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# Cardiac Risk in Non-Cardiac Surgery: Management of Patients with Coronary Stents

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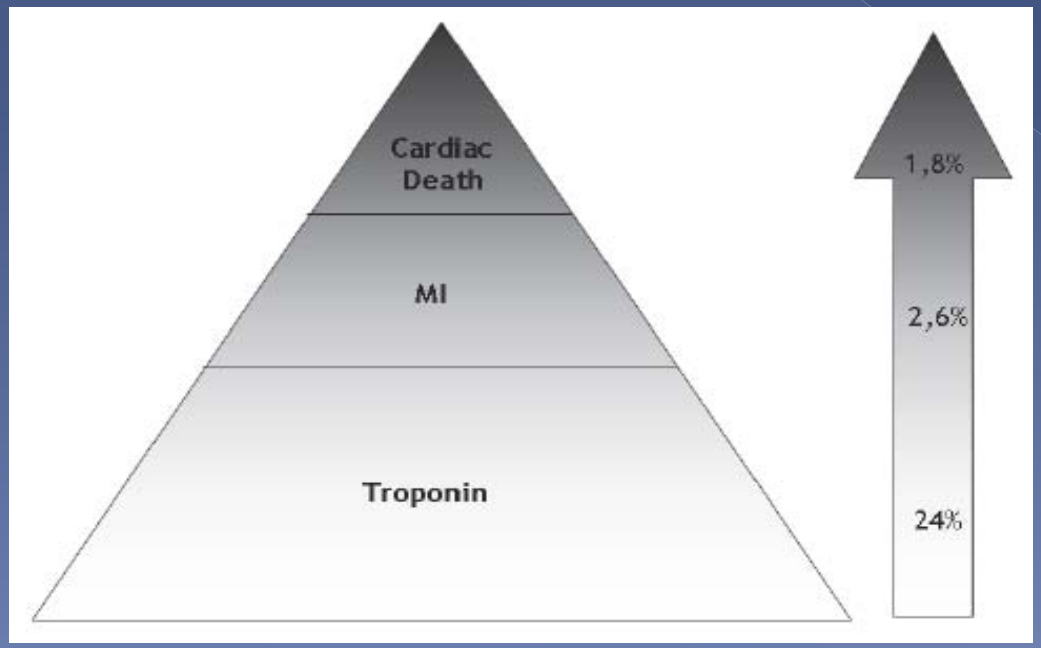
# Outline

- Introduction to the problem
- Patient-specific factors
- Surgery-specific factors
- Disease-specific factors

  Patients with coronary stents
  - Defining the issue
  - Types of stents
  - Preoperative revascularization and patients with pre-existing stents
  - Risk of stent thrombosis vs. Risk of bleeding
  - Management of anticoagulation
- Cardiac risk assessment
- Preoperative testing
- Recommendations

# Introduction to the Problem

- Cardiovascular complications are the leading cause of post-operative mortality in non-cardiac surgeries.
- Increasing number of non-cardiac surgeries in an aging population.




*Poldermans D, et al, J Am Coll Cardiology 2006*

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- At risk population because:

**Patients undergoing major vascular surgery (i.e. with cerebrovascular disease/PAD)**

- Higher incidence of CAD
- 5 times more likely to have LV systolic dysfunction

**Perioperative physiological stress**

- Volume shifts
- Blood loss
- Increased myocardial oxygen demand
- Proinflammatory/Prothrombogenic state
- Acute phase reaction - release of endogenous catecholamines, increased platelet adhesiveness, decreased fibrinolysis

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# Approach to Patient-Specific Factors

- Detailed history
- Functional capacity assessment

1 MET (Metabolic Equivalent of Task)= 3.5 ml $O_2$ uptake/kg/min = resting $O_2$ uptake in sitting position

| Activity | METs |
|---|---|
| Can take care of self, such as eat, dress or use the toilet | 1 |
| Can walk up a flight of steps or a hill | 4 |
| Can do heavy work around the house such as scrubbing floors or lifting or moving heavy furniture | 4-10 |
| Can participate in strenuous sports such as swimming, singles tennis, football, basketball, and skiing | > 10 |

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- Physical examination
  - BP measurement in both arms
  - Carotid artery and jugular venous pulsation exam
  - Precordial palpation and auscultation
  - Specific murmurs
  - Abdominal palpation
  - Extremities for edema and vascular integrity

# Surgery-Specific Factors

**ACC/AHA guideline summary: Cardiac risk stratification for noncardiac surgical procedures**

| |
|---|
| **High risk (reported risk of cardiac death or nonfatal myocardial infarction [MI] often)** |
| • Aortic and other major vascular surgery |
| • Peripheral artery surgery |
| **Intermediate risk (reported risk of cardiac death or nonfatal MI generally 1 to 5 percent)** |
| • Carotid endarterectomy |
| • Head and neck surgery |
| • Intraperitoneal and intrathoracic surgery |
| • Orthopedic surgery |
| • Prostate surgery |
| **Low risk* (reported risk of cardiac death or nonfatal MI generally less than 1 percent)** |
| • Ambulatory surgery |
| • Endoscopic procedures |
| • Superficial procedure |
| • Cataract surgery |
| • Breast surgery |

