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Stent thrombosis after drug-eluting stent implantation: incidence, timing, and relation to discontinuation of clopidogrel therapy over a 4-year period

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Aims To assess the incidence, timing, and relation of drug-eluting stent (DES) thrombosis to discontinuation of clopidogrel therapy.

Methods and results This prospective observational cohort study included 6816 consecutive patients that underwent successful DES implantation. Primary endpoint was definite stent thrombosis (ST). During 4 years of follow-up, definite ST was observed in 73 patients, corresponding to a cumulative incidence of 1.2%. Cumulative incidence of ST at 30 days was 0.5 and 0.8% at 1 year, respectively. Discontinuation of clopidogrel therapy was significantly associated with ST only in the first 6 months after the procedure ($P < 0.001$). During that period, the median time interval from clopidogrel discontinuation to ST was 9 days [interquartile range (IQR) 5.5–22.5] while thereafter it was 104.3 days (IQR 7.4–294.8).

Conclusion The 4 year incidence of ST after DES implantation is low. A relevant number of ST occur early after discontinuation of clopidogrel therapy. The dependence of ST on discontinuation of clopidogrel therapy seems to be mostly confined to the first 6 months after DES implantation. However, specifically designed randomized studies are required to establish the optimal length of clopidogrel therapy after DES implantation.

Keywords Stent thrombosis • Drug-eluting stent • Clopidogrel

Introduction

Drug-eluting stents (DESs) are effective in reducing restenosis and the need for re-intervention after percutaneous coronary interventions (PCIs).[1,2] Although their mid-term safety has been well established, recent pathological[3,4] and clinical data[5–7] have caused concerns about an increased risk of late stent thromboses associated with DES. Registry data have suggested a constant rate of late stent thromboses of 0.6% per year for up to 3 and even 4 years after DES implantation.[8,9] On the other hand, comprehensive meta-analyses found no excess risk in the overall rate of stent thrombosis (ST) with DES. However, there is evidence of a slight increase in the risk of ST associated with DES after the first year.[10–14] Of note, no single trial has had enough power to assess ST as a primary endpoint and it remains an important safety issue in contemporary interventional cardiology due to the attendant high morbidity and mortality of this entity.

The peri-interventional use of thienopyridines in addition to aspirin has greatly reduced the rate of acute thrombotic events in patients treated with coronary stents.[15–19] While the presence of coronary artery disease itself—even without stent implantation—is an indication for lifelong aspirin therapy,[20,21] the optimal duration

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of concomitant thienopyridine therapy after DES implantation is still unknown. On the one hand, premature discontinuation of clopidogrel therapy is associated with an increased risk of ST.[22–25] On the other hand, late ST may still occur despite continued clopidogrel therapy.[8,26,27] Labelling of the two first generation DESs recommends aspirin indefinitely and clopidogrel for 3 months after Cypher and 6 months after Taxus implantation. A landmark analysis of event-free patients of the observational Duke study showed that ongoing clopidogrel usage beyond 6 and even 12 months continued to predict lower rates of death and myocardial infarction after DES implantation.[28] Conversely, the prospective cohort study by Airoldi *et al.*[29] found that the discontinuation of clopidogrel therapy was the most powerful predictor of ST only within the first 6 months but not thereafter. A focused update of the ACC/AHA/SCAI guidelines recommends a duration of clopidogrel therapy of at least 12 months after DES implantation for patients that are not at high risk of bleeding.[30] An unnecessarily prolonged clopidogrel therapy not only represents a financial burden but also a bleeding concern, especially when patients require surgery. Since recent analyses have been limited by insufficient information about clopidogrel therapy and duration of follow-up, we aimed to address these limitations by performing a prospective cohort study. We sought to assess the incidence, timing, and relation of DES thrombosis to discontinuation of clopidogrel therapy in two high-volume PCI centres.

