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## **Management of Antiplatelet Therapy in Patients With Coronary Stents for Noncardiac Surgery**

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### **Stem Case and Key Questions Content**

A 36 year old Caucasian man presents for preoperative assessment one day before a redo anterior cervical discectomy and fusion of C6-7. He states that he had the same surgery six months ago and it went well, but his symptoms have not abated. His history is significant for high cholesterol, type 2 diabetes controlled with oral medications, and controlled hypertension. He previously had an episode of unstable angina 5 years ago for which he underwent percutaneous coronary intervention with implantation of a sirolimus drug-eluting stent. The findings at that time were of >95% LAD stenosis. He was placed on aspirin and clopidogrel and has been on them ever since.

#### **1. What other information is important in determining this patient's risk for surgery?**

He is unable to give any family history of cardiac disease or premature cardiac death because he is adopted. He tolerates some physical activity; he is able to do work around the house and climb stairs without any chest pain or shortness of breath. His medications include ramipril, metoprolol, glucophage, atorvastatin, aspirin, and clopidogrel. He has no known allergies. He does not smoke, use recreational drugs, or drink alcohol.

He does reveal, upon further questioning, that he had a "heart attack" 5 days after his previous cervical fusion about 6 months ago. He states that his antiplatelet therapy was stopped about 7-10 days prior to the surgery, and he was instructed to restart them one week postoperatively. Coronary angiogram at that time showed that his LAD stent was patent but he had multiple other vessels that were diseased. No invasive intervention was taken and he was managed with medications.

#### **2. What should you look for on physical exam? What laboratory tests should be ordered? Should there be any additional cardiac work-up?**

Physical examination shows that he is a Mallampati class one, has no dental problems, has good mouth opening, but he does have discomfort and paresthesia on neck extension. His lungs are clear and he has no murmurs on cardiac exam. He has a normal vascular exam and no evidence of extremity swelling or jugular venous distention. His preoperative laboratory data was significant for an elevated serum glucose at 196 mg/dL. His hemoglobin concentration was 13.7 mg/dL. Otherwise, his lab values were unremarkable. ECG taken in the clinic demonstrated normal sinus rhythm and no evidence of ST changes or Q waves.

#### **3. What is this patient's level of risk for cardiac events during in the perioperative period? What factors contribute to this risk? Should we proceed with the operation?**

***Should his antiplatelet regimen be stopped? Should he have any further cardiac workup? Would your answer be different if he had a CABG instead of stents?***

Upon discussing the risks and benefits of his antiplatelet therapy, he tells you that he has been off of his clopidogrel and aspirin for 2 weeks as instructed by his surgeon's office because "I don't want anything to postpone this surgery. I drove five hours to get here and I have a hotel room in town." You call the surgeon and advise him that the patient should continue his aspirin through the surgery because he is very high risk of stent rethrombosis. He demands that the patient remain off antiplatelet therapy because of the risk of surgical site bleeding.

***4. What is your response? How would deal with the surgeon who demands that all antiplatelet therapy be discontinued 5-7 days before the operation?***

***5. Should you evaluate the platelet function in this patient? What tests are available to evaluate platelet function?***

***6. What special considerations should be made in providing the intraoperative anesthetic care for this patient? Does he need any special monitoring or care? Is there anything you can do to decrease the risk of an intraoperative cardiac event?***

You discuss the risks and benefits of proceeding with the patient and he wishes to undergo the operation. During the operation, he has no evidence of ECG changes, cardiac dysfunction, or instability. He does well perioperatively and is discharged home two days later after an uneventful hospital stay. His aspirin was restarted the day after surgery and the patient was told by his surgeon to restart clopidogrel at the time of discharge.

***7. What special considerations does this patient have in the postoperative period? How soon should he follow up with his doctor?***

***8. When should his antiplatelet therapy be restarted and what is the appropriate way to restart it? What are the risks associated with restarting or not restarting his medications?***

Three days after discharge, the patient calls the anesthesia clinic and says that he is having chest discomfort (mid chest, burning pain, no radiation, lasted few seconds, relieved with rest) and shortness of breath.