# Disease-Specific Factors

**ACC/AHA guideline summary: Clinical predictors of increased perioperative cardiovascular risk (myocardial infarction, heart failure, death)**

| **Major predictors that require intensive management and may lead to delay in or cancellation of the operative procedure unless emergent** |
|---|
| • Unstable coronary syndromes including unstable or severe angina or recent MI |
| • Decompensated heart failure including NYHA functional class IV or worsening or new-onset HF |
| • Significant arrhythmias including high grade AV block, symptomatic ventricular arrhythmias, supraventricular arrhythmias with ventricular rate >100 bpm at rest, symptomatic bradycardia, and newly recognized ventricular tachycardia |
| • Severe heart valve disease including severe aortic stenosis or symptomatic mitral stenosis |
| **Other clinical predictors that warrant careful assessment of current status** |
| • History of ischemic heart disease |
| • History of cerebrovascular disease |
| • History of compensated heart failure or prior heart failure |
| • Diabetes mellitus |
| • Renal insufficiency |

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# Coronary Artery Stents Defining the Issue

- 2 million patients per year undergo coronary artery dilatation in Western countries.
- 90% involve stent placement.
- 5% of patients s/p PCI will undergo non-cardiac surgery within the first year of stenting.

*Steinbuhl SR, et al, A randomized trial (CREDO). JAMA 2002*

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# Coronary Revascularization by PCI

- Balloon angioplasty – PTCA
- Bare Metal Stents (BMS)
  - Expandable tubular wire mesh
  - Stainless steel, cobalt-chromium alloy, nickel-chromium alloy
- Drug Eluting Stents (DES)
  - Metal stents which elute a drug (sirolimus, paclitaxel, everolimus)
  - Limits growth of neointimal scar tissue to decrease restenosis

# Duration of Antiplatelet Therapy

- Dilatation without stenting: 2-4 weeks
  Surgery postponed for 2-4 weeks
- PCI and BMS: 4-6 weeks
  Vital surgery postponed for ≥ 6 weeks
  Elective surgery postponed for ≥ 3 months
- PCI and DES: 12 months
  Elective surgery postponed for ≥ 12 months
- Aspirin: lifelong therapy, irrespective of revascularization technique

*Grines CL, et al, Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents, J Am Coll Cardiol 2007*

# PCI/Stents

2 scenarios

1. Patient requiring non-cardiac surgery, that on preop work up, has a coronary angiogram and has a lesion needing a stent
2. Patient with previous coronary artery stent that needs non-cardiac surgery

# 1 – Preoperative Revascularization

- **CARP: Coronary Artery Revascularization Prophylaxis Trial** *(McFalls E, et al, N Eng J Med 2004)*
  - Hypothesis: Among stable patients with CAD, amenable to CABG or PCI, revascularization prior to elective surgery improves long-term survival.
  - Multicenter RCT from 18 VA Medical Centers including patients scheduled for aortic or infrainguinal vascular operation
  - Primary Endpoint: Long-term survival
  - Secondary Endpoints: MI, Stroke, Renal dialysis, Limb loss
  - n=510, revascularization=258, no revascularization=252
  - Revascularization group – 55% PCI, 38% CABG

- Results: 30-day follow-up, no difference in mortality rate
- At median time of 2.7 years, no difference in mortality rate
- Conclusions
  - In patients with stable cardiac symptoms, coronary artery revascularization prior to a major elective vascular operation, can be done **safely**, but **does not improve short or long-term survival**.

    May delay or prevent the operation.
  - No improvement in long-term survival or provide short-term benefit.

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- **DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography)-V Pilot Study**
  - Feasibility of prophylactic coronary revascularization in patients with preoperative extensive stress induced ischemia
  - 430 high-risk patients, 101 with extensive ischemia, 49 assigned to revascularization
  - **Revascularization did not improve 30-day outcome, no benefit during one year follow-up**

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# Recommendation for Preoperative Revascularization

- Is of no value in preventing perioperative cardiac events
- Only for those patients in whom PCI is independently indicated for an acute coronary syndrome

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# 2 – Pre-existing Stents

Consider

- Indication for stent
- Date of implantation
- Type of stent
- Patient's current oral anti-platelet therapy and proposed duration
- 5-10 days needed for effect of anti-platelet drug to wear off
- Risk of stent thrombosis vs. Bleeding risk

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# Risk of Stent Thrombosis in the Perioperative Period

