jaa Just accepted article

EuroIntervention

Title: Incidence and predictors of outcomes after a first definite coronary stent thrombosis.

Authors: Maria N. Tovar Forero, M.D; Thomas Zanchin, M.D, PhD; Kaneshka Masdjedi, M.D; Laurens van Zandvoort, BSc; Isabella Kardys, M.D, PhD; Felix Zijlstra, M.D, PhD; Jonas Häner, M.D; Stephan Windecker, M.D; Nicolas M. Van Mieghem, M.D, PhD; Lorenz Räber, M.D; Joost Daemen, M.D, PhD

DOI: 10.4244/EIJ-D-19-00219

Citation: Tovar Forero MN, Zanchin T, Masdjedi K, van Zandvoort L, Kardys I, Zijlstra F, Häner J, Windecker S, Van Mieghem NM, Räber L, Daemen J. Incidence and predictors of outcomes after a first definite coronary stent thrombosis. *EuroIntervention* 2019; Jaa-641 2019, doi: 10.4244/EIJ-D-19-00219

Manuscript submission date: 27 February 2019

Revisions received: 05 August 2019

Accepted date: 28 August 2019

Online publication date: 03 September 2019

Incidence and predictors of outcomes after a first definite coronary stent thrombosis

Maria N. Tovar Forero[1], MD; Thomas Zanchin[2], MD, PhD; Kaneshka Masdjedi[1], MD; Laurens van Zandvoort, BSc[1]; Isabella Kardys, MD, PhD[1]; Felix Zijlstra[1], MD, PhD, Prof; Jonas Häner[2], MD; Stephan Windecker[2], MD, Prof; Nicolas M. Van Mieghem[1], MD, PhD; Lorenz Räber[2], MD, Prof; Joost Daemen[1], MD, PhD.

Running title: Predictors of outcomes after stent thrombosis

From:

Thoraxcenter, Erasmus Medical Centre, Rotterdam, the Netherlands[1].

Department of Cardiology, Bern University Hospital, University of Bern, Bern, Switzerland[2]

Corresponding author:

Joost Daemen, MD, PhD

Department of Cardiology, room Rg-628

Erasmus University Medical Centre

P.O. Box 2040

3000 CA Rotterdam, The Netherlands

E-mail: j.daemen@erasmusmc.nl

Conflicts of interest statement:

Joost Daemen: Institutional grant/research support from Abbott Vascular, Boston Scientific, Acist Medical, Medtronic and PulseCath, and consultancy and speaker fees from Pythagoras Medical, Acist medical, Medtronic and Pulse Cath.

Stephan Windecker: Research grants from Amgen, Abbott Vascular, Bayer, Boston Scientific, Biotronik, Medtronic, Edwards Lifesciences, St Jude and Terumo.

Lorenz Räber:Speaker fees from Abbott, Amgen, Sanofi and research grant from Abbott, Sanofi, Regeneron and Heartflow.

Thomas Zanchin:Grant from the Swiss National Science Foundation (grant no. 323530_171146).

The remaining authors have no conflict of interest to declare.

ABSTRACT

Aims: Stent thrombosis (ST) is a rare but potentially fatal complication of coronary artery stenting. Little is known about the optimal treatment strategy at the time of a ST event. We identified the incidence and predictors of adverse cardiac events after treatment of a definite ST.

Methods and results: 695 patients with definite ST were included between 1996 and 2017 in 2 academic medical centres. The primary endpoint was the composite of cardiac death, myocardial infarction (MI) and target vessel revascularization (TVR) (MACE).

Mean age was 62.8 ± 12.1 years and 76.3% were male. ST occurred at a median of 22 days (IQR 3-551 days); 50.8% were early and 49.2% were late/very late ST. At 60 months follow-up, MACE was 43.7%, cardiac death 19.5%, MI 17.9%, TVR 24.8%, and repeat definite ST was 12.1% (10.5% in target vessel). **Independent predictors of MACE were cardiogenic shock (HR 2.54; 95%CI 1.75-3.70; p<0.001), ST in LAD (HR 1.76; 95%CI 1.32-2.35; p<0.001) prior CVA/TIA (HR 1.68; 95%CI 1.08-2.62; p=0.020), peripheral vascular**

disease (HR 1.55; 95%CI 1.00-2.39; p=0.046), multivessel disease (HR 1.53; 95%CI 1.12-2.08; p=0.007), and final TIMI flow 2-3 (HR 0.54; 95% CI 0.34-0.85; p=0.009). No specific treatment of ST influenced MACE, however, new generation P2Y12 inhibitors reduced the risk of MI (HR 0.56; 95% CI 0.32-0.99; p=0.049).

Conclusion: The incidence of adverse events remains high after a first episode of ST. New generation P2Y12 inhibitors reduce the risk of MI. Additional stenting, GpIIb/IIIa inhibitors and thrombectomy did not improve outcomes following ST.

Classifications

ACS / NSTE-ACS; Adjunctive pharmacotherapy; Coronary occlusion; Stent thrombosis; Other technique.

Abbreviations

BMS, Bare Metal Stent; CABG, Coronary Artery Bypass Graft; DES, Drug-Eluting Stent; DAPT, Dual Antiplatelet Therapy; MACE, Major Adverse Cardiac Events; MI, Myocardial Infarction; PCI, Percutaneous Coronary Intervention; ST, Stent Thrombosis; TIMI, Thrombolysis in Myocardial Infarction; TVR, Target Vessel Revascularization.

Condensed abstract

Several patient, lesion and procedural characteristics have been identified at the index procedure as potential factors of stent thrombosis (ST), however, little is known about ST treatment strategies and their impact on future adverse events. We included all first definitive ST from 1996 to 2017 (695 cases). At 60 months, the cumulative incidence of MACE was 43.7%. New P2Y12 inhibitors reduced the incidence of myocardial infarction. Additional stenting, GpIIb/IIIa inhibitors or thrombectomy did not improved outcomes.

INTRODUCTION

Over the years, improvements in stent technology reduced the incidence of future target lesion failure.(1) Conversely, stent thrombosis (ST) emerged as a safety concern associated with high rates of death and myocardial infarction (MI).(2) Amongst others, the problem was linked to stent-related factors like underexpansion, malapposition, polymer-related hypersensitivity reactions, neoatherosclerosis and incomplete stent coverage, and patient-related factors such as premature discontinuation of antiplatelet therapy.(3-5)

The risk of early or late ST appeared to occur at a rate of 0.6% per year after the implantation of a first-generation drug-eluting stent (DES),(6) and up to 0.3% per year in novel generation DES.(7, 8) The latter triggered the development of more biocompatible and bioresorbable polymers and pushed guideline committees to review dual antiplatelet therapy (DAPT) strategies.(9) At the same time, exhaustive attempts were made to identify baseline patient and procedural characteristics associated with an increased risk for ST.(10-13)

To date little is known about ST treatment strategies applied in daily clinical practice and their impact on adverse events, therefore, the purpose of our study was to identify incidence and predictors of future adverse cardiac events after treatment of a first definitive ST.

METHODS

Population

This is a retrospective study including two academic hospitals (Erasmus University Medical Centre, The Netherlands and Bern University Hospital, Switzerland). All patients who presented with a first definite ST between 1996 to 2017 were included.