***9. What is the most likely cause of these symptoms? Could this have been prevented?***

You advise him to go to the emergency room where an ECG reveals ST elevations and ECHO reveals antero-lateral wall loss of contractility. When interrogated, the patient confirmed his clopidogrel was not restarted yet, since "last time I did not restart for a week, and even though the anesthesiologist told me to do it as soon as possible, I was worried my neck wound could bleed". The patient was promptly brought to the cardiac cath lab for deteriorating hemodynamic conditions and a complete occlusion of LAD is found. He was brought back to the CCU after coronary artery reperfusion on an intra-aortic balloon pump.

***10. What should be the continued follow up for this patient? What would you have done differently? What should we be worried to tell the surgeon and the patient?***

## **Model Discussion Content**

### **1. Preoperative evaluation of patients with cardiac risk factors.**

A careful history and physical exam should be undertaken in all patients at risk for cardiac complications. Questions regarding a history of unstable or stable angina, prior MI, operative or percutaneous coronary interventions, and the use of a pacemaker or ICD. Additionally, current symptoms should be assessed including activity tolerance and current medication regimen. Physical exam should account for vital signs, cardiac murmurs, vascular status, and signs of heart failure. Along with the history and physical, hemoglobin concentration and baseline ECG should provide enough information to determine if further testing is warranted. At this point, a decision can be made regarding the patient's risk level relative to the risk level of the operation to be undertaken. In particular, many patients that have had coronary stenting and have known coronary artery disease should have ventricular function, ischemic threshold, and optimization of medical therapy determined prior to undergoing general anesthesia. Clinical judgment and discussion with the patient's cardiologist are important in determining which patients need preoperative echocardiography or stress testing. [1-2; selected reference 1-2]

### **2. Types of stents and recommendations for antiplatelet therapy with the use of each.**

Percutaneous coronary intervention (PCI) may take the form of three different entities: balloon angioplasty, bare metal stent, or drug-eluting stent. Regardless of the type of PCI, antiplatelet therapy with aspirin and/or a thienopyridine (clopidogrel) is recommended after the intervention. [3] Balloon angioplasty was the first type of PCI to be developed and has risks of tissue injury and possible restenosis. Daily use of aspirin is recommended in patients who have undergone balloon angioplasty, and elective operations should be postponed for at least a period of two weeks. Nonelective operations should be undertaken with the continued use of aspirin in the perioperative period with a careful judgment of the risk of thrombosis against the risk of perioperative bleeding. Patients who have bare metal stents have improved outcomes compared to patients with balloon angioplasty, particularly in regard to restenosis and target revascularization. [4] There was, however, a significant risk of stent thrombosis, as high as 16-24% in early studies and approximately 3.5% in later studies using anticoagulation. [5-7] Typically, a dual regimen of clopidogrel and aspirin is prescribed, and the clopidogrel is removed from the regimen after 4-6 weeks when the stent has endothelialized. Aspirin should be continued indefinitely. Drug-eluting stents were developed to help prevent hyperplasia of the endothelium around the stent with subsequent in-stent restenosis. The most common agents used are sirolimus and paclitaxel. They have the advantage of decreasing restenosis further than bare metal stents, but the risk of thrombosis is even higher. Late stent thrombosis (up to 1.5 years after implantation) is a significant concern with the use of drug-eluting stents, and antiplatelet therapy with clopidogrel and aspirin is typically continued for at least 12 months with subsequent lifetime use of aspirin. With both types of stents, dual antiplatelet therapy is continued for life in patients perceived to be at high risk for stent thrombosis, which includes advanced age, diabetes, low ejection fraction, long stents, acute coronary syndrome in the past, LAD stenting, and multiple coronary lesions. [8]

In a patient who is known to require noncardiac surgery within 12 months of a coronary intervention, an assessment of the urgency of the operation weighed with the patient's risk must be undertaken. If the surgery must proceed within 1-2 months, a balloon angioplasty or bare metal stent is preferable to a DES due to the shorter duration of antiplatelet therapy. Another option may be preoperative coronary artery bypass grafting (CABG) to establish a definitive revascularization in which antiplatelet therapy may be stopped at any time. CABG has been

shown to be of little benefit in preventing perioperative ACS when used for preoperative revascularization in lower risk patients having vascular operations. However, in a patient needing urgent or emergent noncardiac surgery and who is determined to absolutely require revascularization, it may be the appropriate choice due to the lesser need for antiplatelet therapy. There is a great deal of debate surrounding the appropriate use of antiplatelet therapy in post-CABG patients; aspirin is generally continued for one year and the use of clopidogrel has shown mixed results.

