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# Risk Reduction Strategies in Early Major Non-Cardiac Surgery after Drug-Eluting Stent Implantation

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## Abstract

Percutaneous coronary intervention with stent implantation has become the predominant revascularization strategy for patients with coronary artery disease. To reduce the risk of thrombotic complications, current guideline recommends dual antiplatelet therapy for 12 months after drug-eluting stent implantation. Dilemma arises when post-stent implantation patients have to undergo non-deferrable noncardiac surgery. In this case report, we presented a patient who have received drug-eluting stent implantation to left circumflex artery for myocardial infarction. Before staged percutaneous coronary intervention to a residual high-grade stenosis in the left anterior descending artery, he was diagnosed with renal cell carcinoma requiring nephrectomy. We describe the case of a patient requiring radical nephrectomy after multiple stent implantations and the strategies we adopted to reduce the risks of perioperative complications. The patient subsequently underwent nephrectomy successfully without perioperative myocardial infarction.

Keywords: Noncardiac surgery; Drug-Eluting stent; Myocardial infarction

## Introduction

Percutaneous coronary intervention (PCI) with stent implantation is the most widely accepted mode of coronary revascularization. Yet, stent thrombosis remains a major hazard limiting the success of PCI. Among others, premature discontinuation of antiplatelet therapy has been identified as an important factor leading to stent thrombosis [1]. Dilemma arises when patients have to undergo noncardiac surgery after stent implantation. From the cardiologist's perspective, antiplatelet therapy is crucial in preventing stent thrombosis and should not be stopped without good reasons; but from the surgeon's perspective, antiplatelet therapy would increase the risk of bleeding complications. We describe the case of a patient requiring radical nephrectomy after multiple stent implantations and the strategies we adopted to reduce the risks of perioperative complications.



Figure 1: (A) Baseline angiography showing occluded mid left circumflex artery (culprit for myocardial infarction) and significant proximal left anterior descending artery lesion. (B) A zotarolimus-eluting stent was implanted to the left circumflex artery. (C) Two endothelial progenitor cell capture stents were implanted to the left anterior descending artery following suboptimal angiographic results after balloon angioplasty.



**Figure 2:** Computed Tomography scan of abdomen. A heterogenously enhancing mass with central hypodensity, suggestive of renal cell carcinoma, is noted in the upper pole of the right kidney with an intact capsule.

# **Case Description**

A 54-year-old Chinese male, with cardiovascular risk factors of smoking, hypertension and diabetes mellitus, presented with non-ST-segment elevation myocardial infarction. PCI to the occluded left circumflex artery with implantation of a zotarolimus-eluting stents (2.25 x 24 mm) was performed successfully (Figure 1). Final

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angiography showed antegrade TIMI 3 flow with < 5% residual stenosis. There was a residual high-grade stenosis at the proximal to mid left anterior descending artery (LAD). The patient was prescribed life-long aspirin (100 mg daily) and clopidogrel (75 mg daily) for 1 year. As part of the work-up for renal impairment (serum creatinine 152  $\mu$ mol/L, creatinine clearance 39mL/min), an abdominal ultrasound examination followed by a CT scan performed two days after PCI showed a renal cell carcinoma in the right kidney (Figure 2). After urological consultation, the consensus was to perform PCI to the residual LAD stenosis the week after, followed by radical nephrectomy another six weeks later. Risk of bleeding for radical neprectomy was quoted to be low to moderate.

In consideration of the upcoming surgical procedure, the initial plan was to revascularize the LAD solely by balloon angioplasty. However, due to suboptimal angiographic results, two endothelial progenitor cell capture stents (Genous<sup>TM</sup>, OrbusNeich, Fort Lauderdale, FL) were implanted in the proximal to mid LAD. Intravascular ultrasound interrogation confirmed optimal stent expansion and apposition.

For the radical nephrectomy, the peri-operative antiplatelet and antithrombin regimens were as follows: aspirin was continued throughout the perioperative period, clopidogrel was stopped 7 days before surgery. Three days prior to surgery, we commenced continuous intravenous infusions of eptifibatide (to prevent platelet activation and adhesion) and unfractionated heparin (to prevent thrombin generation) until 8 hours before the surgery (per pharmacodynamic data from the eptifibatide product information sheet, stopping 4 to 6 hours pre-operatively would suffice if renal function was normal). The right nephrectomy was performed successfully without ischemic complications or excessive bleeding. Clopidogrel 600 mg loading, followed by 75 mg daily, was started the day after surgery. The patient recovered uneventfully and was discharged five days after surgery. Serial haemoglobin and platelet measurements remained stable throughout the peri-operative period.