- Pathophysiology
  - Non-endothelialization (inadequate deployment, delayed healing)
  - Interruption of oral anti-platelet agent (OAA)
  - Prothrombotic state
- Significant thrombosis risk in the perioperative period – 40% of reported cases in non-cardiac surgery where OAA had been held
- Uncommon but devastating – 64% death, 9-45% rate of MI and mortality

*Artang R, et al. Analysis of 36 reported cases of late thrombosis in drug-eluting stents placed in coronary arteries. Am J Cardiol. 2007*
*Iakovou I, et al. Incidence, predictors and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA 2005*
*Cutlip DE, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. Circulation 2001*

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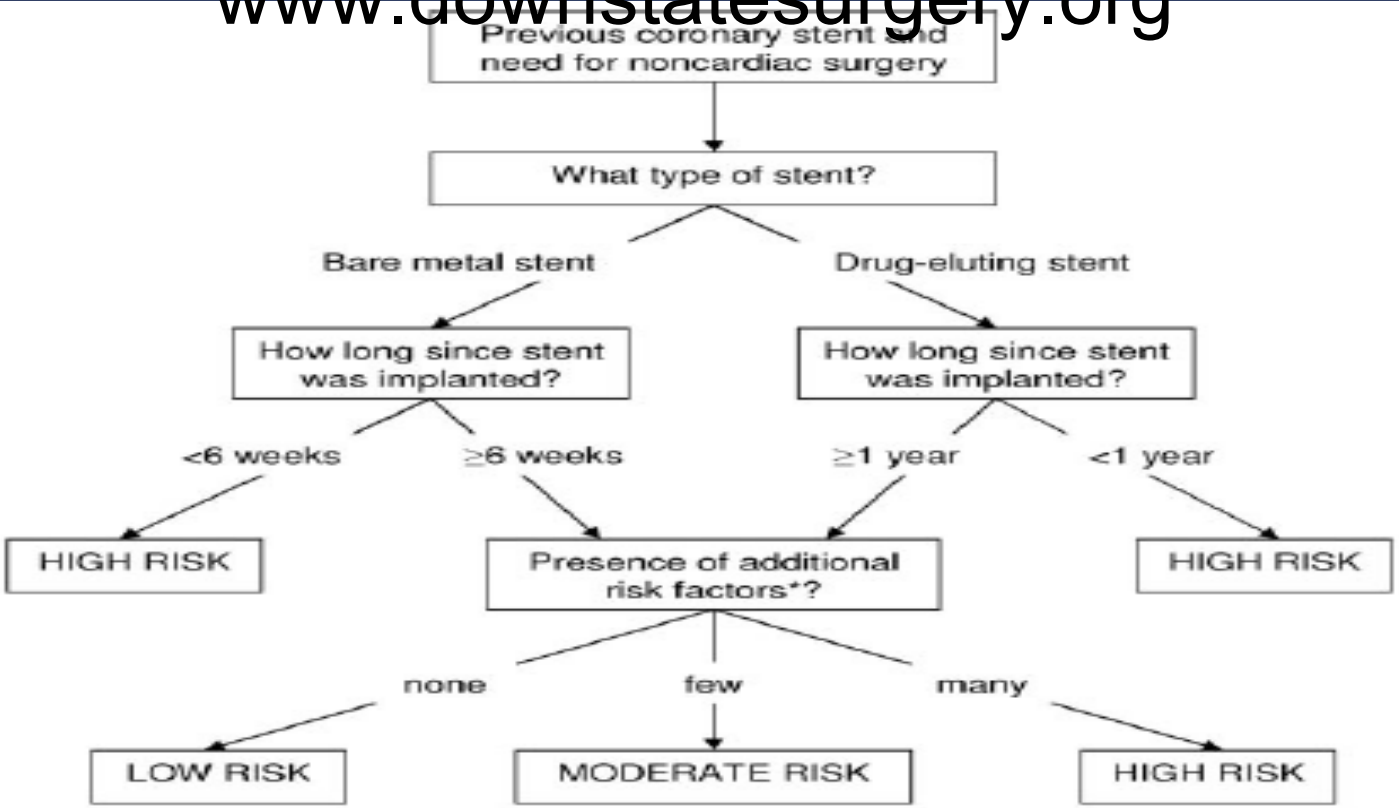


***Additional risk factors for stent thrombosis**

| Coronary anatomy | Stent-indication | Patient |
|---|---|---|
| Bifurcation stenting<br>Ostial stenting<br>Small (<3.0 mm) stent diameter<br>Long (>18 mm) stent length<br>Overlapping stents<br>Multiple stents<br>Suboptimal result | Acute coronary syndrome | Diabetes<br>Renal impairment<br>Advanced age<br>Low ejection fraction<br>Prior brachytherapy |