Methods

Patient population

Patients were included in this prospective cohort study if they had undergone an angiographically successful DES implantation from July 2002 through December 2006 at the Deutsches Herzzentrum or Klinikum rechts der Isar, both tertiary referral, high-volume PCI centres in Munich, Germany. During this period, a total of 10 448 PCIs were performed. Of them, 842 patients underwent balloon angioplasty without stent implantation, 2762 were treated with bare-metal stent implantation and 6844 patients received DESs. Bare metal stents were mostly used within the first 2 years of the study period: in the setting of randomized clinical trials, acute ST-elevation myocardial infarction or lesions in venous bypass grafts. Twenty-eight patients with DES implantation were excluded because of an unsuccessful PCI. Thus, 6816 patients with successful DES implantation could be included in this study.

Angiographic success was defined as a residual stenosis of 30% or less within the stented segment by visual assessment, no evidence of residual dissection, no evidence of thrombus, and achievement of a final thrombolysis in myocardial infarction (TIMI) flow grade $\geq$2.

Interventional procedures

Prior to the intervention all patients received a loading dose of 600 mg clopidogrel and 500 mg aspirin. Interventions were performed according to current practice guidelines for PCI with the final interventional strategy left to the discretion of the operator. Peri-procedural antithrombotic therapy consisted of either intravenously administered unfractionated heparin with or without abciximab or bivalirudin.

Clopidogrel use

Post-interventional antithrombotic therapy consisted of clopidogrel 75 mg twice daily for the remainder of the hospitalization up to 3 days, followed by 75 mg per day. Over the whole period, the recommended duration of clopidogrel therapy was 6–12 months depending on the severity of disease at presentation and complexity of intervention. However, final decision was at the discretion of the operators. In special situations, the recommended duration of clopidogrel therapy was shorter (1–3 months in patients on oral anticoagulation) or longer (indefinitely for stenting of left main coronary vessel[31]) than that shown above. Aspirin 100 mg twice daily was recommended for an indefinite period. Other cardiac medications were prescribed at the discretion of the patient's physician.

Endpoints and definitions

The primary outcome of this study was definite ST. We also calculated the incidence of probable and possible ST according to the criteria of the Academic Research Consortium.[32] Myocardial infarction was defined according to TIMI criteria.[33] A systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg on two separate occasions or the current use of antihypertensive drugs qualified as definition of arterial hypertension. Diabetics had to be on active treatment with insulin or an oral anti-diabetic agent. In diet-controlled patients, an abnormal fasting plasma glucose level or abnormal glucose tolerance test was required.[34] Current smokers were those with regular smoking in the prior 6 months. Hypercholesterolaemia was defined as a total cholesterol value of at least 6.2 mmol/L or the use of lipid-lowering drugs.

Follow-up

Detailed information regarding antiplatelet therapy and the occurrence of adverse events was obtained during the routine follow-up at 30 days, 6 months, 1 year, and annually thereafter. Patients were either interviewed by phone or seen by their physician. Those with cardiac complaints underwent a complete clinical, electrocardiographic, and laboratory check-up. If patients suffered an event at another hospital, the appropriate medical records were solicited (including discharge summaries, laboratory values, and angiograms). General practitioners, referring cardiologists, patients, or their relatives, were contacted for additional information if necessary. Last follow-up visit was performed in August 2008.

Angiographic analysis was performed by operators of the quantitative angiographic core laboratory using identical methods of analysis and definition of the variables. Relevant data were collected from source documents and prospectively entered into a computerized database by specialized personnel of the data coordinating Intracoronary Stenting and Antithrombosis Research (ISAR) centre.

Statistical analysis

Data are presented as means $\pm$ standard deviation (SD), medians [interquartile range (IQR)], or counts (percentages). The incidences of ST, death, and myocardial infarction were calculated as cumulative incidences, estimated by the competing risk approach which takes into account informative censoring.[35] The same method was used for calculating the risk of death and myocardial infarction associated with ST.

