

Stent thrombosis: prevention is the only effective treatment



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Stent thrombosis (ST) is rare but represents the most dramatic mechanism of coronary stent failure¹. In view of the strong association with myocardial infarction (MI) and cardiac death, ST is the primary safety concern of coronary percutaneous coronary interventions (PCI) with stent implantation and represents the key endpoint for the evaluation of the safety profile of coronary stents².

Evolution of PCI techniques, iterations of stent technologies, and optimisation of medical therapy have markedly reduced the risk of ST^{1,3}. However, a considerable number of patients undergoing PCI with stent implantation still suffer from this life-threatening complication.

The pathophysiology of ST is multifactorial, with a number of possible triggers playing different roles over time after stenting^{4,5}. Several studies have investigated potential mechanisms and predictors of ST, with the ultimate objective of providing informative data to prevent it⁶. Conversely, limited evidence is available on treatment strategies for patients suffering from ST and their long-term clinical outcomes.

In this issue of EuroIntervention, Tovar Forero and co-authors⁷ report the findings of a cohort of 695 patients suffering from ST at two large academic hospitals in Bern, Switzerland, and Rotterdam, the Netherlands, between 1996 and 2017. The study aimed to evaluate ST treatment strategies and their impact on outcomes.

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The primary findings of this study underscore the terribly unfavourable outcomes of patients suffering from ST, with excessively high event rates during long-term follow-up. At five years, 25.8% of patients had died, 17.9% had had an MI, 24.8% had undergone a target vessel revascularisation, and 12.1% had had a repeat ST. The strongest independent predictors of major adverse cardiac events after ST were related primarily to an adverse clinical presentation of patients at the time of ST (i.e., cardiogenic shock, ST in the left anterior descending artery, and multivessel disease) or to a suboptimal procedural result at the time of the ST treatment (i.e., Thrombolysis In Myocardial Infarction [TIMI] flow <2). Unfortunately, while predictors are clearly identified by the study findings, the mechanisms underlying ST are

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not fully elucidated since only one out of four patients underwent intracoronary imaging. Among these, the key mechanisms are in line with previously available evidence (i.e., neoatherosclerosis, malapposition, and underexpansion)^{4,5}.

In relation to treatment, approximately 60% of patients underwent repeat stenting and 34% underwent only balloon angioplasty. The latter was frequently used as the treatment strategy (47.9% of cases) in ST events occurring during the first 30 days after PCI, indicating the pivotal role of mechanical triggers of ST in the early phase and the subsequent need to optimise procedural results in these patients. The study also shows a large use of thrombectomy (in 47.9% of patients) and glycoprotein IIb/IIIa inhibitors (57.6% of patients) in the setting of ST, with no apparent benefit on long-term outcomes. The only effective treatment strategy appears to be the use of new-generation P2Y₁₂ inhibitors, which are associated with a risk reduction for MI with borderline statistical significance as compared with clopidogrel (hazard ratio [HR] 0.56, 95% confidence interval [CI]: 0.32-0.99; p=0.049).

The authors should be commended for the exceptional work done in collecting such a granular description of ST cases over two decades. Overall, this study provides valuable findings for the scientific community and for clinical practice. The first and most relevant message is the prognostic relevance of ST. Since ST presents as an acute MI in the majority of cases, in order to put findings into perspective it is reasonable to compare event rates with those observed after primary PCI in patients with acute MI. In **Figure 1**, event rates observed by Tovar Forero and co-authors are compared with those observed in recent major trials on contemporary drug-eluting stents (DES) in patients with ST-segment elevation myocardial infarction (STEMI) at five-year follow-up, i.e., in the COMFORTABLE AMI⁷ and EXAMINATION⁸ trials. It is visually evident how ST is associated with a dramatic prognosis when compared with outcomes after STEMI. Interestingly, 51 out of 118 target vessel revascularisations (43.2%) observed by Tovar Forero and co-authors after a first ST were due to repeat ST. These findings underscore the second key message of the investigators' experience, which

is that currently available treatment for ST is largely ineffective. Future research should, therefore, focus on patients with ST with the aim of developing novel and effective treatment strategies for patients suffering from ST.

In summary, the unfortunate victims of ST have limited treatment options and a dramatic long-term prognosis. At this point in time, all efforts should be implemented to prevent ST by optimising procedural outcomes, tailoring antithrombotic therapy to patients' risk profiles, and intensifying secondary prevention since, in the absence of an effective cure, prevention remains the only effective strategy.

