

THE CURRENT RECOMMENDATIONS AND FUTURE PROSPECTS CONCERNING THE MANAGEMENT OF PATIENTS WITH CORONARY ARTERY STENTS, UNDERGOING NON-CARDIAC SURGERY

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Patients with coronary artery stents in situ present difficult management decisions when they undergo non-cardiac surgery (NCS) and anaesthesia. Many of these difficulties involve the fundamental problem of stopping anti-platelet medications (to prevent major surgical blood loss), which then exposes the patient to the risk of potentially lethal stent thrombosis and MI.

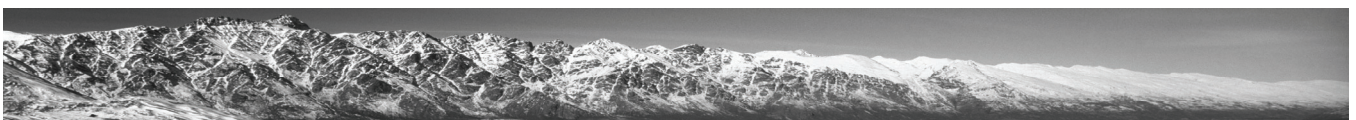
Surgical treatment of coronary artery disease (CAD) started with Murray and Longmire in the 1950's operating on coronary arteries on beating hearts. They were matched by an intrepid Russian, Demikhov. The use of cardiopulmonary bypass (CPB) to assist this surgery arrived in 1968. Coronary artery stents were first used in France in 1986 and in the USA in 1994 and NZ 1994-5. Drug therapy developed considerably alongside this progress and as of today, two statins and clopidogrel are in the top 5 most profitable of all drugs sold worldwide.

Coronary artery stents have an established place in management of acute coronary syndromes (ACS), and are often used for management of coronary artery stenoses whether symptomatic or not. The evidence for this wider stent use as opposed to drugs alone or CABG is constantly changing and is subject to huge commercial pressure and debate. What is not in doubt is that patients will present for NCS with coronary stents in situ and we have to deal with the issues involved. [The rest of this abstract assumes that we all will take note of this kind of patient having all or some of the features of CAD which need perioperative attention-apart from the stent].

Stents have a metal lattice and with respect to bare metal stents (BMS) there is a need for a new endothelium to grow over the exposed metal. This has a major effect of protecting against stent thrombosis and MI. This endothelium can overgrow however and lead to progressive restenosis, especially in diabetics, and in longer narrower vessels, so drug eluting stents (DES) were developed. The drugs which elute are strong inhibitors of endothelial growth and they successfully impair endothelial overgrowth, although most cardiologists believe and hope that over time a protective endothelial layer does develop-albeit more slowly than with BMS. To cover the period when the exposed stent lattice is not covered with endothelium, whether for BMS or for DES, antiplatelet agents are universally used in order to prevent stent thrombosis. The duration of the use of these drugs varies and is increasing. Right now common drug use is one month or more for BMS and a year or more (perhaps for ever) for DES. This therapy is usually aspirin and a thienopyridine such as clopidogrel.

Patients with stents in situ present for NCS at a rate about 5% per year (not counting outpatient operations). 39% of all insured patients over the age of 60 in NZ have a private operation of some sort each year.

When facing NCS a patient with either a BMS or a DES could potentially have their anti-platelet drugs stopped in order to promote safe haemostasis during the operation, but at the risk of causing stent thrombosis with lethal MI. Regrettably this dilemma has not been theoretical. Kaluza in 2000 reported a prohibitive mortality of 32% for NCS, done in patients who had a BMS inserted less than two weeks prior, and often (but not always) in association with cessation of some or all of the antiplatelet drugs. Vicenzi in 2006 reported a group of 103 patients with stents (BMS, DES and unspecified) who had NCS within 12 months of stent insertion. In spite of ICU care, use of heparin, aspirin, and clopidogrel in many patients, the rate of major adverse cardiac events (MACE) was 40% and included a 5% death rate. More recently DES have received specific focus due to continued reports of very late stent thrombosis (more than a year after insertion) with perioperative discontinuation of aspirin suggesting that a protective stent endothelium never developed. These late stent thromboses have a very high MI rate (70-100%) and mortality rate (45% or more). Recently helpful data has been published by the Mayo Clinic and by Poldermans' unit. Taken together they suggest that for stented patients having NCS, low MI and mortality rates are possible if:



- Antiplatelet therapy is continued throughout the perioperative period for elective surgery (and conversely that cessation of these medications conferred considerable risk of MI and death).
- A longer time between stent insertion and NCS was possible.
- It is recognised that particular risk was attached to emergency procedures.