The multivariate adaptive regression splines (MARS) approach[36,37] was employed to determine significant change points of the preventive effect of clopidogrel therapy duration on the risk of ST. By this approach, piecewise linear functions were fitted to the data which allowed for parametrical assessment of risk development by means of statistically reliable change points. Along this procedure, martingale

residuals were used as response variable in a time to event model framework. Subsequently, competing risk regression models (proportional subdistribution hazard regression[38]) including the determined cut off parameter terms and covariables were calculated to assess statistical significance of differences in risk slopes in dependence on clopidogrel therapy duration.

For multivariable analysis, we also used the competing risk regression approach for ST including clinically relevant variables such as age, sex, diabetes, clinical presentation, and vessel size.

Proportional hazard assumption implied by the regression approach was verified by investigation of Schoenfeld-residual plots with fitting spline-functions and simultaneous confidence bands.

To account for the dependency of a more extended clopidogrel treatment on a longer follow-up period (better prognosis per definition), time to occurrence of ST was defined from the end of clopidogrel therapy within the event analysis.

The statistical software package R version 2.7.1 (R Foundation for Statistical Computing, Vienna, Austria) with function polymars (polspline package, Kooperberg 2006) was used for MARS analyses. The R package cmprisk (Gray 2008) was used to perform the competing risk analyses. Further statistical analyses were performed using S-PLUS statistical package (S-PLUS version 4.5, Insightful Corp, Seattle, Washington, DC).

A two-sided *P*-value <0.05 was considered to indicate statistical significance.

Because of the low number of statistical tests performed in this study, no corrections for multiple testing were done. In patients with multilesion interventions, only one lesion was selected for the analysis. This was either the stented lesion which presented the occlusion or a lesion at random.

There was no industry involvement in the study design, data collection, analysis, or writing of the manuscript.

Results

Patient population

During 4 years of follow-up, 4.2% of the patient population had incurred a myocardial infarction and 8.6% had died. Definite ST were observed in 73 patients, corresponding to a cumulative incidence of 1.2% at 4 years. Cumulative incidence of definite ST was 0.5% at 30 days and 0.8% at 1 year. At 4 years of follow-up, 2.8% of the patients had probable (0.3%) or possible (2.5%) ST (*Figure 1*). Among patients with probable ST, there were 14 unexplained deaths within 30 days after the procedure and 8 acute myocardial infarctions involving the target-vessel territory without angiographic confirmation.

Baseline, angiographic, and procedural characteristics

Baseline, angiographic, and procedural characteristics of the overall patient population are displayed in *Tables 1–3*. Total stent length per patient was 34.7 ± 22.1 mm and the number of stents implanted per patient was 1.8 ± 1.1, respectively.

Figure 2 depicts the number of patients experiencing ST while on clopidogrel therapy and patients with ST after cessation of clopidogrel.

Clinical outcomes of stent thrombosis

In comparison to patients without ST, patients with ST carried a higher risk of myocardial infarction [89 vs. 3%; HR 50.4 (95% CI 39.4–64.5)] and death [42 vs. 8%; HR 5.2 (95% CI 3.4–8.1)].

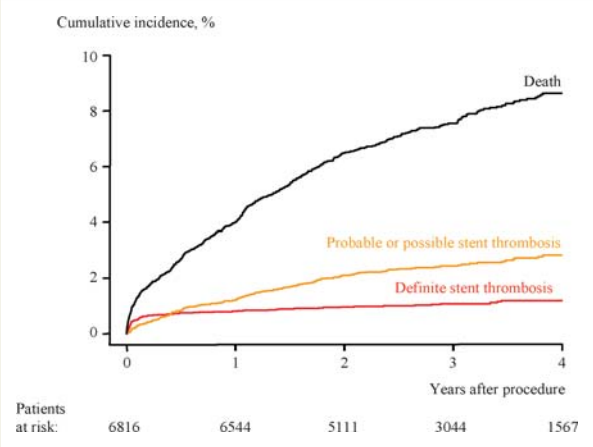

Figure 1 Cumulative incidence of death, probable or possible, and definite stent thrombosis in the overall population during 4 years of follow-up. The numbers below show the number of patients at risk at different time points.