## Discussion

Stent placement into the coronary artery denudes the endothelium of the arterial wall. The process of re-endothelialization (passivation) of the stent strut takes place soon after stent implantation, but the time required to complete the process differs greatly between bare metal stents and drug-eluting stents. With bare metal stents, approximately four weeks are needed for re-endothelialization. With drug-eluting stents, healing of the endothelium over stent struts has been shown to be impaired secondary to the drug and/or polymer coating resulting in significantly delayed re-endothelialization. In keeping with this, the risk of late (>1 year) stent thrombosis following drug-eluting stent implantation is higher than that after bare metal stent implantation; and this stays true for up to four years after drug-eluting stent implantation [2]. Recent guidelines recommend uninterrupted dual antiplatelet therapy with aspirin and thienopyridine for four weeks after bare metal stent implantation, and twelve months after drug-eluting stent implantation [3]. In our patient, the diagnosis of renal cell carcinoma was made after implantation of the zotarolimus-eluting stent. This makes interruption of antiplatelet therapy before nephrectomy particularly risky.

The endothelial progenitor cell capture stent is a stent coated with murine monoclonal antihuman CD34 antibodies designed to attract circulating endothelial progenitor cells to rapidly establish a functional endothelial layer and promote healing. Therefore, there is a valid theoretical reason to postulate that endothelial progenitor cell capture stent could be a favorite choice in patients undergoing noncardiac surgery following PCI. The endothelial progenitor cell capture stent has been shown to be safe in real world clinical situations, including patients with ST-segment elevation myocardial infarction who were given only 1-month dual antiplatelet therapy [4]. Although an angiographic study showed that the restenosis rate is greater than that of drug-eluting stents, the theoretical lowered risk of stent thrombosis may be appealing to patients undergoing noncardiac surgery. With multiple adjunctive measures such as intravascular ultrasound-guided implantation, bridging glycoprotein IIb/IIIa inhibitor/unfractionated heparin infusion and adequate time (six weeks) for re-endothelialization of the Genous stents, the surgery was performed successfully without ischaemic nor bleeding complications. A recent study reported a series of 22 patients in whom endothelial progenitor cell capture stent was used before life-saving and undeferable major noncardiac surgery. Despite a mean duration of antiplatelet therapy of only 12.5 days, no perioperative cardiac complications were reported [5].

Noncardiac surgery should ideally be deferred until completion of dual antiplatelet therapy after coronary stent implantation. However, this is not feasible in our patient, despite the history of recent zotarolimus-eluting stent implantation, as the malignant nature of the underlying disease precludes the 12-month waiting period. In a recently released European guideline, it was suggested that if surgery cannot be delayed, bypass surgery, bare metal stents or balloon angioplasty should be considered. In patients with semi-urgent surgery, the decision to prematurely stop one or both antiplatelet agents (at least 5 days preoperatively) has to be taken after multidisciplinary consultation, evaluating the individual thrombotic and bleeding risk [6]. A pilot study explored the potential role of perioperative administration of short-acting glycoprotein IIb/IIIa inhibitor in patients who have undergone drug-eluting stent implantation and have to undergo an urgent noncardiac surgery [7]. Clopidogrel was withdrawn five days before surgery. A bridging glycoprotein IIb/IIIa inhibitor (tirofiban) was started and continued until four hours before surgery. There were no cases of major adverse cardiac events or surgical re-exploration due to bleeding complication. Although limited by the small sample size, it suggests that in patients with recently implanted drug eluting stents needing urgent noncardiac surgery, a 'bridging strategy' using intravenous glycoprotein IIb/IIIa inhibitor is a safe and feasible option. In view of the shorter duration of antiplatelet effect, eptifibatide and tirofiban (rather than abciximab) may be the preferrable bridging glycoprotein IIb/IIIa inhibitor before noncardiac surgery.

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