"Fit for GA?"

Perspective of an anaesthetist on preoperative optimization

Alice Joeng, Resident

Department of Anaesthesia, Princess Margaret Hospital

Why Bother?

- *Surgery is a stressful event*
  - Bleeding, extensive fluid shift
  - Pain
  - Stress response
  - Procedure –specific risk eg: aortic cross-clamping, bone reaming , thoracotomy
- *Most require anaesthesia*
  - Amnesia, muscle paralysis and analgesia
  - Effect of anaesthetic agent/technique
- *High risk patients*
  - Underlying condition require surgical treatment –eg sepsis, ruptured AAA
  - Pre-existing +/- acute organ failure

Aim of optimization

- Realistic assessment of risk
  - Identify high risk patients
  - Identify correctable factors and correct them
  - Make appropriate decision when considering a patient for surgical procedure
  - Implement prophylactic measures where possible
  - Apply appropriate degree of monitoring in a suitable environment
  - Anticipate complications
  - Have a well thought out management plan (pre/intra/postop) to manage the risk
- **Improve overall patient outcome and survival (perioperative and long term)**

Our role

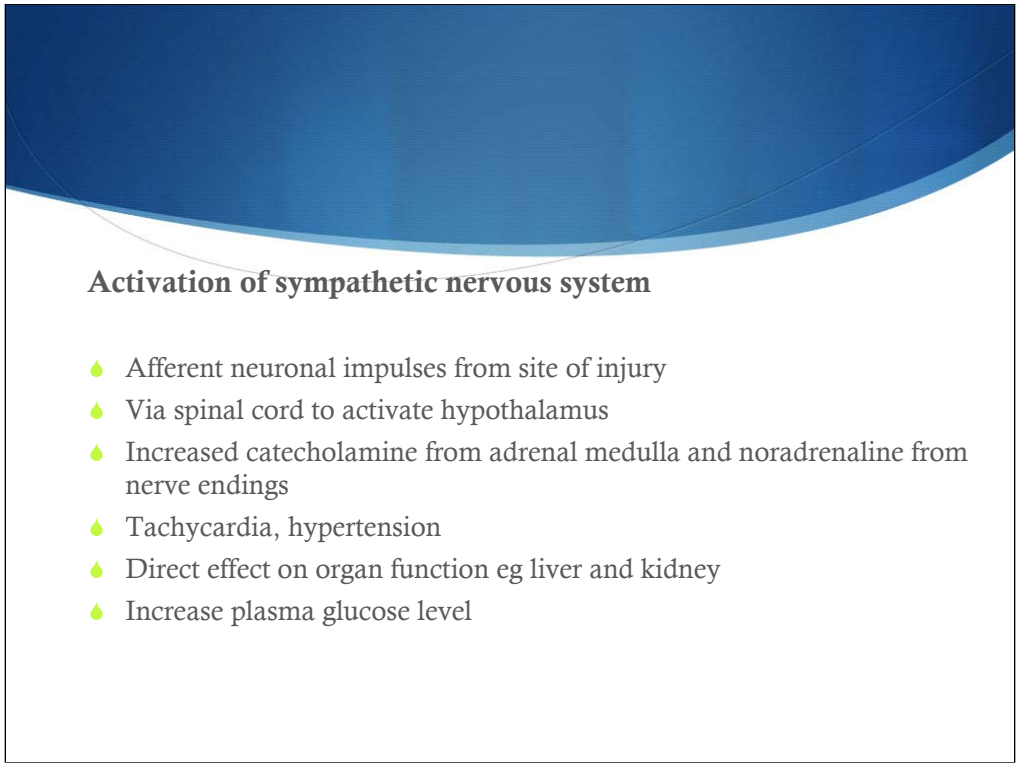
- "Perioperative physician"
- Discuss with all parties of management team (eg surgical team, ICU) with regard to perceived risk vs benefit of proposed surgery, as well as timing of surgery
- Once all information is available, the choices are
  - Proceed to surgery
  - Proceed to less extensive or palliative surgical option
  - Recommend against surgery
- If decide to proceed to surgery, optimize patient's condition by pharmacological or non-pharmacological means
  - Optimize organ function
  - Reduce stress response
  - Appropriate anaesthetic technique and provide good analgesia
  - Appropriate postoperative care and monitoring