### **3. Current recommendations for preoperative suspension of antiplatelet agents.**

The risk of holding antiplatelet therapy in the perioperative period is that these patients may develop stent thrombosis and subsequent cardiac events. In appropriately treated patients, the risk of stent thrombosis with bare metal stents is around 1.5% at one month. The risk of thrombosis is even higher in patients with drug-eluting stents (0.5-3.1%). The reason for this is due to the nature of the stents. Early thrombosis (less than one month) is usually due to mechanical stimulation of clot formation from the stent itself. Late thrombosis in bare metal stents is potentially related to the significance of restenosis after implantation. Drug-eluting stents, however, as a product of their inhibition of endothelial growth, often lead to the exposure of prothrombotic surface molecules on the endothelium, and sirolimus and paclitaxel themselves promote platelet aggregation. Stent thrombosis in drug-eluting stents is most often identified by a major cardiac event. One of the most common causes of thrombosis, aside from patient factors, is the early discontinuation of antiplatelet therapy in the post-PCI period.[4,5,7]

Currently, the recommendations are to postpone any elective noncardiac surgery within the post-PCI period where dual antiplatelet therapy is required (4-6 weeks for bare metal stents and 1 year for drug-eluting stents). Any nonelective surgery may be undertaken with the understanding that risk for stent thrombosis is very high and at least aspirin (preferably clopidogrel also) should be continued in the perioperative period. After the initial post-PCI period, there are no specific guidelines on the best course of action. Clinical judgement and coordination with the surgeon are very important in the discontinuation of antiplatelet therapy preoperatively. High consideration should be given to continuing aspirin in all patients, and the risk of thrombosis should be weighed with the risk of bleeding based on patient factors and surgical factors. Some institutions admit patients several days prior to the operation to discontinue therapy and substitute it with a shorter acting anticoagulation therapy, such as heparin/low molecular weight heparin or a GPIIb/IIIa inhibitor; the use of GPIIb/IIIa inhibitors in particular may be a prudent course of action in the highest risk patients. The use of heparin/LWMH is likely not of great benefit because they do not inhibit the platelet aggregation that is the critical and inciting event in stent thrombosis. Overall, brief pauses in antiplatelet therapy may not be detrimental to the patient, but the length of time that a patient is not on antiplatelet therapy may be related to the likelihood of developing stent thrombosis. [selected reference 1-2]

### **4. Current recommendations for postoperative reinstatement of antiplatelet therapy.**

The broadest recommendation regarding the reinstatement of antiplatelet therapy is to restart as soon as possible after the surgery. Aspirin is often restarted on the same day of surgery, although in higher risk patients it should not be stopped at all. Clopidogrel, if discontinued, should be restarted as soon as possible. Careful assessment of the patient's postoperative bleeding risk along with their thrombosis risk is critical. Continuation of antiplatelet therapy has been shown to increase bleeding tendency in surgical patients, but the morbidity and mortality of that bleeding has not been well established. There is conflicting evidence of the need for

increased blood transfusions and possible reoperation, but the benefit of protection from stroke and MI is clear. [7-8]

## ***5. Discussion of postoperative complications in relation to coronary artery stent placement and antiplatelet therapy.***

The most feared complications in relation to antiplatelet therapy and coronary stents are of postoperative major cardiac events and death. The incidence of perioperative MI in patients with known coronary artery disease is about 4%. When a MI results from stent thrombosis, as is most likely in patients with previous PCI, the mortality is close to 50%. Stent thrombosis tends to be occlusive and catastrophic, so its prevention and recognition is of utmost importance. Surgery is known to cause a stress state in the body, which results in a prothrombotic and proinflammatory environment in which stent thrombosis, MI, and stroke can occur. The treatment of major cardiac events postoperatively is the same; it is the prevention and recognition of them that is the most important aspect of the perioperative care of patients with known cardiac disease. [6]