*Riddel JW, et al. Circulation 2007*

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# Bleeding Risk

Consider

- Anti-platelet agents
- Nature of surgery

# Anti-platelet agents

## Aspirin

- Complete/irreversible blockade of platelet COX-1
- 50-150 mg/day (up to 325 mg for high BW)
- 4–5 days after stopping aspirin for effect to wear off
- Never stop aspirin if it is for secondary prevention; safe to dc for 7 days if for primary prevention
- Literature review
  - Increased risk of bleeding complications and procedural bleeding (RR 1.5)
  - No increase in the **severity** or perioperative mortality due to bleeding complications
  - Exceptions: intracranial surgery and prostatectomy

*Burger W, et al. Low-dose aspirin for secondary cardiovascular prevention - cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. J Intern Med. 2005*

*Eikelboom JW, et al. Bleeding and management of bleeding. Eur Heart J. 2006*

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# Clopidogrel (thienopyridine)

- Platelet ADP-receptor antagonist
- Loading dose: 300 mg, daily dose: 75 mg
- Decreases the risk of MI in unstable angina by 18% and the risk of coronary stent thrombosis and recurrent stroke by 30%
- Increases the risk of spontaneous hemorrhage by 38% (incidence 1–2%)
- Short half-life (4 h), but prolonged recovery from drug (7 d) – irreversible platelet inhibition

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# Dual Anti-platelet Therapy

- Increased rate of severe spontaneous bleeding compared with patients on aspirin alone (ATC Trial – 37% increase in RR, CURE Trial – 27% increase in RR)

- Diffuse bleeding and oozing in areas of difficult surgical hemostasis leads to delayed blood loss

# Glycoprotein IIb/IIIa Antagonists

- Used for prevention of immediate thrombosis of coronary stents (24-48 hours)
- Abciximab (ReoPro®)
- Tirofiban (Aggrastat®)
- Eptifibatide (Integrilin®)

# New Agents

- Bivalirudin
  - IV direct antithrombin agent
  - 25 minute half-life
- Short-acting $P2Y_{12}$ antagonist
  - Reversible ADP receptor blockers
  - IV and PO

| Continuing OAA | Stopping OAA |
| --- | --- |
| Bleeding risk<br>• Aspirin 2.5-20%<br>• Dual OAA 30-50% | Hypercoagulability due to pathology and response to surgery |
| 30% increase in transfusion rate | Increased post-op MI and mortality rate from stent thrombosis |
| Non-fatal MI 2-6%, cardiac mortality 1-5% | Perioperative death rate increased 5-10 times |

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# Recommendations for OAA Based on Thrombosis vs. Bleeding Risk

| Surgical haemorrhagic risk | Cerebro- and cardiovascular risk | | |
|---|---|---|---|
| | Low | Intermediate | High |
| | >6 months after MI, PCI, BMS, CABG, stroke >12 months if complications | 6–24 weeks after MI, PCI+BMS, CABG, or stroke (Ø complication); >12 months after DES; high-risk stents (long, proximal, multiple, overlapping, small vessels, bifurcation); low EF, diabetes | <6 weeks after MI, PCI, BMS, CABG; <6 months after same if complications; <12 months after high-risk DES; <2 weeks after stroke |
| *Low risk* | | | |
| Transfusion normally not required; peripheral, plastic, and general surgery, biopsies; minor orthopaedic, ENT, and general surgery; endoscopy; eye anterior chamber; dental extraction and surgery | Elective surgery: OK; maintain aspirin | Elective surgery: OK; maintain aspirin, clopidogrel (if prescribed) | Elective surgery: postpone; vital or emergency surgery: OK; maintain aspirin and clopidogrel |
| *Intermediate risk* | | | |
| Transfusions frequently required; visceral surgery; cardiovascular surgery; major orthopaedic, ENT, reconstructive surgery; endoscopic urology | Elective surgery: OK; maintain aspirin | Elective surgery: postpone; surgery absolutely required: OK; maintain aspirin, clopidogrel (if prescribed) | Elective surgery: postpone; vital or emergency surgery: OK; maintain aspirin and clopidogrel |
| *High risk* | | | |
| Possible bleeding in a closed space; intracranial neurosurgery; spinal canal surgery; eye posterior chamber surgery | Elective surgery: OK; maintain statin; withdraw aspirin (maximum 7 days) | Elective surgery: postpone; surgery absolutely required: OK; maintain aspirin, or replace aspirin by ibuprofen; stop clopidogrel | OK only for vital or emergency surgery; maintain aspirin Bridge with tirofiban/eptifibatide and heparin |

*Chassot PG, et al. Br J Anaesth 2007*

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# Urgent/Emergent Surgery

## Platelet transfusion and antagonism

- Current OAAs – irreversible
- Fresh platelets to re-establish normal coagulation
- Hemostasis needs 50% normal circulating platelets
- **No evidence to recommend prophylactic platelet transfusion**
- Recommendations to transfuse platelets if active/uncontrolled bleeding
- Effective after 6-8 hours of last clopidogrel dose