Endpoints and definitions

The primary endpoint was Major Adverse Cardiac Events (MACE), a composite of cardiac death, non-fatal MI, and ischemia-driven target vessel revascularization (TVR) at 60 months follow-up after the first ST event. Death was classified as cardiac or non-cardiac. Secondary endpoints included the components of MACE and repeat definite ST in the target vessel (ST-TV). Cardiac death was defined as any death due to a clear cardiac cause, unwitnessed death or death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment. Coronary artery bypass grafting (CABG) revascularization was considered an event if not part of the initial ST treatment. TVR MI and ST were defined according to the Academic Research Consortium definitions.(14) Repeat ST-TV was identified as any new definite ST in the target vessel after the successful treatment of the index ST.

Clinical follow-up

Survival data were obtained from municipal civil registries. A health questionnaire was sent to all living patients with questions on re-admission and major adverse cardiac events. For patients who had an adverse event at another centre, medical records or discharge summaries were systematically reviewed. General practitioners, referring cardiologists, and patients were contacted as necessary for additional information. There was no independent or external monitoring of data entry. We performed censoring at 60 months with 14 patients lost to follow-up. **Clinical events were adjudicated by trained study personnel not involved in the specific procedures during the course of the study. All patients provided written informed consent for the procedure and the use of anonymous datasets for research purposes in alignment with the Dutch Medical Research Acts and the appropriate Health Insurance Portability and Accountability Act waiver/authorization or the appropriate informed consent documentation per institutional policy for the collection of data in Switzerland.**

Statistical analysis

Categorical variables are expressed as numbers and frequencies and compared using χ^2 test or Fisher's exact test when appropriate. Continuous variables are presented as the mean ± standard deviation (SD) and tested using Student's t-test or as the median and Inter-quartile range (IQR: 25^{th}-75^{th} percentile) and tested with Mann-Whitney rank sum test.

Missing values for covariates were present in less than 5%, except for smoking (6.6% missing values), statins prescription (6.8% missing values) index stent type (15.5% missing values) multivessel disease (MVD) (17.6% missing values), and estimated glomerular filtrate rate <60 ml/min/1.73m2 (34.2% missing values). Therefore, we applied multiple imputation to handle missing values. Values were imputed using a regression approach based on patients' clinical data. Results from 5 imputed data sets were pooled to obtain risk estimates.

Univariate predictors of outcomes were identified using Cox proportional-hazards models. Predictors with a p value < 0.1 were introduced in the multivariate Cox proportional-hazards model using the 'enter' method. In case of outcomes with insufficient number of events, the most strongly associated covariates were included in the model. Data are presented as Hazard-Ratios (HRs) with 95% confidence intervals (CI 95%). All tests were two-tailed and a P value <0.05 was considered statistically significant. The Kaplan-Meier method was applied to show the cumulative incidence of the primary and secondary endpoints.

SPSS software version 24.0 for Windows (SPSS, Inc., Chicago, USA) was used to execute all the analysis.

RESULTS

Clinical presentation

A total of 695 patients presenting with a first episode of definite ST were included. Mean age was 62.8 ± 12.1 years and 76.3% were male. The first ST occurred at a median of 22 days (25-

75th percentile: 3–551 days; min 0, max 5859 days) after the index PCI. Early ST (0-30 days) and late/very late ST (>30 days) occurred in 50.8% and 49.2% of the cases respectively. MI was the presenting symptom in 87.2% of the cases and accompanied by cardiogenic shock in 11.8%. Aspirin was used by 88.9% of the patients at baseline and 53.8% used P2Y12 inhibitors.*(Table 1 and 2).*

According to the timing of ST (Early vs late/very late), patients with early ST were older (64.1 ± 12.1 vs 61.4 ± 11.9 years respectively, p=0.004), presented more often with MI (93.4% vs 80.6% respectively p<0.001) and hemodynamic instability (16.9% vs 6.9% respectively p<0.001), had multivessel ST (5.2% vs 1.5% p=0.007) or left coronary system as culprit (for LAD 58.6% vs 48.5% p=0.009; for left circumflex artery 21.2% vs 14.1% respectively p=0.015).*(Supplementary tables 1 and 2).*

Treatment

Thrombectomy and Glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors were used in 47.9% and 57.6% of the patients, respectively. In 27.6% of the patients, intracoronary imaging was used to assess the mechanism of the ST, with neoatherosclerosis (31.8%), malapposition (25.5%) and underexpansion (17.7%) as the main findings.*(Table 2)* Additional stenting was performed in 59.8% of the patients with the use of DES in 90.8%. Balloon angioplasty alone (POBA) was performed in 34.4% of the cases and CABG in 0.9%. DAPT was prescribed in 95.7% of the patients, of which 28.1% received either Prasugrel or Ticagrelor. The remaining patients were treated with a combination of oral anticoagulant (OAC) and 1 antiplatelet therapy (ATP) (1.1%), 1 ATP (1.8%) or OAC alone (0.3%); in 1.1% of the cases no ATP or OAC was prescribed due to concomitant major bleeding.*(Table 2)*

As compared to late/very late ST, patients with early ST received more often treatment with POBA (45.6% vs 24.3% respectively p < 0.001) and GpIIb/IIIa inhibitors (66.6% vs 47.9 %

p<0.001), but fewer patients with early ST underwent intracoronary imaging assessment as compared to those with late/very late ST (24.3% vs 30.8% respectively p=0.058).*(Supplementary table 2).*

Outcomes

At 60 months, the cumulative incidence of the primary composite endpoint was 43.7% (238 cases). Cardiac death occurred in 19.5% (111 cases), MI in 17.9% (82 cases) and TVR in 24.8% (118 cases). Repeat definite ST occurred in 12.1% (58 cases) and repeat definite ST-TV in 10.5% (51 cases) (acute 9.8% (5 cases), subacute 27.5% (14 cases), late 23.5% (12 cases), and very late 39.2% (20 cases)).*Figure 1*.

Independent predictors of MACE were cardiogenic shock (HR 2.54; 95%CI 1.75-3.70; p<0.001), ST in LAD (HR 1.76; 95%CI 1.32-2.35; p<0.001) prior CVA/TIA (HR 1.68; 95%CI 1.08-2.62; p=0.020), peripheral vascular disease (HR 1.55; 95%CI 1.00-2.39; p=0.046) and MVD (HR 1.53; 95%CI 1.12-2.08; p=0.007). Final TIMI flow 2-3 was inversely associated with MACE (HR 0.54; 95% CI 0.34-0.85; p=0.009) and cardiac death (HR 0.33; 95% CI 0.18-0.60; p<0.001) at 60 months. Treatment with new generation P2Y12 inhibitors was inversely associated with future MI events (HR 0.56; 95% CI 0.32-0.99; p=0.049), and the use of intracoronary imaging was associated with an increased risk for repeat ST-TV (HR 1.85; 95% CI 1.06-3.23; p=0.032). No other modifiable procedural characteristics predicted any of the outcomes.(*Table 3).*

According to the timing of the ST, similar predictors were found for MACE following early ST as for the total population. Cardiogenic shock and final TIMI flow 2-3 were the only independent predictors for MACE in patients with late/very late ST. Intracoronary imaging increased the risk for future MI, TVR and ST-TV in patients with early ST, and index stent type DES reduced future MI events in patients with late/very late ST. No procedural

characteristics predicted any of the outcomes in patients presenting with late/very late ST.*(Supplementary tables 3 and 4).*

When considering the time point of the index ST (years 1996-2007 and 2008-2017), similar predictors of MACE were found for both groups as for the total population, except for additional stenting which increased the risk of adverse events in the first group (HR 1.82; 95% CI 1.16–2.86; p=0.008).*(Supplementary table 5).*

DISCUSSION

Patients presenting with ST have a significantly increased risk for morbidity and mortality following PCI. While extensive research has been performed on finding predictors of ST,(10-13) little to no evidence is available on the optimal treatment strategy of those presenting with the event. Furthermore, the low incidence of ST and the lack of systematic follow-up entail great difficulty in recognizing the real incidence of adverse events and their predictors. In the present investigation we assessed the incidence and predictors of future MACE after the treatment of a first definitive ST in the largest series of patients thus far.