Surgery-specific factors

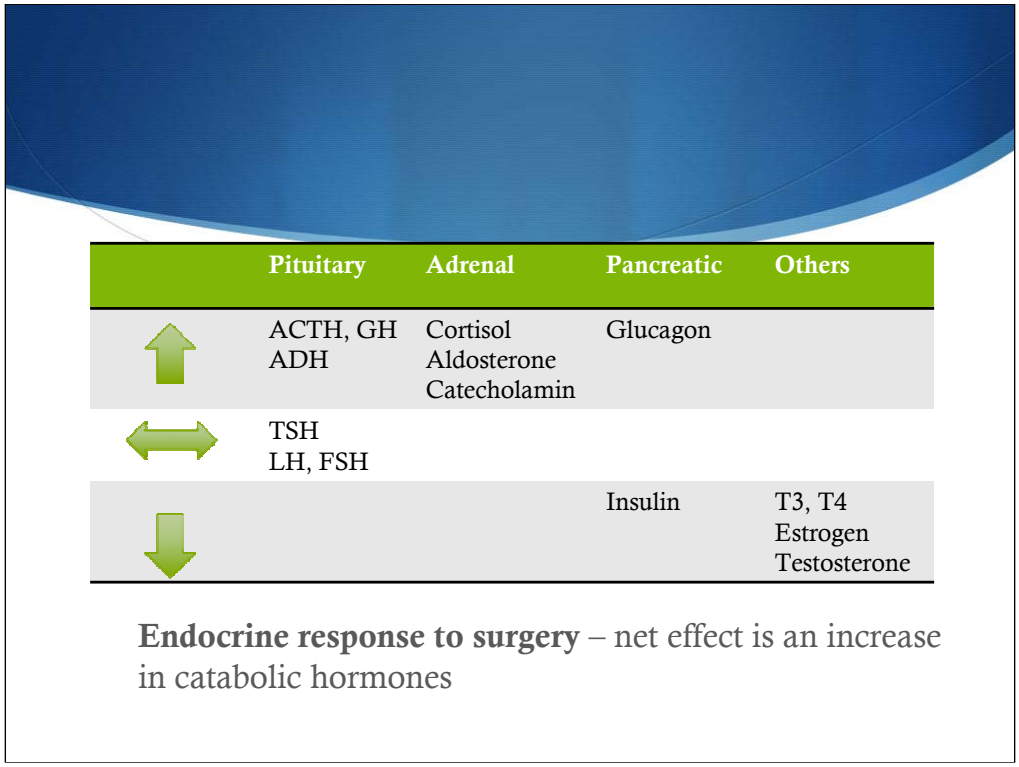
- Bleeding + blood transfusion
- Pain
- Extensive fluid shift, electrolyte imbalance
- Specific eg:
  - Aortic cross-clamping, cardiopulmonary bypass
  - Pneumoperitoneum
  - Tourniquet
  - Positioning
    - Eg lithotomy, prone, trendelenburg position

Stress response to surgery

- Hormonal, metabolic and inflammatory changes following surgery
  - Magnitude and duration related to degree of tissue trauma and development of complications eg sepsis
  - Also occurs in settings of trauma, severe sepsis, burn, acute pancreatitis
- evolutionary advantage for survival
- It has been argued that the response is unnecessary in current surgical and anaesthetic practice



Liver: alpha and beta receptor for hepatic artery, alpha for portal vein. SNS → portal venous constriction, initial vasoconstriction then vasodilation of hepatic artery → effect : dec liver blood flow
Kidney: SNS constricts afferent and efferent arteriole, reduce renal blood flow and GFR



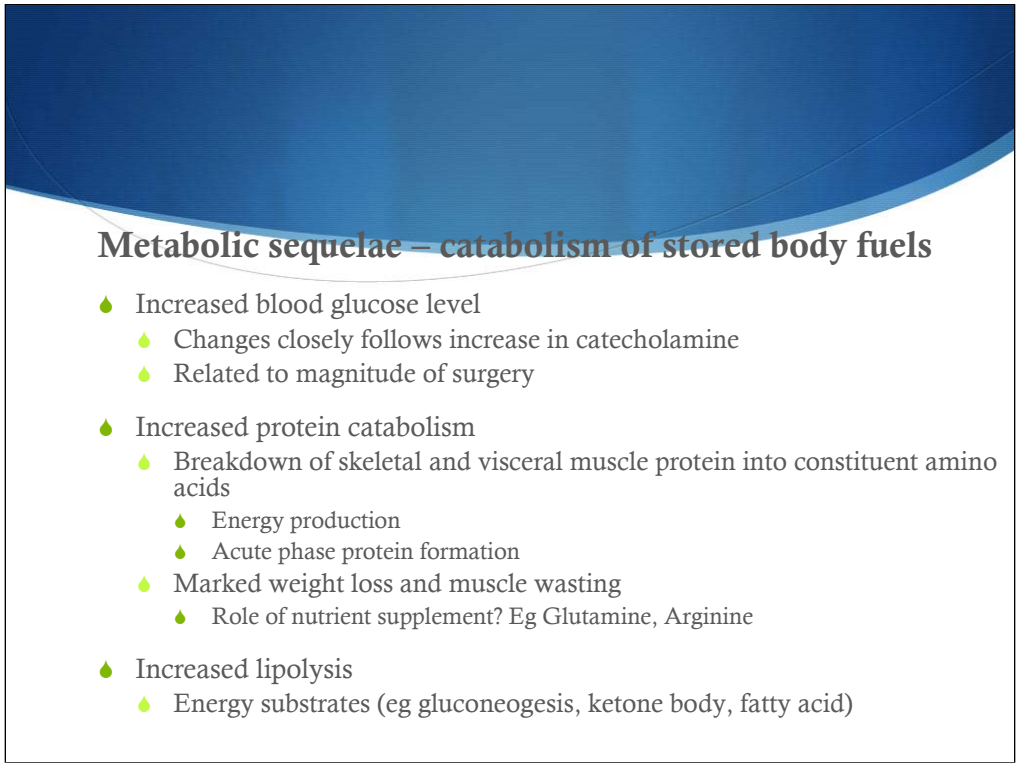
	Pituitary	Adrenal	Pancreatic	Others
↑	ACTH, GH ADH	Cortisol Aldosterone Catecholamin	Glucagon	
↔	TSH LH, FSH			
↓			Insulin	T3, T4 Estrogen Testosterone