Table 1 Base-line characteristics of the patients[a]

Base-line characteristics	*n* = 6816
Age, years	66.8 ± 10.8
Women	1640 (24.0)
Diabetes	1925 (28.0)
Insulin-treated	630 (9.2)
Arterial hypertension	4503 (66.0)
Current smoker	1042 (15.0)
Hypercholesterolaemia	4841 (71.0)
Body mass index, kg/m^2	27.2 ± 4.0
Clinical presentation	
Acute myocardial infarction	1188 (17.4)
ST-elevation myocardial infarction	627 (9.2)
Non-ST-elevation myocardial infarction	561 (8.2)
Unstable angina	1197 (17.6)
Stable angina	4431 (65.0)
Prior myocardial infarction	2349 (34.0)
Prior aortocoronary bypass surgery	866 (13.0)

[a]Data are presented as numbers (%) or means ± SD.

Effect of clopidogrel therapy duration on the risk of stent thrombosis

The median clopidogrel therapy duration was 360 days (IQR 360–556). The MARS model (*Figure 3*) revealed a significant change point in the risk of ST after 6 months of clopidogrel therapy. As illustrated in *Figure 3*, the risk of ST was highest early after PCI. There was a rapid risk decrement within the first 29 days

Table 2 Angiographic characteristics[a]

Angiographic characteristics	*n* = 6816
Left ventricular ejection fraction, %	53.9 ± 12.3
Multivessel disease	5626 (83.0)
Target vessel	
Left main coronary artery	255 (3.7)
Left anterior descending	2781 (40.9)
Left circumflex coronary artery	1761 (25.8)
Right coronary artery	1813 (26.6)
Venous bypass graft	206 (3.0)
Complex (type B2/C) lesions	4973 (73.0)
Ostial lesions	1220 (18.0)
Bifurcation lesions	1542 (23.0)
Restenotic lesions	1269 (19.0)
Chronic occlusions	288 (4.2)
Initial TIMI flow grade	
0	391 (5.7)
1	189 (2.8)
2	635 (9.3)
3	5601 (82.2)
Vessel reference diameter, mm	2.8 ± 0.6
Diameter stenosis prior to procedure, %	60.9 ± 15.8

[a]Data are presented as numbers (%) or means ± SD.

Table 3 Procedural characteristics[a]

Procedural characteristics	*n* = 6816
Balloon-to-vessel ratio	1.1 ± 0.1
Balloon diameter, mm	3.1 ± 0.6
Maximal balloon pressure, atm	14.7 ± 3.0
Number of stents	1.2 ± 0.4
Length of stented segment, mm	22.5 ± 9.7
Type of drug-eluting stent	
Cypher stent	2073 (30.4)
Taxus stent	1287 (18.9)
ISAR stent	2866 (42.0)
others	590 (8.7)
Overlapping stents	1237 (18.0)
Diameter stenosis after procedure, %	9.8 ± 5.9
Final TIMI flow grade	
2	114 (1.7)
3	6702 (98.3)

[a]Data are presented as numbers (%) or means ± SD.

(hazard reduction per 1 day treatment continuation: 0.95, 95% CI 0.91–0.99) and a less prominent (but not statistically different, $P = 0.073$) decrease from 1 to 6 months of treatment (hazard reduction per 1 day treatment continuation: 0.98, 95% CI 0.94–1.04). A nearly constant risk was observed after 6 months (hazard change per 1 day treatment continuation: 1.00, 95% CI 0.99–1.01). Overall, the risk decrease throughout the first 6 months of clopidogrel therapy was significantly greater compared with the risk decrease in the subsequent interval (hazard reduction per day: 0.98, 95% CI 0.97–0.99 vs. 1.00, 95% CI 0.99–1.01, $P < 0.001$).

The multivariable regression model confirmed the change point of the risk of ST at 6 months of clopidogrel treatment duration (*Figure 3*). Even though the risk decrease attributable to clopidogrel therapy was lower after multivariable adjustment, the difference in the risk of ST before and after 6 months of clopidogrel therapy remained highly significant ($P < 0.001$; *Figure 3*).