At first, we quantified the incidence of MACE after the index ST. At 60 months, almost every second ST patient suffered from MACE (43.7%), mainly driven by a high mortality rate (25.8%), of which 75% were cardiac. Furthermore, the incidence of TVR was as high as 24.8%. Interestingly, 51 out of 118 TVR (43.2%) resulted from a repeat ST-TV event, indicating that the applied ST treatment was ineffective in a substantial proportion of patients. Looking for baseline predictors, we found that cardiogenic shock, ST in LAD and post-procedural TIMI flow were strong predictors of MACE; similar patient and lesion-related factors have been found in previous studies with smaller patients' cohorts and shorter follow-up. (15-19)

With a specific focus on modifiable procedural characteristics, we found that 59.8% of the patients were treated with additional stents (90.8% were DES). Their use, however, did not

impact future MACE. The latter, puts the findings of the Dutch Stent Thrombosis registry (DSR) in which the use of additional stents increased cardiac death and repeat ST up to 73% at 3 years in perspective.(17) Merely 26% of the patients in the DSR presented with late or very late ST as compared to 49.2% in our study; an important difference given the substantially higher incidence of neoatherosclerosis in patients with late or very late ST as compared to early ST. Furthermore, the difference in timing between both studies should be taken into account resulting in significant difference in the use of BMS and new P2Y12 inhibitors (± 50% and 0% respectively in the DSR).

Thrombus aspiration did not emerge as protective measure against future MACE. The latter extends the findings of several recent randomized trials in which thrombus aspiration failed to reduce future events in STEMI patients.(17, 20, 21)

Significant improvement in the risk of future MI was also found with the use of either Prasugrel or Ticagrelor in patients presenting with ST, a finding that adds to previous studies including ACS populations.(22-24)

Differences in treatment profiles were found in patients presenting with early versus late/very late ST. Patients with early ST event were more likely to receive treatment with POBA and GpIIb/IIIa inhibitors which is in line with the assumption that stent-deployment related issues and an initial impaired response to ADP-receptor antagonist therapy during a prothrombotic state mostly explain an early ST event.(2, 25) Intravascular imaging findings confirmed a higher incidence of procedure-related issues (underexpansion and edge dissections) in this population. Moreover, additional stenting was more frequent in patients with late or very late ST, which could suggest a higher incidence of neoatherosclerosis.

A stratified analysis following either early or late/very late ST revealed one remarkable finding: the risk for future MI, TVR and repeat ST-TV appeared to be significantly increased when intravascular imaging was performed. **Intravascular imaging was performed more**

frequently in younger and male patients, cases where the index stent was bioresorbable, the LAD was the culprit, and the presentation of the ST was "very late". Furthermore, those patients also received more often treatment with GpIIb/IIIa inhibitors, thrombectomy, and direct stenting, with a larger stent number and length. However, we were not able to identify a consistent and significantly higher risk profile of patients receiving imaging versus those who did not.*(Supplementary table 6)* Finally, a play of chance could not be excluded.

It is essential to remark that including patients over almost 20 years is both our strength and our main limitation. Several important changes have taken place in the coronary field and this entails great difficulty in finding individual predictors of future outcomes. **Periprocedural treatment strategies have been influenced by novel insights, the availability of pharmacological and technical resources, and improvements in stent technology; as such, optical coherence tomography was only introduced in 2008, the new generation P2Y12 inhibitors became available in 2009, and stents have evolved from BMS to DES (1st and 2nd generations) to platforms with bioresorbable polymers/backbone). Nevertheless, a sensitivity analysis regarding the time of presentation showed similar predictors as for the whole population; of note, additional stenting was a strong predictor of MACE only in the population 1996-2007, which could be explained by a higher use of earlier stent technologies. (26)**

Limitations:

This a retrospective study including patients over a long period of time; changes in treatment strategies over the years might have influenced our results. An important selection bias might

be present on the use of intracoronary imaging. Information on lesion complexity was not available. Data on compliance to antiplatelet agents was not accessible. Finally, given the retrospective nature of the study analysis, there was some missing baseline data and multiple imputation technique was performed. Hence, our results are hypothesis-generating only and must be confirmed with larger-scaled randomized studies.

CONCLUSION

The incidence of adverse events remains high after a first episode of ST. Treatment with new generation P2Y12 inhibitors reduces the risk of future MI. The use of new stents, GpIIb/IIIa inhibitors and thrombectomy was not associated with improved cardiovascular outcomes following ST.

Impact on daily practice

There is a significantly increased risk for morbidity and mortality following the treatment of a first ST episode. While placing stents and using GpIIb/IIIa inhibitors did not show to improve outcome, treatment with new generation P2Y12 inhibitors might be preferable to Clopidogrel in order to reduce the risk of myocardial infarction. Larger and randomized studies are needed to compare the effect of procedural and medical treatment strategies of ST in the current era.

Funding

The authors received no specific funding for this work

REFERENCES

1. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE, Investigators S. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med. 2003;349(14):1315-23.
2. Claessen BE, Henriques JP, Jaffer FA, Mehran R, Piek JJ, Dangas GD. Stent thrombosis: a clinical perspective. JACC Cardiovasc Interv. 2014;7(10):1081-92.
3. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, Kutys R, Skorija K, Gold HK, Virmani R. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. J Am Coll Cardiol. 2006;48(1):193-202.
4. 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, Heestermans T, Buysschaert 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 Global European Effort I. 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(11):1007-21.
5. 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, Juni P, Cook S, Koskinas KC, Windecker S, Raber L. Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography. Circulation. 2016;133(7):650-60.
6. Daemen J, Wenaweser P, Tsuchida K, Abrecht L, Vaina S, Morger C, Kukreja N, Juni P, Sianos G, Hellige G, van Domburg RT, Hess OM, Boersma E, Meier B, Windecker S, Serruys PW. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. Lancet. 2007;369(9562):667-78.
7. Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Genereux P, Branzi A, Stone GW. Stent thrombosis with drug-eluting stents: is the paradigm shifting? J Am Coll Cardiol. 2013;62(21):1915-21.
8. Silber S, Windecker S, Vranckx P, Serruys PW, investigators RAC. Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial. Lancet. 2011;377(9773):1241-7.
9. Daemen J, Simoons ML, Wijns W, Bagust A, Bos G, Bowen JM, Braunwald E, Camenzind E, Chevalier B, Dimario C, Fajadet J, Gitt A, Guagliumi G, Hillege HL, James S, Juni P, Kastrati A, Kloth S, Kristensen SD, Krucoff M, Legrand V, Pfisterer M, Rothman M, Serruys PW, Silber S, Steg PG, Tariah I, Wallentin L, Windecker SW, Aimonetti A, Allocco D, Baczynska A, Bagust A, Berenger M, Bos G, Boam A, Bowen JM, Braunwald E, Calle JP, Camenzind E, Campo G, Carlier S, Chevalier B, Daemen J, de Schepper J, Di Bisceglie G, Dimario C, Dobbels H, Fajadet J, Farb A, Ghislain JC, Gitt A, Guagliumi G, Hellbardt S, Hillege HL, Ten Hoedt R, Isaia C, James S, de Jong P, Juni P, Kastrati A, Klasen E, Kloth S, Kristensen SD, Krucoff M, Legrand V, Lekehal M, Lenarz L, Ni Mhullain F, Nagai H, Patteet A, Paunovic D, Pfisterer M, Potgieter A, Purdy I, Raveau-Landon C, Rothman M, Serruys PW, Silber S,