Conflict of interest statement

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References

1. Stefanini GG, Byrne RA, Windecker S, Kastrati A. State of the art: coronary artery stents - past, present and future. *EuroIntervention*. 2017;13:706-16.
2. Byrne RA, Serruys PW, Baumbach A, Escaned J, Fajadet J, James S, Joner M, Oktay S, Jüni P, Kastrati A, Sianos G, Stefanini GG, Wijns W, Windecker S. Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions task force on the evaluation of coronary stents in Europe: executive summary. *Eur Heart J*. 2015;36:2608-20.
3. Klingenberg R, Heg D, Räber L, Carballo D, Nanchen D, Gencer B, Auer R, Jaguszewski M, Stähli BE, Jakob P, Templin C, Stefanini GG, Meier B, Vogt P, Roffi M, Maier W, Landmesser U, Rodondi N, Mach F, Windecker S, Jüni P, Lüscher TF, Matter CM. Safety profile of prasugrel and clopidogrel in patients with acute coronary syndromes in Switzerland. *Heart*. 2015;101:854-63.
4. Taniwaki M, Radu MD, Zaugg S, Amabile N, Garcia-Garcia HM, Yamaji K, Jorgensen E, Kelbaek H, Pilgrim T, Caussin C, Zanchin T, Veugeois A, Abildgaard U, Jüni P, Cook S, Koskinas KC, Windecker S, Räber L. Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography. *Circulation*. 2016;133:650-60.
5. Adriaenssens T, Joner M, Godschalk TC, Malik N, Alfonso F, Xhepa E, De Cock D, Komukai K, Tada T, Cuesta J, Sirbu V, Feldman LJ, Neumann FJ, Goodall AH, Heestermaans T, Buyschaert I, Hlinomaz O, Belmans A, Desmet W, Ten Berg JM, Gershlick AH, Massberg S, Kastrati A, Guagliumi G, Byrne RA; Prevention of Late Stent Thrombosis by an Interdisciplinary

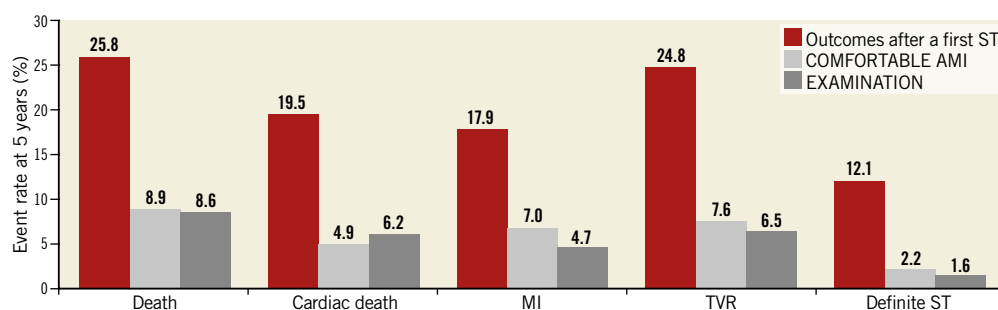


Figure 1. Five-year outcomes after a first ST versus outcomes after a STEMI in contemporary DES trials. Five-year clinical outcomes after a first ST in the Bern-Rotterdam experience as compared to outcomes after a STEMI in selected contemporary trials evaluating drug-eluting stents in patients with STEMI (COMFORTABLE AMI⁷ and EXAMINATION⁸ trials). DES: drug-eluting stent; MI: myocardial infarction; ST: stent thrombosis; STEMI: ST-segment elevation myocardial infarction

- Global European Effort (PRESTIGE) Investigators. Optical Coherence Tomography Findings in Patients With Coronary Stent Thrombosis: A Report of the PRESTIGE Consortium (Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort). *Circulation*. 2017;136:1007-21.
6. Taniwaki M, Stefanini GG, Räber L, Brugaletta S, Cequier A, Heg D, Iniguez A, Kelbaek H, Serra A, Ostojic M, Hernandez-Antolin R, Baumbach A, Blöchlinger S, Juni P, Mainar V, Sabate M, Windecker S. Predictors of adverse events among patients undergoing primary percutaneous coronary intervention: insights from a pooled analysis of the COMFORTABLE AMI and EXAMINATION trials. *EuroIntervention*. 2015;11:391-8.
7. Tovar Forero MN, Zanchin T, Masdjedi K, van Zandvoort LJ, Kardys I, Zijlstra F, Häner J, Windecker S, Van Mieghem NM, Räber L, Daemen J. Incidence and predictors of clinical outcomes after a first definite coronary stent thrombosis. *EuroIntervention*. 2020;16:e344-50.
8. Räber L, Yamaji K, Kelbaek H, Engstrom T, Baumbach A, Roffi M, von Birgelen C, Taniwaki M, Moschovitis A, Zaugg S, Ostojic M, Pedrazzini G, Karagiannis-Voules DA, Lüscher TF, Kornowski R, Tüller D, Vukcevic V, Heg D, Windecker S. Five-year clinical outcomes and intracoronary imaging findings of the COMFORTABLE AMI trial: randomized comparison of biodegradable polymer-based biolimus-eluting stents with bare-metal stents in patients with acute ST-segment elevation myocardial infarction. *Eur Heart J*. 2019;40:1909-19.
9. Sabaté M, Brugaletta S, Cequier A, Iniguez A, Serra A, Jiménez-Quevedo P, Mainar V, Campo G, Tsepili M, den Heijer P, Bethencourt A, Vazquez N, van Es GA, Backx B, Valgimigli M, Serruys PW. Clinical outcomes in patients with ST-segment elevation myocardial infarction treated with everolimus-eluting stents versus bare-metal stents (EXAMINATION): 5-year results of a randomised trial. *Lancet*. 2016;387:357-66.