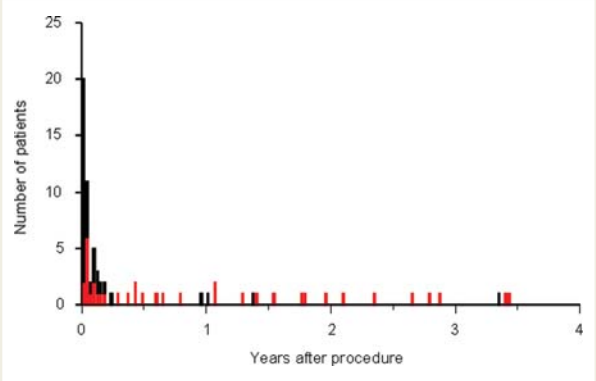

Figure 2 Number of patients incurring stent thrombosis during 4 years of follow-up. Black bars indicate patients on clopidogrel therapy and red bars those off clopidogrel therapy at the time of stent thrombosis.

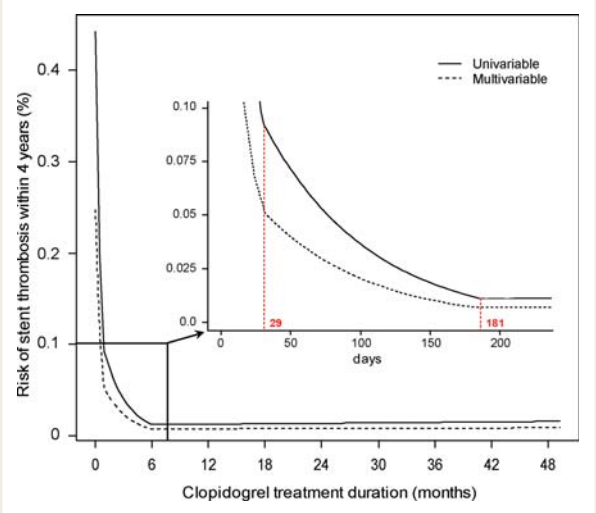

Figure 3 Change in the risk of stent thrombosis in dependence on clopidogrel treatment duration in the univariable (solid line) and multivariable MARS-model (dashed line).

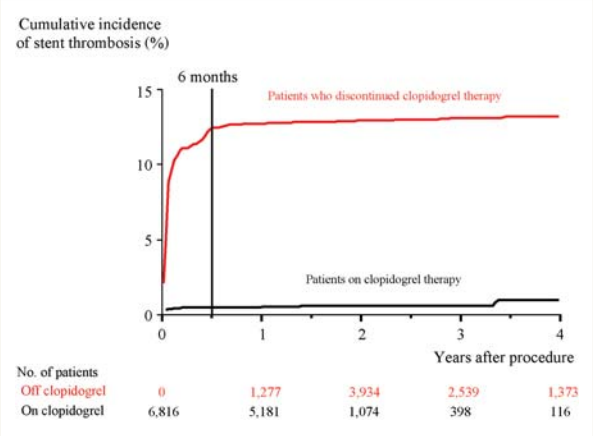

Figure 4 Cumulative incidence of stent thrombosis in patients who continued (black) and those who discontinued clopidogrel therapy (red). Patients switched from one group to the other as soon as they stopped taking clopidogrel.

The MARS analysis was repeated after excluding the polymer-free ISAR DES yielding the same relation pattern between clopidogrel therapy duration and the risk of ST as that shown in *Figure 3*.

Figure 4 depicts the cumulative incidence of ST in patients who continued and those who discontinued clopidogrel therapy with patients switching from one group to the other as soon as they stopped taking clopidogrel. The increase in the cumulative incidence of ST was low in patients who discontinued clopidogrel beyond 6 months of therapy.