Simoons ML, Steg PG, Tariah I, Ternstrom S, Van Wuytswinkel J, Waliszewski M, Wallentin L, Wijns W, Windecker SW. ESC Forum on Drug Eluting Stents European Heart House, Nice, 27-28 September 2007. Eur Heart J. 2009;30(2):152-61.
10. van Werkum JW, Heestermans AA, Zomer AC, Kelder JC, Suttorp MJ, Rensing BJ, Koolen JJ, Brueren BR, Dambrink JH, Hautvast RW, Verheugt FW, ten Berg JM. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol. 2009;53(16):1399-409.
11. Iqbal J, Sumaya W, Tatman V, Parviz Y, Morton AC, Grech ED, Campbell S, Storey RF, Gunn J. Incidence and predictors of stent thrombosis: a single-centre study of 5,833 consecutive patients undergoing coronary artery stenting. EuroIntervention. 2013;9(1):62-9.
12. Waksman R, Kirtane AJ, Torguson R, Cohen DJ, Ryan T, Raber L, Applegate R, Waxman S, Gordon P, Kaneshige K, Leon MB, Investigators D. Correlates and outcomes of late and very late drug-eluting stent thrombosis: results from DESERT (International Drug-Eluting Stent Event Registry of Thrombosis). JACC Cardiovasc Interv. 2014;7(10):1093-102.
13. D'Ascenzo F, Bollati M, Clementi F, Castagno D, Lagerqvist B, de la Torre Hernandez JM, ten Berg JM, Brodie BR, Urban P, Jensen LO, Sardi G, Waksman R, Lasala JM, Schulz S, Stone GW, Airoldi F, Colombo A, Lemesle G, Applegate RJ, Buonamici P, Kirtane AJ, Undas A, Sheiban I, Gaita F, Sangiorgi G, Modena MG, Frati G, Biondi-Zoccai G. Incidence and predictors of coronary stent thrombosis: evidence from an international collaborative meta-analysis including 30 studies, 221,066 patients, and 4276 thromboses. Int J Cardiol. 2013;167(2):575-84.
14. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW, Academic Research C. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. 2007;115(17):2344-51.
15. Secemsky EA, Matteau A, Yeh RW, Steg PG, Camenzind E, Wijns W, McFadden E, Mauri L, Investigators PT. Comparison of Short- and Long-Term Cardiac Mortality in Early Versus Late Stent Thrombosis (from Pooled PROTECT Trials). Am J Cardiol. 2015;115(12):1678-84.
16. Moon JY, Jeong MH, Kim IS, Jeong HC, Sim DS, Hong YJ, Kim JH, Ahn Y, Kang JC. Long-term clinical outcome and prognosis after treatment of the first generation drug-eluting stent thrombosis. Int J Cardiol. 2010;145(3):564-6.
17. van Werkum JW, Heestermans AA, de Korte FI, Kelder JC, Suttorp MJ, Rensing BJ, Zwart B, Brueren BR, Koolen JJ, Dambrink JH, van't Hof AW, Verheugt FW, ten Berg JM. Long-term clinical outcome after a first angiographically confirmed coronary stent thrombosis: an analysis of 431 cases. Circulation. 2009;119(6):828-34.
18. Almalla M, Schroder J, Hennings V, Marx N, Hoffmann R. Long-term outcome after angiographically proven coronary stent thrombosis. Am J Cardiol. 2013;111(9):1289-94.
19. Burzotta F, Parma A, Pristipino C, Manzoli A, Belloni F, Sardella G, Rigattieri S, Danesi A, Mazzarotto P, Summaria F, Romagnoli E, Prati F, Trani C, Crea F. Angiographic and clinical outcome of invasively managed patients with thrombosed coronary bare metal or drug-eluting stents: the OPTIMIST study. Eur Heart J. 2008;29(24):3011-21.
20. Waldo SW, Armstrong EJ, Yeo KK, Patel M, Reeves R, Macgregor JS, Low RI, Mahmud E, Rogers JH, Shunk K. Procedural success and long-term outcomes of aspiration thrombectomy for the treatment of stent thrombosis. Catheter Cardiovasc Interv. 2013;82(7):1048-53.

21. Mahmoud KD, Vlaar PJ, van den Heuvel AF, Hillege HL, Zijlstra F, de Smet BJ. Usefulness of thrombus aspiration for the treatment of coronary stent thrombosis. Am J Cardiol. 2011;108(12):1721-7.
22. Gan XD, Wei BZ, Fang D, Fang Q, Li KY, Ding SL, Peng S, Wan J. Efficacy and safety analysis of new P2Y12 inhibitors versus clopidogrel in patients with percutaneous coronary intervention: a meta-analysis. Curr Med Res Opin. 2015;31(12):2313-23.
23. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM, Investigators T-T. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007;357(20):2001-15.
24. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA, Investigators P, Freij A, Thorsen M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009;361(11):1045-57.
25. Armstrong EJ, Feldman DN, Wang TY, Kaltenbach LA, Yeo KK, Wong SC, Spertus J, Shaw RE, Minutello RM, Moussa I, Ho KK, Rogers JH, Shunk KA. Clinical presentation, management, and outcomes of angiographically documented early, late, and very late stent thrombosis. JACC Cardiovasc Interv. 2012;5(2):131-40.
26. Stefanini GG, Holmes DR, Jr. Drug-eluting coronary-artery stents. N Engl J Med. 2013;368(3):254-65.

FIGURE LEYENDS

Figure 1. Outcomes at 60 months follow-up.

Major adverse cardiac events (MACE), Stent thrombosis (ST); Target vessel revascularization (TVR).