- If procedure needed soon after PCI and IV GP IIb/IIIa antagonist
  - Abciximab – platelet transfusion required if within 48 hours since stopping infusion
  - Tirofiban and eptifibatide – short-acting, usually do not require platelet transfusion

- Aprotinin
  - Basic pancreatic trypsin inhibitor, reduces fibrinolysis
  - Shown to decrease postoperative bleeding in patients undergoing CABG

# Substitutes

- No recommendations for heparin, warfarin, or GP IIb/IIIa agents reduce the risk of stent thrombosis
- Some evidence for bridging therapy with IV tirofiban +/- IV heparin during urgent surgery
  - Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study (*N Engl J Med 1998*)

- Urgent surgery in patients with a recently implanted coronary drug-eluting stent: a phase II study of 'bridging' antiplatelet therapy with tirofiban during temporary withdrawal of clopidogrel (*Savonitto S, et al. Br J Anaesth 2010*)
  - 30 patients with recently implanted DES and high stent thrombosis risk undergoing urgent major surgery
  - Clopidogrel withdrawn 5 days prior and tirofiban started 24 hours later
  - Tirofiban stopped 4 hours before surgery and resumed 2 hours after surgery
  - No increased risk of bleeding

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# Cardiac Risk Assessment

## Revised Goldman cardiac risk index (RCRI)

| Six independent predictors of major cardiac complications[1] |
|---|
| High-risk type of surgery (examples include vascular surgery and any open intraperitoneal or intrathoracic procedures) |
| History of ischemic heart disease (history of MI or a positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, or ECG with pathological Q waves; do not count prior coronary revascularization procedure unless one of the other criteria for ischemic heart disease is present) |
| History of HF |
| History of cerebrovascular disease |
| Diabetes mellitus requiring treatment with insulin |
| Preoperative serum creatinine >2.0 mg/dL (177 µmol/L) |
| **Rate of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest according to the number of predictors[2]** |
| No risk factors - 0.4 percent (95% CI: 0.1-0.8) |
| One risk factor - 1.0 percent (95% CI: 0.5-1.4) |
| Two risk factors - 2.4 percent (95% CI: 1.3-3.5) |
| Three or more risk factors - 5.4 percent (95% CI: 2.8-7.9) |

*References:*

1. *From: Lee TH, Marcantonio ER, Mangione CM, et al. Circulation 1999; 100:1043.*
2. *From: Devereaux PJ, Goldman L, Cook DJ, et al. CMAJ 2005; 173:627.*

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# NSQIP database risk model

- Type of surgery
- Dependent functional status
- Abnormal creatinine
- ASA class
- Increased age

# Preoperative Evaluation

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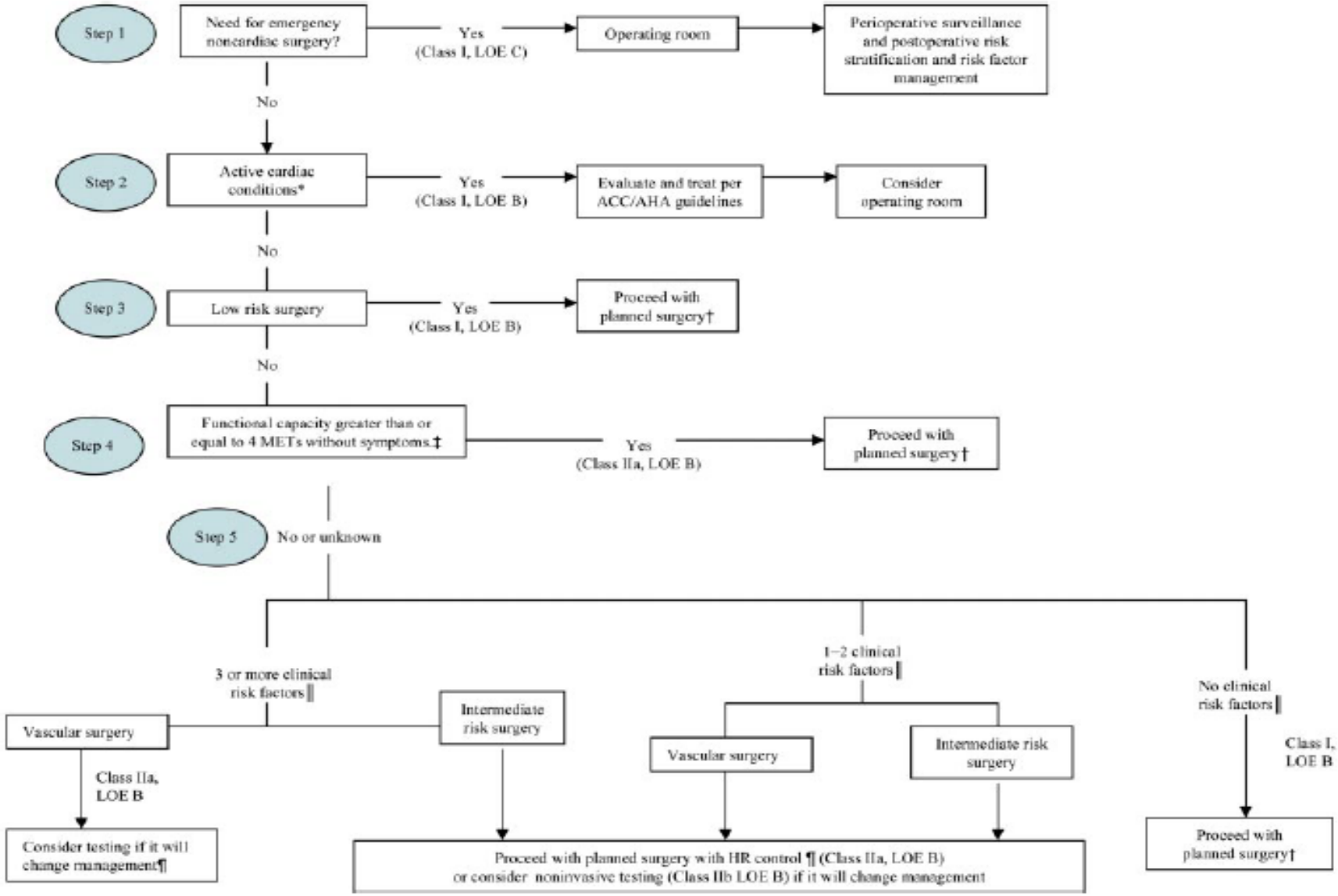