Temporal relationship between clopidogrel therapy discontinuation and stent thrombosis

The median time interval from clopidogrel discontinuation to ST was 9 days (IQR 5.5–22.5) within the first 6 months after DES implantation and 104.3 days (IQR 7.4–294.8) thereafter.

Discussion

The purpose of this study was to assess the relation of DES thrombosis to discontinuation of clopidogrel therapy in a prospective cohort of 6816 patients with successful DES implantation during a follow-up period of 4 years.

The main findings of our study are that (i) the incidence of definite ST in this cohort of patients treated with DES in two high volume, tertiary referral centres is low, (ii) most ST events occur early after DES implantation, (iii) ST is associated with a high morbidity and mortality, and (iv) the preventive effect of clopidogrel from ST is mostly confined to the first 6 months after DES implantation with no substantial benefit thereafter.

The expanded use of DES for off-label indications was not only associated with a marked reduction of restenosis,[1,2] but was also credited with an increased risk of ST.[39–41] The incidence of definite ST observed in this study (0.5, 0.8, and 1.2% at 30 days, 1 and 4 years of follow-up, respectively) is low compared with the rates reported in other registries.[8,9,29,41] The results are more in keeping with those reported in the pivotal FDA approval trials for the Cypher and Taxus stents that included mainly low-risk patients.[13] They are also within the expected range of ST observed after BMS implantation.[13,42] Even though DES thrombosis was rare, it turned out to be a deleterious event for most patients, with 89% of the patients with ST sustaining myocardial infarction and a fatality rate of 42%. The reasons underlying the low incidence of ST in this study are speculative. In fact, all patients were preloaded with 600 mg of clopidogrel prior to the intervention. Although specific large randomized trials are pending, there are data that support the routine use of a high loading dose of 600 mg of clopidogrel prior to PCI.[43–48] Likewise, a recent *post hoc* analysis of the HORIZONS-AMI trial showed a significant reduction in the overall rate of ST in STEMI patients that were pre-treated with 600 mg clopidogrel compared with those that received only 300 mg.[49] Although the proportion of patients presenting with an acute coronary syndrome is low (35%) compared with a previous registry (59% in the Bern-Rotterdam Registry[8]), the patient population of this study is characterized by many complex features (e.g. 28% diabetics, 83% multivessel disease, 73% complex lesions, 23% bifurcational lesions, and 3% PCI in venous bypass grafts) that are known to be associated with an increased risk of ST.[23] However, ST rates are higher in patients with more severe risk profile such as those in SYNTAX (three vessel and left main disease),[50] TRITON-TIMI 38 (moderate to high-risk acute coronary syndrome),[51] and HORIZONS-AMI (ST-elevation myocardial infarction).[52]

Reports about an increased risk of late and very late ST in DES recipients have caused not only an intensive debate within the cardiology community,[5–7] but also disseminated great concerns about the long-term safety of these permanent devices in the lay press. Necropsy studies showing delayed endothelialization and ongoing inflammation provided the presumed pathophysiological mechanism for late susceptibility to ST in these patients.[3,4] However, a number of meta-analyses failed to find a difference in the cumulative incidence of ST between DES and BMS.[11–13] Nevertheless, the time distribution of thrombotic events appears to differ between BMS and DES recipients with more events occurring very late after DES implantation. In light of these results, cardiologists advocated an extension in the duration of clopidogrel therapy to at least 1 year[53] and some even for an indefinite period. In fact, by reducing acute ischaemic events, the peri-interventional use of thienopyridines was the prerequisite for the safe performance of PCI.[15] Premature discontinuation before the recommended 3–6 months of clopidogrel therapy has proven as one of the strongest predictors of ST.[22–24] However, there is a little evidence that the simple lengthening of clopidogrel therapy has the potential to prevent late ST. A landmark-analysis of event-free patients in a large single-centre registry found an increased risk of death and myocardial infarction in DES recipients not taking clopidogrel after 6 months and even after 1 year compared with those on clopidogrel and those with BMS.[28]

In contrast, the present study suggests that there is no substantial benefit of a prolonged clopidogrel therapy beyond 6 months. Moreover, the lack of a temporal relationship between clopidogrel discontinuation and the incidence of ST after 6 months further implies the lack of a causal association.