TABLES

Table 1. Baseline characteristics

Characteristics	Patients (695)
Age	62.8 ± 12.1
Male	530/695 (76.3)
Prior myocardial infarction	368/692 (53.2)
Prior cerebrovascular accident/transient ischemic attack	52/685 (7.6)
Peripheral vascular disease	60/685 (8.8)
Coronary artery bypass graft	54/685 (7.9)
Dyslipidaemia	415/692 (60)
Hypertension	367/692 (53)
Diabetes Mellitus	152/693 (21.9)
Current smoking	203/649 (31.3)
Estimated glomerular filtration rate <60 ml/min/1.73 m2	91/457(19.9)
Family history of cardiovascular disease	248/691 (35.9)
Index stent	
Bare metal stent	76/587 (12.9)
Drug-eluting stent	446/587 (76)
Bare metal stent + Drug-eluting stent	4/587 (0.7)
Bioresorbable scaffold	15/587 (2.6)
Bioresorbable polymer	46/587 (7.8)
Aspirin	576/648 (88.9)
P2Y12 inhibitor	

Clopidogrel	286/648 (44.1)
Ticagrelor	33/650 (5.1)
Prasugrel	30/650 (4.6)
Anticoagulation	40/672 (6)
Presentation	
Myocardial infarction	592/679 (87.2)
Unstable angina	69/679 (10.2)
Stable angina	18/679 (2.7)
Cardiogenic shock	82/693 (11.8)
Stent thrombosis timing	
Acute	104/679 (15.3)
Subacute	241/679 (35.5)
Late	115/679 (16.9)
Very late	219/679 (32.3)

Categorical data are presented as counts and percentages. Continuous data are presented as mean ± SD or median and Inter-Quartile Range (IQR25th-75th).

Table 2. Peri-procedural characteristics

Characteristics	Patients (695)
Multivessel disease	257/573 (44.9)
Multivessel stent thrombosis	23/695 (3.3)
Stent thrombosis location:	
Left main	14/695 (2)
Left anterior descending coronary	372/695 (53.5)
Left circumflex coronary	124/695 (17.8)
Right coronary artery	194/695 (27.9)
Bypass Graft	24/695 (3.5)
Bifurcation involved	144/695 (20.7)
Thrombolysis in myocardial infarction flow pre	
0	475/683 (69.5)
1	65/683 (9.5)
2	67/683 (9.8)
3	76/683 (11.1)
Thrombolysis in myocardial infarction flow post	
0	28/683 (4.1)
1	13/683 (1.9)
2	36/683 (5.3)
3	606/683 (88.7)
Intracoronary imaging	192/695 (27.6)
IVUS	117/695 (16.8)
OCT	80/695 (11.5)
Intracoronary imaging findings:	

Underexpansion	34/192 (17.7)
Malapposition	49/192 (25.5)
Edge dissection	27/192 (14.1)
Edge disease	17/192 (8.9)
Neoatherosclerosis	61/192 (31.8)
Uncovered struts	2/192 (1)
Gap	9/192 (4.7)
Broken stent	2/192 (1)
Glycoprotein IIb/IIIa inhibitor	392/680 (57.6)
Thrombectomy	322/672 (47.9)
Rheolytic	77/283 (27.2)
Aspirin prescribed	649/666 (97.4)
P2Y12 Inhibitor prescribed	
Clopidogrel	431/666 (64.7)
Ticagrelor	76/666 (11.4)
Prasugrel	139/666 (20.9)
Anticoagulation prescribed	43/666 (6.5)
Statins prescribed	635/648 (98)
Treatment of stent thrombosis	
Additional stent	415/694 (59.8)
Balloon angioplasty alone (POBA)	239/694 (34.4)
Coronary artery bypass graft	6/694 (0.9)
Conservative	34/694 (4.9)
Additional stent characteristics	
Direct stenting	102/410 (24.9)

Bare metal stent	35/413 (8.5)
Drug-eluting stent	375/413 (90.8)
Drug-eluting stent + Bare metal stent	3/413 (0.7)
Number	1 (1-2)
Average diameter (mm)	3 (2.75-3.5)
Length (mm)	28 (16-40)
Overlapping	190/415 (45.8)
POBA characteristics	
Non-compliant	54/236 (22.9)
Plain (No drug-eluting balloon)	177/236 (75)
Cutting	3/236 (1.3)
Drug-coated	3/239 (1.3)

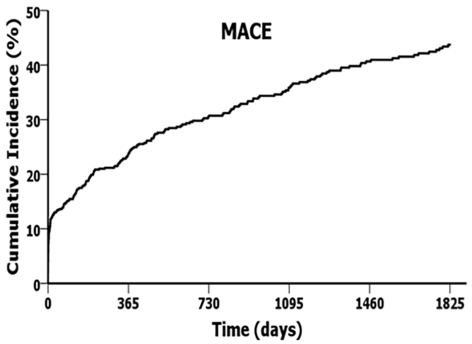
Categorical data are presented as counts and percentages. Continuous data are presented as mean ± SD or median and Inter-Quartile Range (IQR25th-75th).

Table 3. Independent predictors of outcomes at 60 months

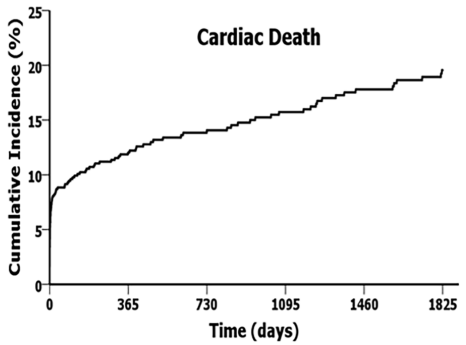
Events	HR (CI 95%)	P value
Major adverse cardiac events		
Cardiogenic shock at ST	2.54 (1.75-3.70)	<0.001
ST in LAD	1.76 (1.32-2.35)	<0.001
Prior CVA/TIA	1.68 (1.08-2.62)	0.020
Peripheral vascular disease	1.55 (1.00-2.39)	0.046
Multivessel disease	1.53 (1.12-2.08)	0.007
TIMI flow post 2-3	0.54 (0.34-0.85)	0.009
Cardiac death		
Cardiogenic shock at ST	3.41 (2.17-5.38)	<0.001
ST in LAD	1.76 (1.16-2.67)	0.007
Estimated glomerular filtration rate <60 ml/min/1.73 m2	1.64 (1.02-2.63)	0.040
Age	1.04 (1.02-1.06)	<0.001
TIMI flow post 2-3	0.33 (0.18-0.60)	<0.001
Myocardial Infarction		
Multivessel ST	2.54 (1.09-5.94)	0.031
Peripheral vascular disease	2.22 (1.17-4.22)	0.014
Male	1.84 (1.03-3.28)	0.039
ST in LAD	1.72 (1.08-2.72)	0.021
Prasugrel/Ticagrelor prescribed	0.56 (0.32-0.99)	0.049
Target vessel revascularization		
Prior CVA/TIA	1.97 (1.11-3.51)	0.021
Stent thrombosis in target vessel		

Prior coronary artery bypass graft	4.02 (1.72-9.39)	0.001
ST in LAD	2.50 (1.28-4.89)	0.007
Intracoronary imaging	1.85 (1.06-3.23)	0.032

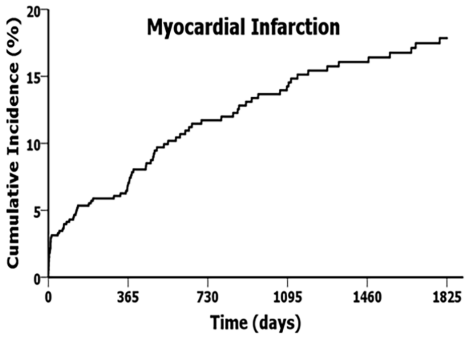
Cerebrovascular accident/transient ischemic attack (CVA/TIA). Left Anterior Descending Coronary (LAD). Stent thrombosis (ST). Thrombolysis In Myocardial Infarction (TIMI). Data are presented as Hazard ratios (HR) and 95% Confidence Intervals (CI).



