1. Introduction

The introduction of coronary stents in the early 1990s has drastically improved the outcome of percutaneous coronary intervention (PCI) for obstructive coronary artery disease. To date, two different types of stents are available: bare metal stents (BMSs) and the newer drug-eluting stents (DESs). Various randomised controlled trials have demonstrated great advantages of DESs with respect to significant reduction of restenosis and recurrence of symptoms and improvement of clinical outcomes after PCI as compared to BMSs [1]. Since the introduction a few years ago, millions of DESs have been implanted. However, acute (≤24 h), subacute (1–30 d), and late (>30 d after stent implantation) stent thrombosis is still the major downside to coronary stents (both BMSs and DESs) because this inevitably leads to myocardial infarction (90%) and death in up to 40% of the cases [2]. To prevent stent thrombosis, patients are treated with aggressive antiplatelet therapy. The current guidelines recommend a dual antiplatelet regimen with acetylsalicylic acid (ASA) and clopidogrel after PCI with stenting (Fig. 1, mechanisms of action of antiplatelet drugs). Clopidogrel maintenance therapy is recommended after BMS implantation for at least 4 wk (level of evidence 1a) and after DES implantation for 6–12 mo (level of evidence 1c) [3]. However, despite these narrowly evidence-based recommendations, the optimal duration of clopidogrel has not yet been established. Moreover, it is...
becoming clear that an extension of the duration of clopidogrel will probably further reduce the incidence of late stent thrombosis [4].

The problem with the current dual antiplatelet regimen with aspirin and clopidogrel is the fact that patients with coronary heart disease often have concomitant urologic problems that require adequate treatment as well, including surgery. This sometimes creates a dilemma for the clinician with respect to the most appropriate treatment, that is, when to operate and whether or not to stop antiplatelet therapy. The presented case demonstrates such a difficulty in decision-making.

2. Case report

A 77-yr-old man with no cardiovascular history, but with a positive family history for cardiovascular disease and dyslipidemia, underwent an elective coronary angiogram because of stable angina pectoris. Angiography revealed a significant stenosis in the proximal left anterior descending coronary artery. Stenting of the lesion was undertaken with implantation under high pressure of four DESs with a total length of 100 mm (Taxus® [paclitaxel], Boston Scientific, Natick, MA, USA, 2.75 × 32 mm, 2.5 × 24 mm, 2.5 × 24 mm, and 2.5 × 20 mm). Prior to stent implantation, the patient was prescribed clopidogrel for at least 6 mo and lifelong aspirin. Exactly 2 mo after stent placement, he discontinued the clopidogrel for a scheduled laparoscopic pelvic lymph node dissection for staging of prostate cancer. Several hours after his surgery, he suddenly experienced heavy chest pain. Electrocardiography showed ST-segment depression in leads II, III, and aVF, and ST-segment elevation in V2 till V4, and a myocardial infarction was diagnosed. The patient was transported to the catheterisation laboratory and urgent angiography demonstrated that the stents were occluded by a massive thrombus (Fig. 2). Balloon angioplasty restored coronary blood flow but the patient remained hemodynamically unstable. An intra-aortic balloon pump was placed, but his clinical situation deteriorated and the patient died several hours later. At autopsy, a fresh thrombus was observed occluding the coronary DESs (Figs. 3 and 4).

3. Discussion

Stent thrombosis is a serious complication and is associated with a high morbidity and mortality [2]. Recent studies have identified major risk factors that are associated with an increased risk for the occurrence of a stent thrombosis, including early discontinuation of antiplatelet therapy and factors that lead to a prothrombotic state, such as renal failure, diabetes, and (major) surgical procedures. Specifically, recent studies have demonstrated that surgical procedures trigger “wound” monocytes to accelerate the activation of factor VII and factor X, which eventually leads to high plasma levels of thrombin [5]. In addition, increased concentrations of circulating plasma tissue factors and sympathetic physical stress (leading to decreased fibrinolytic activity, vasospasm, and increased shear stress) during surgery also heighten the risk for atherothrombotic events.

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4. **A Historical perspective**

Studies in the late 1990s demonstrated that preoperative preparation of patients with coronary artery disease minimises cardiac-related events and death during surgery [6]. However, this was in the era of balloon angioplasty without stent implantation. Surprisingly, after the widespread introduction of coronary BMSs, several studies revealed that preoperative preparation with stent implantation resulted in higher perioperative mortality rates, especially if surgery is performed within 4–6 wk of stenting [7]. The current American College of Cardiology/American Heart Association (ACC/AHA) Guideline Update for perioperative cardiovascular evaluation for noncardiac surgery is based on later studies and recommends an interval of 4–6 wk before surgery to allow for at least 4 wk of dual antiplatelet therapy [8]. However, these guidelines are based on outdated evidence because we are currently in the era of the DES. As yet, evidence is accumulating that the endothelialisation of a DES is delayed because the encoated (cytostatic) drug inhibits the endothelialisation process. The type of drug influences coverage of the stent as well; a paclitaxel DES takes more time to receive full endothelialisation than a sirolimus DES.