## ***6. Measuring the effectiveness of antiplatelet therapy pre and postoperatively.***

There are monitoring tests that can be undertaken to assess the effectiveness of antiplatelet activity and guide treatment, but current recommendations are against using platelet function tests to predict thrombosis risk because they are expensive and fail to provide a complete picture of each patient's true risk. Additionally, the appropriate tests are not universally available. Platelet aggregation studies, assessment of platelet receptor function, and assays of platelet released factors (such as thromboxane) may shed some light into the effectiveness of antiplatelet therapy with both aspirin and clopidogrel. Additionally, point of care tests, such as the thromboelastogram, may be useful in assessing platelet function intraoperatively or postoperatively. Platelet count, prothrombin time, partial thromboplastin time, factor assays, and bleeding time are not useful tests in the monitoring of antiplatelet therapy. No one test will address all aspects of antiplatelet agent effectiveness, and the use of these tests may have more of a role in evaluating a patient that has thrombosis in spite of dual therapy, indicating resistance. [9-11]

## ***Summary***

The risk of holding antiplatelet therapy in the perioperative period in patients with stent and coronary artery bypass, is thrombosis and subsequent cardiac events. In appropriately treated patients, the risk of stent thrombosis with bare metal stents is around 1.5% at one month (probably similar to by pass grafts). The risk of thrombosis is even higher in patients with drug-eluting stents (0.5-3.1%). The incidence of perioperative MI in patients with known coronary artery disease is about 4%. When a MI results from stent thrombosis, as is most likely in patients with previous PCI, the mortality is close to 50%. Continuation of antiplatelet therapy keeps the incidence of MACE similar to CAD general risk also for patients with stents. What evidences do we have to justify continuation, suspension or alteration of therapy, based on functional assays? Current guidelines still lack insights of most recent evidences which correlate platelet function testing with effective therapy titration that would reduce risk of thrombosis while avoiding excessing bleeding. This PBLD will help guiding the practicing anesthesiologist to critically appraise literature and evidences, as well develop a strategic plan of care in accordance to practice management guidelines and evidence-based knowledge.

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## References

1. Merritt JC, Bhatt DL. "The Efficacy and Safety of Perioperative Antiplatelet Therapy." *J Thromb Thrombolysis* 2004; 17(1): 21-27.
2. Metzler H, Huber K, Kozek-Langenecker S. "Anaesthesia in patients with drug-eluting stents." *Curr Opin Anaesthesiol* 2008; 21: 55-59.
3. Newsome LT, Kutcher MA, Royster RL. "Coronary Artery Stents: Part 1. Evolution of Percutaneous Coronary Intervention." *Anesth Analg* 2008; 107(2): 552-569.
4. Newsome LT, Weller RS, Gerancher JC, Kutcher MA, Royster RL. "Coronary Artery Stents: Part 2. Perioperative Considerations and Management." *Anesth Analg* 2008; 107(2): 570-590.
5. Gurbel PA, Becker RC, et al. "Platelet Function Monitoring in Patients with Coronary Artery Disease." *J Am Coll Cardiol* 2007; 50(19): 1822-1834.
6. Iakovou I, Schmidt T, et al. "Incidence, Predictors, and Outcome of Thrombosis After Successful Implantation of Drug-Eluting Stents." *JAMA* 2005; 293(17): 2126-2130.
7. Schouten O, van Domburg RT, et al. "Noncardiac Surgery After Coronary Stenting: Early Surgery and Interruption of Antiplatelet Therapy are Associated with an Increase in Major Cardiac Events." *J Am Coll Cardiol* 2007; 49(1): 122-124. Correspondence.
8. King SB, Smith SC, Hirshfeld JW, et al. "2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines." *J Am Coll Cardiol* 2008; 51: 172-209.
9. Cattano D, Altamirano AV, Kaynak HE, Seitan C, Paniccchia R, Chen Z, Huang H, Prisco D, Hagberg CA, Pivalizza EG.
10. Collyer TC, Gray DJ, Sandhu R, Berridge J, Lyons G. Assessment of platelet inhibition secondary to clopidogrel and aspirin therapy in preoperative acute surgical patients measured by Thrombelastography Platelet Mapping. *Br J Anaesth*. 2009 Apr;102(4):492-8.
11. Korte W, Cattaneo M, Chassot PG, Eichinger S, von Heymann C, Hofmann N, Rickli H, Spannagl M, Ziegler B, Verheugt F, Huber K. Peri-operative management of antiplatelet therapy in patients with coronary artery disease: joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the working group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (ÖGARI) and the Working Group Thrombosis of the European Society for Cardiology (ESC). *Thromb Haemost*. 2011 May;105(5):743-9.