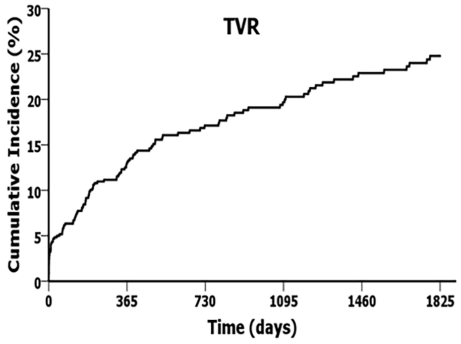
Risk (n)	695	438	297	256	206	175
Events (n)	0	156	189	210	228	238
Cum. Incidence (%)	0	23.9	30.7	35.9	40.7	43.7



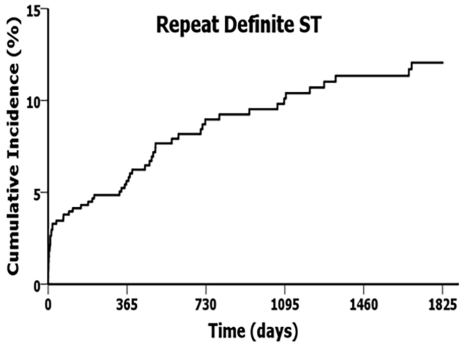
Risk (n)	695	510	380	347	299	262
Events (n)	0	80	90	97	105	111
Cum. Incidence (%)	0	12	14.1	15.7	17.8	19.5



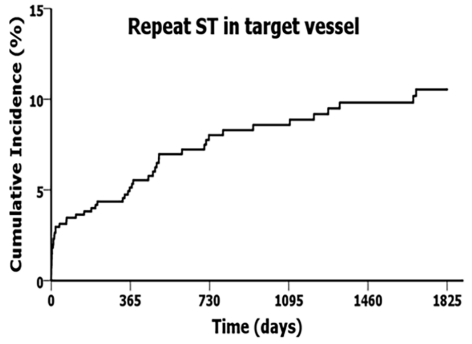
Risk (n)	695	474	332	295	246	213
Events (n)	0	42	62	71	77	82
Cum. Incidence (%)	0	7	11.7	14.3	16.1	17.9



Risk (n)	695	437	305	270	219	187
Events (n)	0	77	94	103	113	118
Cum. Incidence (%)	0	13.1	17.1	19.7	22.9	24.8



Risk (n)	695	479	340	309	259	229
Events (n)	0	34	48	52	56	58
Cum. Incidence (%)	0	5.6	9	10.1	11.3	12.1



Risk (n)	695	480	343	314	264	231
Events (n)	0	31	43	45	49	51
Cum. Incidence (%)	0	5.1	8	8.6	9.8	10.5

Supplementary material

Supplement to: **Incidence and predictors of outcomes after a first definite coronary stent thrombosis**

Index

Supplementary table 1. Baseline characteristics according to ST timing

Characteristics	Early ST (345)	Late/Very late ST (334)	P value*
Age	64.1 ± 12.1	61.4 ± 11.9	0.004
Male	256/345 (74.2)	267/334 (79.9)	0.076
Prior MI	159/343 (46.4)	203/333 (61)	<0.001
Prior CVA/TIA	24/338 (7.1)	26/331 (7.9)	0.711
Prior PVD	24/338 (7.1)	36/331 (10.9)	0.087
Prior CABG	21/338 (6.2)	33/331 (10)	0.075
Dyslipidaemia	185/342 (54.1)	221/334 (66.2)	0.001
Hypertension	175/342 (51.2)	183/334 (54.8)	0.346
Diabetes Mellitus	81/343 (23.6)	69/334 (20.7)	0.354
Current smoking	89/312 (28.5)	109/321 (34)	0.141
eGFR <60 ml/min/1.73 m2	38/213 (17.8)	51/237 (21.5)	0.328
Family history of CVD	113/341 (33.1)	132/334 (39.5)	0.085
Index stent			
BMS	38/321 (11.8)	38/266 (14.3)	0.379
DES	240/321 (74.8)	206/266 (77.4)	0.450
BMS + DES	2/321 (0.6)	2/266 (0.8)	1.000
BRS	8/321 (2.5)	7/266 (2.6)	0.915
BRP	33/321 (10.3)	13/266 (4.9)	0.016
Aspirin	297/329 (90.3)	270/309 (87.4)	0.245
P2Y12 inhibitor			

Clopidogrel	221/329 (67.2)	65/309 (21)	<0.001
Ticagrelor	29/330 (8.8)	4/310 (1.3)	<0.001
Prasugrel	21/330 (6.4)	9/310 (2.9)	0.038
Anticoagulation	20/330 (6.1)	20/327 (6.1)	0.976
Presentation			
MI	311/333 (93.4)	266/330 (80.6)	<0.001
Unstable angina	19/333 (5.7)	49/330 (14.8)	<0.001
Stable angina	3/333 (0.9)	15/330 (4.5)	0.004
Cardiogenic shock	58/344 (16.9)	23/333 (6.9)	<0.001
ST timing			
Acute	104/345 (30.1)	N/A	N/A
Subacute	241/345 (69.9)	N/A	N/A
Late	N/A	115/334 (34.4)	N/A
Very late	N/A	219/334 (65.6)	N/A

Bare Metal Stent (BMS). Bioresorbable scaffold (BRS). Bioresorbable polymer (BRP). Cardiovascular Disease (CVD). Cerebrovascular Accident/Transient Ischemic Attack (CVA/TIA). Coronary Artery Bypass Graft (CABG). Diabetes Mellitus (DM). Drug Eluting Stent (DES). Estimated Glomerular Filtration Rate (eGFR). Myocardial Infarction (MI). Peripheral Vascular Disease (PVD). Stent Thrombosis (ST). Categorical data are presented as counts and percentages. Continuous data are presented as mean ± SD or median and Inter-Quartile Range (IQR25th-75th).

*** P values represent early vs. late/very late ST**

Supplementary table 2. Peri-procedural characteristics according to ST timing

Characteristics	Early ST (345)	Late/Very late ST (334)	P value*
Multivessel disease	113/249 (45.4)	136/308 (44.2)	0.772
Multivessel ST	18/345 (5.2)	5/334 (1.5)	0.007
2 vessel ST	17/345 (4.9)	5/334 (1.5)	0.012
3 vessel ST	1/345 (0.3)	0/334 (0)	1.000
ST location:			
LM	6/345 (1.7)	8/334 (2.4)	0.548
LAD	2.02/345 (58.6)	162/334 (48.5)	0.009
LCX	73/345 (21.2)	47/334 (14.1)	0.015
RCA	85/345 (24.6)	105/334 (31.4)	0.048
Bypass Graft	3/345 (0.9)	21/334 (6.3)	<0.001
Bifurcation involved	78/345 (22.6)	62/334 (18.6)	0.193
TIMI flow pre			
0	250/338 (74)	215/329 (65.3)	0.015
1	25/338 (7.4)	39/329 (11.9)	0.051
2	30/338 (8.9)	33/329 (10)	0.610
3	33/338 (9.8)	42/329 (12.8)	0.220
TIMI flow post			
0	19/338 (5.6)	9/329 (2.7)	0.063
1	8/338 (2.4)	5/329 (1.5)	0.429
2	20/338 (5.9)	14/329 (4.3)	0.329