Registry data showing an ongoing risk of ST despite continued dual antiplatelet therapy are supportive of the results of the present study. In the 8146 patients Bern/Rotterdam Registry, there was no significant difference in the rate of ST in patients in Bern routinely receiving clopidogrel for 12 months and those in Rotterdam receiving clopidogrel for 3–6 months.[8] Moreover, patients experiencing late or very late ST in the REWARDS registry were receiving dual antiplatelet therapy as often as and even more often than patients who stopped clopidogrel.[27]

Our data substantiate those from Airoldi *et al.*[29] With their study of 58 cases with ST in a cohort of 3021 patients during a follow-up period of 18 months, the authors demonstrated that the discontinuation of clopidogrel therapy was a strong predictor for ST within the first 6 months but not thereafter.

The existence of a point after DES implantation when the benefits of clopidogrel are no longer significant implicates that continuing therapy beyond that time point might expose patients to unnecessary risks and side effects. Recent studies have highlighted the relevance of bleeding as a predictor of mortality.[54] While often discounted in the past bleeding has become recognized as a major factor in current trials of antithrombotic therapy. Indisputable, a certain degree of platelet inhibition is important to the treatment of arteriosclerotic disease, particularly in the setting of PCI. However, incremental reductions in ischaemic endpoints achieved with the use of aspirin,[21] the additional use of clopidogrel,[55] and its substitution for the more potent prasugrel[51] were all at the expense of an increased risk of bleeding. Defining the time point where the benefit of treatment no longer exceeds risks should be the focus of future investigations. The randomized MATCH trial is a good example where the balance point was exceeded. Of patients with recent ischaemic stroke or transient ischaemic attack, the combination of aspirin and clopidogrel over 18 months increased the risk of life-threatening or major bleedings compared with clopidogrel alone, while there was no significant difference in the reduction of major vascular events.[56] Furthermore surgery, either elective or urgent, poses a largely unsolved problem for patients on dual antiplatelet therapy and their treating physicians.

Limitations of this study include the inherent lack of randomization of the comparison groups. Treatment duration may have been dependent on unmeasured confounders, which could not be taken into account in the multivariable analysis. Patients not at high risk of ST could have been prescribed a shorter duration of clopidogrel therapy thereby creating a selection bias in favour of a shorter therapy duration. The number of ST and especially late ST is low in comparison with other registries. Despite the large number of 6816 patients included in this study, there were only 37 thrombotic events after discontinuation of antiplatelet therapy. A common reason for this is a failure of case detection. Moreover, the number of patients on clopidogrel therapy for more than 2 years becomes insufficient to allow a meaningful assessment of this therapy duration. The use of definite ST likely results in an underestimate of the true incidence but avoids the dilution of case certainty if probable or possible events were included. Another limitation of this study is that clopidogrel use was defined at discrete follow-up time points. No compliance information was available for the entire period. Thus, recall bias cannot be excluded. Moreover, the distribution of clopidogrel treatment duration was multimodal with peaks at about 30 days, 3 months, 6 months, and 1 year after stent implantation which may have weakened the statistical power of the piecewise continuous model approach.

In conclusion, the low 4 year incidence of ST observed in this study may add some reassurance regarding the long-term safety profile of DES. The present findings should not be interpreted in such a way that a 6 month course of clopidogrel therapy is sufficient in every DES recipient. Optimal duration of antiplatelet therapy after DES implantation is still unclear and can only be determined by means of a randomized controlled study.

Conflict of interest: Dr J.M. has received lecture fees from Daiichi Sankyo and Cordis. Dr A.K. has received lecture fees from Bristol-Meyers Squibb, Cordis, Eli Lilly, Medtronic and Sanofi-Aventis.