They also reported no important differences in bleeding complications between those who stopped antiplatelet medications and those who continued them.

This and other evidence lead to recommendations published in Anesthesiology in 2009. They suggest:

1. For BMS defer elective surgery until a complete course of antiplatelet medication has been completed, i.e. not till 4-6 weeks after stent insertion.
2. For DES defer elective surgery until the antiplatelet medication has been completed, i.e. for a year after stent insertion.
3. Bridging therapy of many kinds has been incompletely studied and is not yet confirmed as helpful.
4. Consider the use of antiplatelet therapy beyond the times above in patients at risk of stent thrombosis.
5. If surgery cannot be deferred then please consider keeping antiplatelet therapy going, and if you have to stop the thienopyridine, keep the aspirin going if possible and re-start the thienopyridine soon after the surgery. Others have suggested appropriately that only for unavoidable neurosurgery or eye surgery should all antiplatelet agents be stopped.
6. If the planned elective surgery involves much bleeding wait until a full course of antiplatelet medication has been completed. (They leave out the potential options of stopping or continuing with the antiplatelet medications once the full course is finished).

These recommendations leave out certain important topics such as where to do the NCS, how to approach patient consent, how to monitor such patients perioperatively, what to do if you suspect a stent thrombosis, and interactions with surgeons.

Patients must know the risks being confronted and many do not know. Cardiologists have to be asked for drug and stent specifics. Planned restenting is the aim if perioperative stent thrombosis occurs and some thought has to be given to how such a procedure would be performed. Surgeons have to be re-educated about this whole issue, and have to be told to consider operating with antiplatelet agents being used.

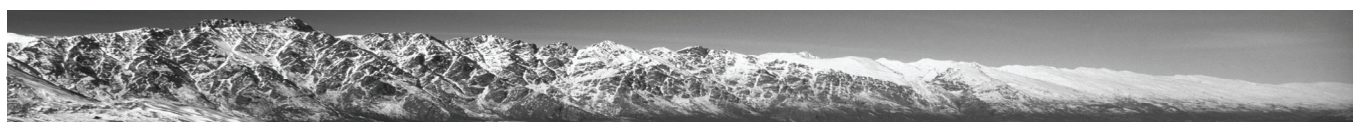
Future developments in CAD and stent management are inevitable and will improve this story. Correct stent deployment is an increasingly recognized critical factor in getting good stent results and higher pressures (up to 22 atmospheres) create better apposition, less room for thrombosis to develop, and better lumen size. DES are not all the same and some feel that the sirolimus stents develop an endothelium quicker and better than the paclitaxel stents (I am sure this debated). Stent polymers are under huge examination as some evidence suggests that stent thrombosis has some similarities to a hypersensitivity reaction. Novel agents are being looked at for drug elution. They include genes which can create endothelium in 10 days, aspirin, everolimus et al. Techniques to visualize the endothelium presence are being investigated. Biodegradable stents have made some progress but have both positive and negative features. Better bridging anticoagulant drugs are being developed including the attractive new area of aptamers. The genetics of clopidogrel and aspirin action are better understood and will in future allow better more accurate use of these drugs and better studies about stents. Platelet function monitors are in use and will create the potential to titrate antiplatelet drugs better. Lastly there is continual progress towards understanding and treating CAD outside the confines of stenting (think what statins have done) and this will continue.

Lastly, do you know your own LDL, HDL and what drugs are you taking to optimize this if you need to? Please be able to answer the question. Treating CAD is not as good as preventing it!!!

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NB **= very good

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