The process described above underlines the importance of continuing antiplatelet therapy during and after the operation. However, if the risk for major bleeding complications exceeds the risk for thromboembolic events, discontinuation can be preferred [9]. For urologic procedures a wide variation exists in the management of antithrombotic

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**Fig. 2 -** A stent thrombosis has occurred in the left anterior descending artery. All four paclitaxel-eluting stents are occluded with thrombus.

**Fig. 3 -** Histologic section taken from a Taxus stent in the left anterior descending (LAD) artery, which is totally occluded by a platelet-rich thrombus. (This histologic section was generously provided by Dr. Renu Virmani.)
drugs. Prospective studies demonstrate conflicting results on the effect on bleeding complications differing from no significant blood loss to a postoperative blood loss twice as high in patients using ASA undergoing transurethral resection of the prostate [9]. General practice seems to discontinue ASA 10 d preoperatively. For patients on clopidogrel or dual antiplatelet therapy, undergoing urologic surgery, no data are available.

5. The dilemma of the presented case

The relatively early surgery after DES implantation together with the withdrawal of antiplatelet drugs has inevitably caused the stent thrombosis in our case. However, did we have any other option before we brought our patient to surgery?

1. We could have continued the dual antiplatelet regimen instead of the single antiplatelet regimen during surgery. However, numerous studies have shown that perioperative continuation of dual antiplatelet therapy enhances postoperative bleeding and transfusion rates [10]. Therefore, most experts recommend, although unproven, to continue ASA throughout surgery and our practice in the presented case was according this widespread habit.

2. We could have postponed the laparoscopic pelvic lymph node dissection until full re-endothelialisation of the implanted DES occurred. However, several case series have demonstrated that the endothelialisation process of a DES may take >1 yr. This was of course impossible in our patient who needed urgent surgery for staging of his malignancy. In addition, current guidelines recommend nonstop continuation of dual antiplatelet therapy for at least 12 mo after DES implantation [11]. However, even this delay was unacceptable in the presented case.

3. Perioperative administration of heparin instead of dual antiplatelet therapy would have been another alternative; however, no evidence supports this antithrombotic strategy. Moreover, cases were reported with stent thrombosis despite heparinisation in the perioperative phase of surgery.

4. Unfortunately, the prostate cancer was not diagnosed before the elective percutaneous coronary intervention. Otherwise, the cardiologist undeniably would have implanted a BMS. In some cases, this choice could have been foreseen; however, in our case it could not.

6. Conclusions

The current practice of withdrawing any form of antiplatelet therapy before surgery has been challenged by the introduction of DESs since evidence is accumulating that a DES requires dual antiplatelet therapy for at least a year [11]. However, convincing evidence regarding the optimal management of antiplatelet therapy throughout surgery in patients with a recently implanted coronary stent is still lacking. Although it is very likely that the risk of atherothrombotic events far outweighs the risk of prolonged and enhanced bleeding in patients undergoing urologic surgery, a revision of the current guidelines is urgently needed and clinicians must be aware of the dark side of DES usage. When it comes to stent implantation it is of course important to balance the benefits and risks for BMSs and DESs. For patients with comorbidities that could require surgery soon, a DES should be avoided and treatment should take place with a BMS. Elective surgery after recent stent implantation should be postponed so patients can complete the dual antiplatelet regimen (at least 1 yr for DES and 4 wk for BMS). Patients with an implanted BMS or DES who require instant surgery (before safe discontinuation of antiplatelet therapy can occur) should be evaluated individually in consultation with the cardiology department. Perioperative risk with respect to bleeding and thromboembolic complications will be estimated, based on type of operation, interval between stent implantation and operation, stent characteristics, and comorbidities. This leads to a recommendation with respect to antiplatelet therapy perioperatively.
EU-ACME question

Please visit www.eu-acme.org/europeanurology to answer the below EU-ACME question on-line (the EU-ACME credits will be attributed automatically). The answer will be published online next month.

Question:

A 74-yr-old man underwent successful implantation of a DES 2 wk ago because of an acute myocardial infarction. Since then, he has been treated according to the ACC/AHA guidelines with aspirin and clopidogrel for the period of at least 1 yr. Coincidently, he is scheduled to undergo a surgical biopsy for the staging of his prostate cancer. What is the best treatment option at this specific time point?

A. Postpone transurethral resection until 12 mo after stent implantation.
B. Perform the scheduled transurethral resection and continue both antiplatelet drugs.
C. Perform the scheduled transurethral resection and discontinue one of the antiplatelet drugs to avoid bleeding.
D. Perform the scheduled transurethral resection and discontinue both antiplatelet drugs to avoid bleeding.

References