**Figure 1.** Cardiac evaluation and care algorithm for noncardiac surgery based on active clinical conditions, known cardiovascular disease, or cardiac risk for patients 50 years of age or greater.

ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for noncardiac surgery

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# Cardiac Risk Reduction Strategy

- Define urgency of surgery (may supercede risk stratification)
- Initial risk assessment
- Refinement of risk assessment with non-invasive testing and selective invasive testing
- Consideration of therapy/medication (revascularization, beta blockers, statins, anticoagulants)

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# Managing Patients on Dabigatran (Pradaxa®)

- Direct thrombin inhibitor
- Anticoagulation in patients with a-fib to prevent strokes and thromboembolism
- No known reversal agent
- Measurement of effect
  - aPTT and TT useful for negative predictive value
  - Ecarin Clotting Time (ECT): not influenced by other anticoagulants

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# Dabigatran and Elective Surgery

| | High Bleeding Risk Procedure (e.g. Most major surgical procedures) (desire no or minimal anticoagulant effect at time of procedure) | Moderate Bleeding Risk Procedure (desire mild-moderate anticoagulant effect at time of procedure) |
|---|---|---|
| | | |
| Normal or Mild Renal Impairment (CrCl >50 mL/min) | PRE: Hold 4 doses (2 days) pre-procedure | PRE: Hold 2 doses (1 day) pre-procedure |
| | POST: Resume 48-72 hours post-procedure (consider prophylactic heparin/LMWH until reinitiated) | POST: Resume 24-48 hours post-procedure |
| | | |
| Moderate Renal Impairment (CrCl 30-50 mL/min) | PRE: Hold 6-8 doses (3-4 days) pre-procedure | PRE: Hold 4 doses (2 days) pre-procedure |
| | POST: Resume 48-72 hours post-procedure (consider prophylactic heparin/LMWH until reinitiated) | POST: Resume 24-48 hours post-procedure |
| | | |
| Severe Renal Impairment (CrCl <30 mL/min) | Thrombosis or Hematology consult | Thrombosis or Hematology Consult |

Package insert. Pradaxa (dabigatran etexilate). Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc., 2010.