3	291/338 (86.1)	301/329 (91.5)	0.027
Intracoronary imaging	84/345 (24.3)	103/334 (30.8)	0.058
IVUS	58/345 (16.8)	57/334 (17.1)	0.930
OCT	26/345 (7.5)	51/334 (15.3)	0.001
Intracoronary imaging findings:			
Underexpansion	18/84 (21.4)	15/103 (14.6)	0.221
Malapposition	19/84 (22.6)	30/103 (29.1)	0.314
Edge dissection	24/84 (28.6)	3/103 (2.9)	<0.001
Edge disease	1/84 (1.2)	15/103 (14.6)	0.001
Neoatherosclerosis	2/84 (2.4)	55/103 (53.4)	<0.001
Uncovered struts	0/84 (0)	2/103 (1.9)	0.503
Gap	5/84 (6)	4/103 93.9)	0.733
Broken stent	1/84 (1.2)	1/103 (1)	1.000
GpIIb/IIIa inhibitor	221/332 (66.6)	159/332 (47.9)	<0.001
Circulatory support	29/340 (8.5)	21/330 (6.4)	0.286
Thrombectomy	147/332 (44.3)	164/324 (50.6)	0.104
Rheolytic	42/114 (36.8)	33/158 (20.9)	0.004
Aspirin prescribed	312/322 (96.9)	321/328 (97.9)	0.438
P2Y12 Inh prescribed			
Clopidogrel	200/322 (62.1)	219/328 (66.8)	0.215
Ticagrelor	41/322 (12.7)	33/328 (10.1)	0.284
Prasugrel	71/322 (22)	66/328 (20.1)	0.547
Anticoagulation prescribed	25/322 (7.8)	18/328 (5.5)	0.243

Statins prescribed	314/321 (97.8)	307/313 (98.1)	0.815
Treatment of ST			
Additional stent	165/344 (48)	235/334 (70.4)	<0.001
POBA	157/344 (45.6)	81/334 (24.3)	<0.001
CABG	1/344 (0.3)	5/334 (1.5)	0.118
Conservative	21/344 (6.1)	13/334 (3.9)	0.187
Additional stent characteristics			
Direct stenting	32/162 (19.8)	64/233 (27.5)	0.079
BMS	20/164 (12.2)	15/234 (6.4)	0.045
DES	141/164 (86)	219/234 (93.6)	0.011
DES + BMS	3/164 (1.8)	0/234 (0)	0.069
Number	1 (1-2)	1 (1-2)	0.814
Av. Diam (mm)	3 (2.5-3.25)	3 (2.75-3.5)	<0.001
Length (mm)	23.5 (14-37.5)	28 (20-43)	0.001
Overlapping	81/165 (49.1)	101/235 (43)	0.227
POBA characteristics			
NC	35/156 (22.4)	19/79 (24.1)	0.781
Plain (No DEB)	120/156 (76.9)	56/79 (70.9)	0.313
Cutting	0/156 (0)	3/79 (3.8)	0.037
Drug-coated	1/157 (0.6)	2/81 (2.5)	0.268

Average diameter (Av. Diam). Coronary Artery Bypass Graft (CABG). Bare Metal Stent (BMS). Drug Eluting Stent (DES). Drug-Eluting Balloon (DEB). Intravascular Ultrasound

(IVUS). Left Anterior Descending coronary artery (LAD). Left Circumflex coronary artery (LCX). Left Main (LM). Non-Compliant (NC). Optical Coherence Tomography (OCT). Plain Old Balloon Angioplasty (POBA). Right Coronary Artery (RCA). Stent Thrombosis (ST). Thrombolysis In Myocardial Infarction (TIMI). Categorical data are presented as counts and percentages. Continuous data are presented as mean ± SD or median and Inter-Quartile Range (IQR25th-75th).

*** P values represent early vs. late/very late ST.**

Supplementary table 3. Independent predictors of outcomes up to 60 months in patients presenting with early ST

Early ST (0-30 days)	Hazard ratio (CI 95%)	P value
MACE		
Cardiogenic shock at ST	2.07 (1.30-3.31)	0.002
ST in LAD	1.87 (1.22-2.87)	0.004
Multivessel disease	1.65 (1.01-2.72)	0.046
TIMI flow post intervention 2-3	0.43 (0.24-0.77)	0.005
Cardiac death		
Cardiogenic shock at ST	2.69 (1.55-4.66)	<0.001
ST in LAD	2.16 (1.25-3.73)	0.005
Multivessel disease	2.13 (1.14-3.97)	0.018
Age	1.04 (1.02-1.06)	<0.001
TIMI flow post intervention 2-3	0.32 (0.15-0.65)	0.002
MI		
Multivessel ST	4.73 (1.83-12.20)	0.001
ST in LAD	3.15 (1.99-4.98)	0.012
Intracoronary imaging at ST	2.24 (1.11-4.53)	0.024
TVR		
Multivessel ST	3.17 (2.20-4.58)	0.022
Intracoronary imaging at ST	2.37 (1.29-4.37)	0.005
Diabetes Mellitus	2.03 (1.10-3.74)	0.023
ST in LAD	2.02 (1.06-3.87)	0.041

ST-TV		
Multivessel ST	7.68 (2.33-25.31)	0.001
Intracoronary imaging at ST	5.36 (2.07-13.89)	0.001

Cardiovascular disease (CVD). Cerebrovascular Accident/Transient Ischemic Attack (CVA/TIA). Left Anterior Descending coronary artery (LAD). Major Adverse Cardiac Events (MACE). Myocardial Infarction (MI). Target Vessel Revascularization (TVR). Stent Thrombosis (ST). Stent Thrombosis in Target Vessel (ST-TV). Data is presented as Hazard ratio (HR) and 95% Confidence Interval (CI).

Supplementary table 4. Independent predictors of outcomes up to 60 months in patients presenting with late/very late ST

Late/very late ST (>30 days)	Hazard ratio (CI 95%)	P value
MACE		
Cardiogenic shock at ST	3.03 (1.67-5.51)	<0.001
TIMI flow post intervention 2-3	0.46 (0.21-0.99)	0.047
Cardiac death		
Cardiogenic shock at ST	10.06 (4.69-21.61)	<0.001
Age	1.06 (1.03-1.10)	<0.001
MI		
ST in RCA	0.32 (0.14-0.74)	0.007
Index stent DES	0.46 (0.22-0.94)	0.035
TVR		
Peripheral vascular disease	2.04 (1.04-4.00)	0.038
ST-TV		
No predictors found	N/A	N/A

Major Adverse Cardiac Events (MACE). Myocardial Infarction (MI). Right Coronary Artery (RCA). Target Vessel Revascularization (TVR). Stent Thrombosis (ST). Stent Thrombosis in Target Vessel (ST-TV). Data is presented as Hazard ratio (HR) and 95% Confidence Interval (CI).

