presenting as acute myocardial infarction, and optimal reperfusion is achieved in only two-thirds of the patients because of a high clot burden. Consequently, the 30-day mortality following ST is high (10%–25%).[2,3] Nearly 1 in 5 patients with ST are likely to experience a recurrent episode.[2]

See Article by Enomoto et al.

Although previous studies have established multiple patient and procedural factors for index ST, the incidence and predictors of recurrent ST (RST) have been less extensively studied. Prior studies have noted *patient* (diabetes mellitus, smoking, left ventricular ejection fraction <45%), *lesion* (complex lesions, long total stent length) and *procedural* (Thrombolysis in Myocardial Infarction flow grade <3, residual stenosis/dissection, implantation of additional stents, postprocedural renal failure) factors as independently predictive of RST. A multicenter registry from California found prior ST at a coronary bifurcation and large proximal reference vessel diameter as independent predictors of definite/probable angiographic RST.[4]

In this issue of the *Journal of the American Heart Association* (*JAHA*), Enomoto et al[5] provide data regarding the epidemiology of RST. Using data from the REAL-ST registry (Retrospective Multicenter Registry of ST After First- and Second-Generation DES Implantation) from 46 hospitals in Japan, they identified a total of 595 patients with definite ST of first-generation (n=314) and second-generation drug-eluting stents (n=281). Over a median follow-up of 31 months, 32 patients experienced RST. The incidence of RST was 4.5% at 1 year and 6% at 5 years respectively compared with previous studies that have reported RST incidence of 16% at 1 year and 24% at 5 years.[4,6] Although the large difference in incidence could be explained by inclusion of a larger proportion of patients who received second-generation drug eluting stents and consideration of only definite ST as opposed to both probable and definite ST in prior studies, loss of follow-up in a multicenter study cannot be excluded. Surprisingly, the incidence of RST was similar between first-generation and second-generation drug eluting stents. As expected, RST was associated with nearly a 3-fold higher risk of mortality. In multivariable analysis, early ST and multivessel ST were predictive of recurrent events but these analyses are limited by the overall small number of events and the violation of the proportional hazard assumption. Most of the RST events were reported within 30 days after the index ST, which is consistent with prior studies. More than 70% of RST occurred within 30 days of the index event in a study by van Werkum et al.[2] The median time for RST incidence was 4 to 5 days following index ST in a study by Lemesle et al.[7]

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Correspondence to: Sidakpal S. Panaich, MD, Department of Cardiology, University of Iowa, 200 Hawkins Drive, Iowa City, IA 52241. E-mail: sidakpal-panaich@uiowa.edu

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Although these findings highlight the clinical impact of RST, certain key details are not included in this paper, which make it difficult to interpret these findings in the context of existing literature. Although the authors report use of imaging in ≈70% of the patients in this study, no imaging data are provided that might shed further light on the major causes of recurrent events. Intravascular ultrasound (IVUS) or optical coherence tomography can provide critical information regarding mechanical factors such as stent underexpansion, tissue protrusion, residual inflow/outflow disease, and edge dissection that contribute to the risk of ST.[8] Identifying the underlying mechanism of ST can be very useful for guiding treatment—high pressure balloon dilation for stent underexpansion versus stenting to cover any residual dissection or disease or stent fracture. In the ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions) trial that compared IVUS-guided versus angiography guided drug eluting stents implantation in 1448 all-comer patients undergoing PCI, IVUS-guided PCI was associated with lower frequency of target vessel failure (2.9% versus 5.4%, *P*=0.019). Notably, no definite ST was noted in IVUS guided PCI group compared with 4 definite ST events in the angiography group at 1 year.[9] At 3-year follow-up, there continued to be a significantly lower incidence of ST in IVUS group compared with the angiography group (0.1% versus 1.1%, *P*=0.02). However, despite strong evidence from randomized controlled trials, demonstrating its superiority in terms of improving hard clinical outcomes, intravascular imaging remains grossly underused in the contemporary practice.[10]

In addition to mechanical factors, achieving adequate platelet inhibition especially during the early period after PCI is an important factor in reducing the risk of ST. Although the present study did not have detailed information regarding antiplatelet regimens adopted following index ST, 78% of the patients were on dual antiplatelet therapy at the time of index ST. The role of high on treatment platelet reactivity in guiding antiplatelet therapy using platelet function testing in routine care is debatable with none of the randomized trials showing a benefit of such a strategy. Nonetheless, if ST occurs on dual antiplatelet therapy that includes clopidogrel, replacing it with a more potent agent like prasugrel or ticagrelor is reasonable. The addition of rivaroxaban to dual antiplatelet therapy was found to reduce the risk of ST in the ATLAS-ACS TIMI 51 (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome–Thrombolysis in Myocardial Infarction 51) trial and may be considered in patients who have a low risk of bleeding.[11,12] Recently, the role of a genotype-guided strategy to tailor oral antiplatelet therapy in patients with CYP2C19 loss of function alleles (*2 or *3) was studied in a randomized controlled trial by Pereira et al.[13] The study narrowly missed its primary outcome of cardiovascular death, myocardial infarction, stroke, ST, or recurrent ischemia at 12 months (hazard ratio [HR], 0.66; *P*=0.056). However, when considering time to multiple recurrent events including ST, there was a benefit with genotype-guided strategy (HR, 0.60; *P*=0.011) lending support to this strategy in preventing recurrent events in patients with ST. Although using genotyping to guide antiplatelet therapy routinely does not seem to be supported by the data, it might be of value in patients who experience ST while compliant and in absence of any other underlying cause.

Although ST is increasingly rare, when it occurs it can have devastating consequences. Prevention of RST starts with appropriate patient selection, procedural optimization with intravascular imaging, and ensuring medical compliance with antiplatelet agents including consideration of more potent therapy in high-risk patients and close surveillance. Although much progress has been made in this field, there are still a lot of unknowns that need to be addressed in future studies to confront this rare but serious complication.

ARTICLE INFORMATION

Affiliation

Department of Cardiovascular Medicine, University of Iowa Hospitals & Clinics, Iowa City, IA.

Disclosures

None.

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