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CARDIOVASCULAR FLASHLIGHT

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Severe right bivalvular carcinoid heart disease

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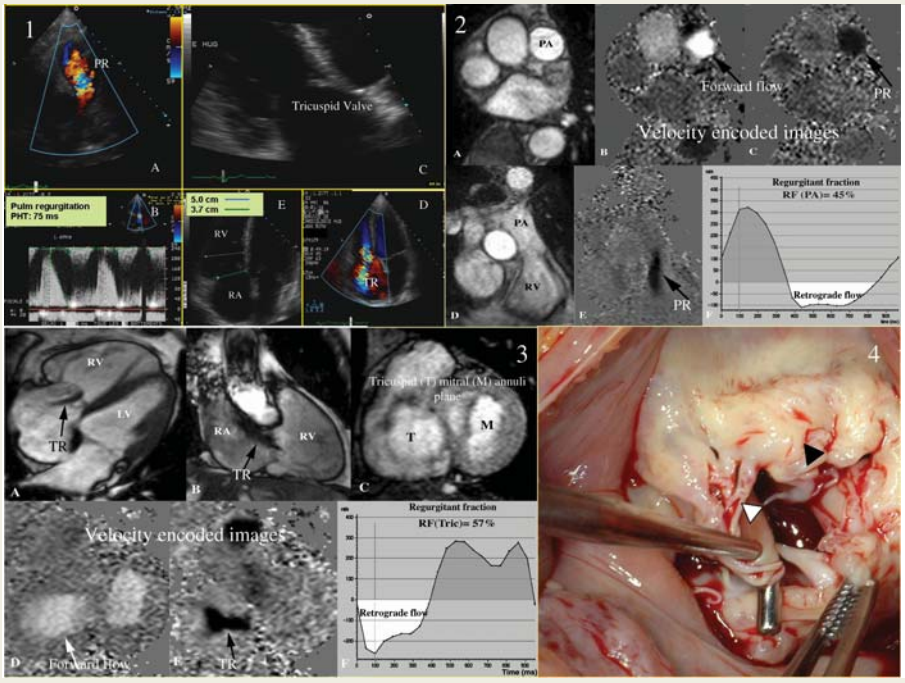

A 65-year-old man with a 1-year clinical history of recurrent flush and diarrhoea was admitted to our hospital for severe right-sided heart failure. Abdominal computed tomography scan showed carcinoid tumour originating from gut with hepatic metastases. Chemotherapy with octreotid and arterial chemo-embolization of the hepatic metastases was initiated. Transthoracic echocardiography revealed severe tricuspid and pulmonary valve regurgitation with dilation of the right heart chambers (*Figure 1A–E*). Together with the history and the thickened, retracted, and immobile leaflets, this was suggestive of carcinoid heart disease. Velocity-encoded cardiac-magnetic resonance imaging confirmed the severity of pulmonary [*Figure 2A–F*; regurgitant fraction (RF) = 45%] and tricuspid valve regurgitations (*Figure 3A–F*). Tricuspid regurgitant volume was calculated as the difference of the net pulmonary forward volume and the tricuspid inflow in diastole as well as direct quantification of flow at the tricuspid annulus (illustrated here) with similar results (RF calculated at 58 and 57%, respectively). The patient underwent successful cardiac surgery with placement of bioprosthetic valves, less prone to thrombotic and haemorrhagic complications in this situation. The operative settings showed pathological findings suggestive of carcinoid heart disease (*Figure 4*) with thickened and retracted leaflets (black arrow) and chordae (white arrow) confirmed by histology revealing valvular fibrosis and no inflammatory changes. Early post-operative follow-up showed substantial clinical improvement of right-sided heart failure.

Carcinoid heart disease is a rare cause of intrinsic tricuspid and pulmonary valve disease and leads to important morbidity and mortality caused by right-sided heart failure. Medical and in appropriate cases surgical treatment can improve quality of life and in same cases survival. This case illustrates the importance of quantification of valve regurgitations, especially in the pulmonary position, as pre-operative strategy for optimal clinical decision-making in carcinoid heart disease.