Supplementary table 5. Independent predictors of MACE up to 60 months according to the time-point of the ST event

Predictors of MACE	HR (CI 95%)	P value
ST between 1996-2007 (296 patients)		
ST in LAD	1.99 (1.29-3.09)	0.002
Cardiogenic shock at ST	1.77 (1.03-3.04)	0.039
Additional stent	1.82 (1.16-2.86)	0.008
TIMI flow post intervention 2-3	0.34 (0.16-0.70)	0.004
ST between 2008-2017 (399 patients)		
Cardiogenic shock	3.22 (1.90-5.46)	<0.001
Multivessel disease	1.66 (1.03-2.68)	0.037
Age	1.02 (1.00-1.03)	0.015
TIMI flow post intervention 2-3	0.47 (0.25-0.87)	0.016

Major Adverse Cardiac Events (MACE). Left Anterior Descending coronary artery (LAD). Stent Thrombosis (ST). Thrombolysis In Myocardial Infarction (TIMI). Data is presented as Hazard ratio (HR) and 95% Confidence Interval (CI).

Supplementary table 6. Differences between patients receiving intravascular imaging (IVUS/OCT) during the index stent thrombosis event.

Baseline and procedural characteristics	No imaging (503)	Imaging (192)	P value*
Age	63.7 ± 12.1	60.6 ± 11.8	**0.002**
Male	373/503 (74.2)	157/192 (81.8)	**0.035**
Prior MI	265/500 (53)	103/192 (53.6)	0.879
Prior CVA/TIA	36/493 (7.3)	16/192 (8.3)	0.647
Prior PVD	47/493 (9.5)	13/192 (6.8)	0.251
Prior CABG	44/493 (8.9)	10/192 (5.2)	0.105
Dyslipidemia	300/500 (60)	115/192 (59.9)	0.980
Hypertension	268/500 (53.6)	99/192 (51.6)	0.631
Diabetes Mellitus	109/501 (21.8)	43/192 (22.4)	0.856
Current smoking	148/457 (32.4)	55/192 (28.6)	0.348
eGFR <60 ml/min/1.73 m2	66/319 (20.7)	25/138 (18.1)	0.527
Family history of CVD	167/499 (33.5)	81/192 (42.2)	**0.032**
Index stent			
BMS	53/435 (12.2)	23/152 (15.1)	0.351
DES	332/435 (76.3)	114/152 (75)	0.743
BMS + DES	2/435 (0.5)	2/152 (1.3)	0.277
BRS	6/435 (1.4)	9/152 (5.9)	**0.005**
BRP	42/435 (9.7)	4/152 (2.6)	**0.006**
Aspirin	406/466 (87.1)	170/182 (93.4)	**0.022**

New P2Y12 inhibitor	43/468 (9.2)	20/182 (11)	0.486
Anticoagulation	35/483 (7.2)	5/189 (2.6)	**0.023**
Presentation			
MI	421/487 (86.4)	171/192 (89.1)	0.359
Unstable angina	50/487 (10.3)	19/192 (9.9)	0.885
Stable angina	16/487 (3.3)	2/192 (1)	0.101
Cardiogenic shock	73/501 (14.6)	9/192 (4.7)	**<0.001**
ST timing			
Acute ST	80/492 (16.3)	24/187 (12.8)	0.268
Subacute ST	181/492 (36.8)	60/187 (32.1)	0.253
Late ST	87/492 (17.7)	28/187 (15)	0.400
Very late ST	144/492 (29.3)	75/187 (40.1)	**0.007**
Year of ST			**0.043**
1996-2007	226/503 (44.9)	70/192 (36.5)	
2008-2017	277/503 (55.1)	122/192 (63.5)	
Multivessel disease	200/389 (51.4)	57/184 (31)	**<0.001**
Multivessel ST	19/503 (3.8)	4/192 (2.1)	0.264
ST location:			
LM	8/503 (1.6)	6/192 (3.1)	0.198
LAD	255/503 (50.7)	117/192 (60.9)	**0.015**
LCX	94/503 (18.7)	30/192 (15.6)	0.346
RCA	149/503 (29.6)	45/192 (23.4)	0.104
Bypass Graft	22/503 (4.4)	2/192 (1)	**0.031**

Bifurcation involved	98/503 (19.5)	46/192 (24)	0.193
TIMI flow pre 0-1	400/492 (81.3)	140/191 (73.3)	**0.021**
TIMI flow post 2-3	454/492 (92.3)	188/191 (98.4)	**0.002**
GpIIb/IIIa inhibitor	249/488 (51)	143/192 (74.5)	**<0.001**
Thrombectomy	191/481 (39.7)	131/191 (68.6)	**<0.001**
Aspirin prescribed	457/474 (96.4)	192/192 (100)	**0.008**
New P2Y12 inhibitor prescribed	150/474 (31.6)	65/192 (33.9)	0.581
Anticoagulation prescribed	34/474 (7.2)	9/192 (4.7)	0.237
Statins prescribed	454/467 (97.2)	181/181 (100)	**0.023**
Treatment of ST			
Additional stent	292/502 (58.2)	123/192 (64.1)	0.156
POBA	186/502 (37.1)	53/192 (27.6)	**0.019**
CABG	6/502 (1.2)	0/192 (0)	0.195
Conservative	18/502 (3.6)	16/192 (8.3)	**0.010**
Additional stent characteristics			
Direct stenting	57/287 (19.9)	45/123 (36.6)	**<0.001**
BMS	26/290 (9)	9/123 (7.3)	0.582
DES	263/290 (90.7)	112/123 (91.1)	0.906
DES + BMS	1/290 (0.3)	2/123 (1.6)	0.213
Number	1 (1-2)	1 (1-2)	**0.043**
Av. Diam (mm)	3 (2.75-3.50)	3.12 (2.88-3.50)	**0.006**
Length (mm)	26 (16-40)	31 (18-43)	**0.041**

Overlapping	133/292 (45.5)	57/123 (46.3)	0.882
POBA characteristics			
NC	33/184 (17.9)	21/51 (40.4)	**0.001**
Plain (No DEB)	146/184 (79.3)	31/52 (59.6)	**0.004**
Cutting	3/184 (1.6)	0/52 (0)	1.000
Drug-coated	3/186 (1.6)	0/53 (0)	1.000

Average diameter (Av. Diam). Bare Metal Stent (BMS). Bioresorbable scaffold (BRS). Bioresorbable polymer (BRP). Cardiovascular Disease (CVD). Cerebrovascular Accident/Transient Ischemic Attack (CVA/TIA). Coronary Artery Bypass Graft (CABG). Drug Eluting Stent (DES). Estimated Glomerular Filtration Rate (eGFR). Intravascular Ultrasound (IVUS). Left Anterior Descending coronary artery (LAD). Left Circumflex coronary artery (LCX). Left Main (LM). Myocardial Infarction (MI). Non-Compliant (NC). Optical Coherence Tomography (OCT). Plain Old Balloon Angioplasty (POBA). Peripheral Vascular Disease (PVD). Right Coronary Artery (RCA). Stent Thrombosis (ST). Thrombolysis In Myocardial Infarction (TIMI). Categorical data is presented as counts and percentages and tested by χ^2 test or Fisher's exact test when appropriate. Continuous data is presented as mean ± SD and tested by the student's t-test or median and Inter-Quartile Range (IQR25th-75th) and tested by Mann-Whitney rank sum test.