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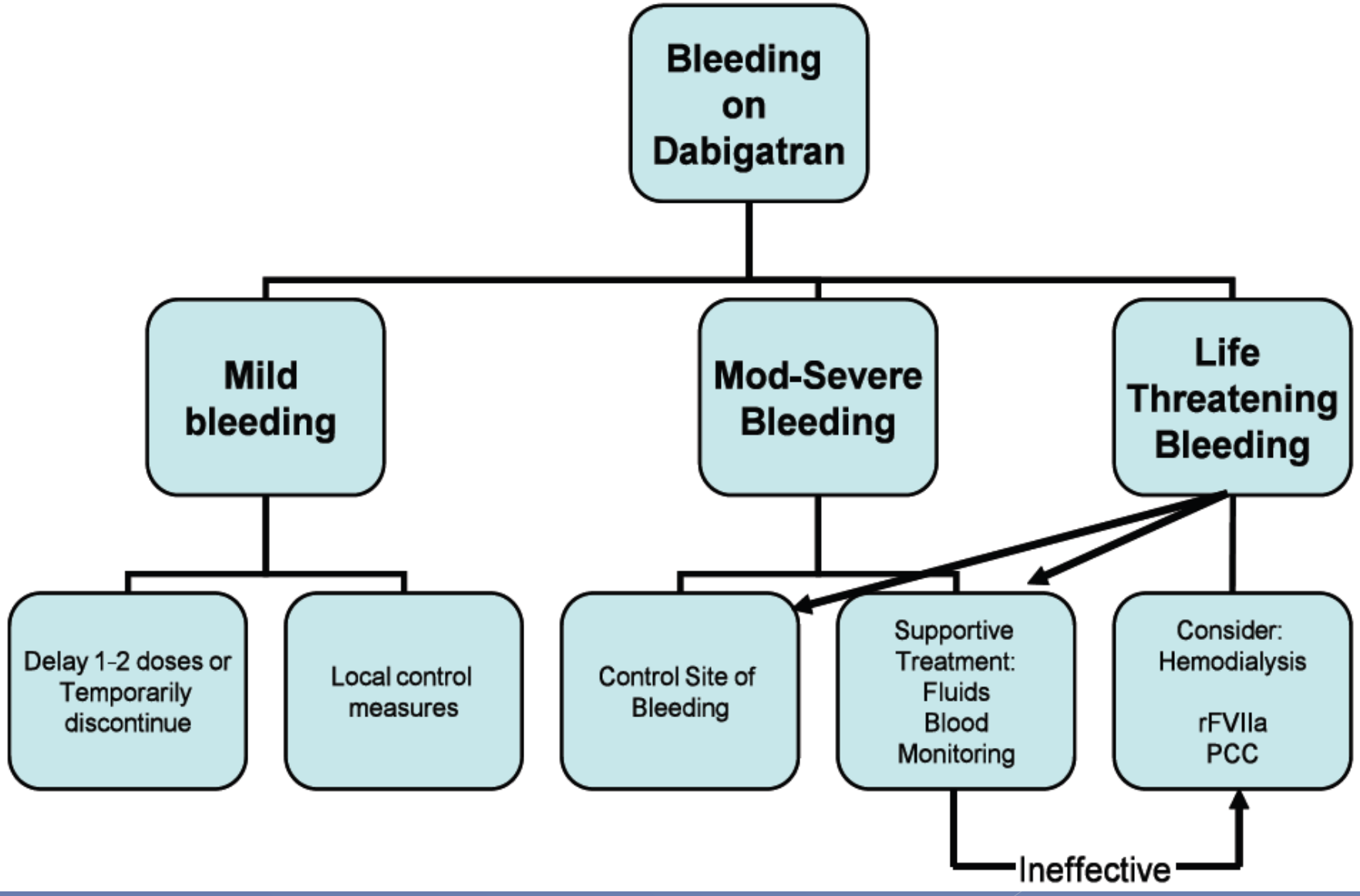
# Dabigatran and Urgent Surgery



# Summary

- Cardiovascular complications are the leading cause of postoperative mortality in non-cardiac surgeries
- Consider patient-specific, surgery-specific and disease-specific issues
- Cardiac risk assessment tools
- Preoperative evaluation with selective non-invasive and invasive testing
- Perioperative management of risk factors including medications in elective vs. emergent operations

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# Summary (continued)

- Patients with coronary stents
  - Surgeons must contact patient's cardiologist prior to surgery
  - Try to defer surgery until course of dual anti-platelet therapy is complete
  - If a procedure is planned within this time – should be done with 24 hour availability of cardiac cath services
  - Weighing stent thrombosis risk against bleeding risk
  - Urgent/emergent operation
    - Proceed with at least aspirin in most cases
    - Involve anesthesia and cardiology
    - Inform patient of relative risks of both stent thrombosis and bleeding
  - Recommence oral anti-platelet therapy as soon as possible post-procedure

# Thank You

# Question 1

Following coronary revascularization, which of the following is **NOT** an appropriate option for managing anticoagulation for elective non-cardiac operations?

A. Elective procedures involving any significant risk of bleeding should be deferred for 12 months after drug-eluting stent (DES) placement
B. Elective procedures involving any significant risk of bleeding should be deferred for 4 to 6 weeks after bare metal stent (BMS) placement
C. Patients with DES placed 12 months previously who have thienopyridines stopped perioperatively should continue to receive aspirin perioperatively
D. Aspirin should be continued indefinitely in patients with DES
E. Patients with DES should have thienopyridine derivatives stopped, aspirin continued, and be given warfarin (Coumadin) perioperatively

# Question 2

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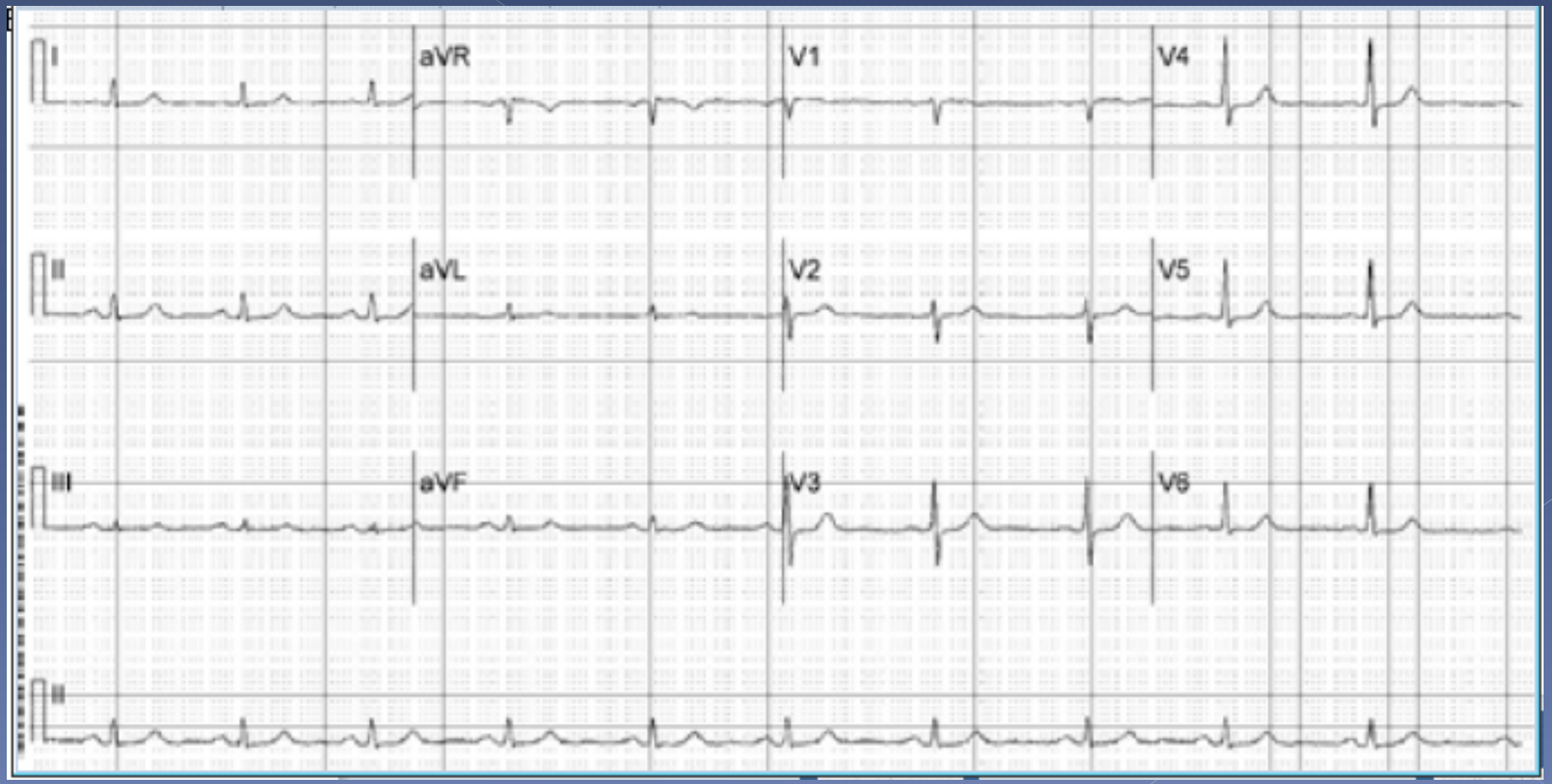
*A 69-year-old man scheduled for colon resection for a near-obstructing colon cancer had an acute MI and drug-eluting stents placed 3 months ago. His current cardiac evaluation is normal. The preoperative EKG is shown. His medications include clopidogrel (Plavix) and aspirin.*



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The surgical procedure is performed without incident, but in the recovery room the patient develops chest tightness and pain. An EKG is obtained, as shown.

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Appropriate management includes all of the following immediate interventions **EXCEPT**:

A. morphine sulfate
B. cardiac catheterization
C. beta blockers
D. nitroglycerin
E. pulmonary artery catheterization

# Question 3

Preoperative noninvasive testing for the presence of inducible myocardial ischemia would be most appropriate for which of the following patients?

A. A healthy 60-year-old man without historical cardiac risk factors scheduled for gastrectomy because of gastric carcinoma
B. A patient with a history of MI 1 year previously and good exercise tolerance undergoing laparoscopic cholecystectomy
C. A patient with diabetes and renal insufficiency undergoing inguinal hernia repair
D. A patient with limited exercise tolerance and diabetes undergoing right hemicolectomy
E. All of the above