Endocrine response to surgery – net effect is an increase in catabolic hormones

Highlight cortisol , GH, insulin
Increased catabolism promote provision of substrate for survival

- **Cortisol**
  - Increases rapidly after starting of surgery, reaching maximum at 4-6 hours, may last up to 72 hours
  - Usual negative feedback response of cortisol on ACTH secretion is ineffective
  - Promotes lipolysis, protein breakdown
  - Promotes gluconeogenesis + inhibits glucose utilization by cells
    - Increases plasma glucose level
  - Anti-inflammatory activity
    - Inhibits synthesis of prostaglandin and accumulation of macrophage/neutrophils
- **Growth Hormone**
  - Stimulate glycogenolysis in liver
  - Anti-insulin effect

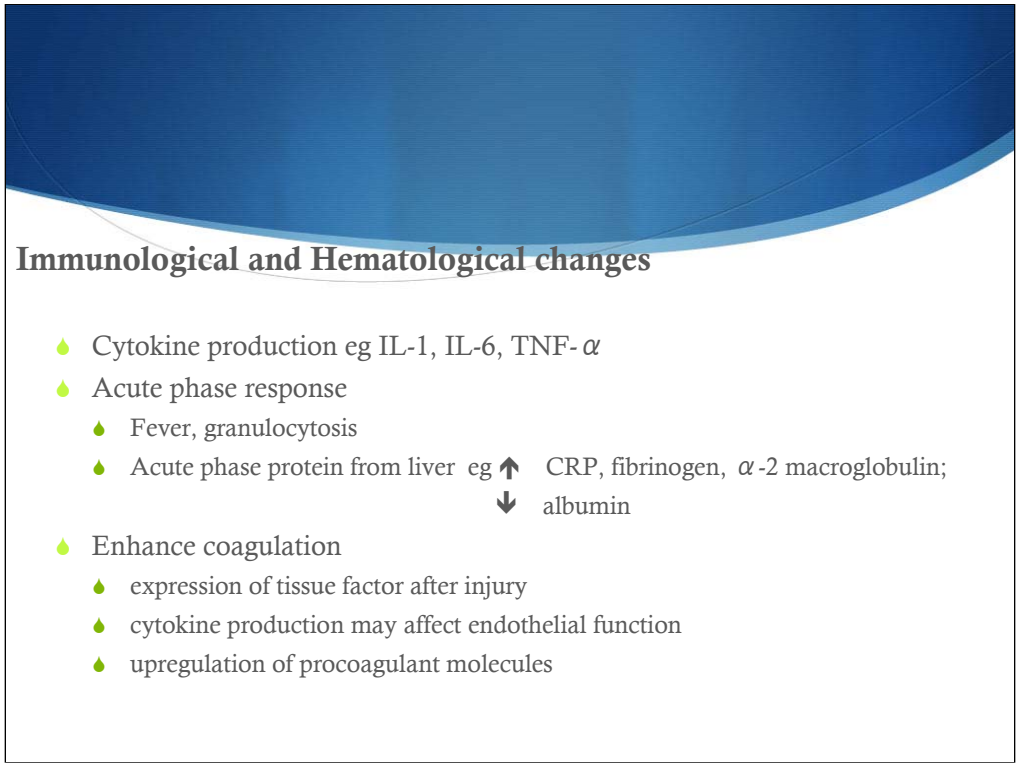
- **Insulin**
  - Key anabolic hormone
  - Decrease plasma glucose level
    - Promote uptake of glucose into cells, conversion of glucose into glycogen and fat
  - Inhibit protein breakdown and lipolysis
  - Secretion fails to match catabolic, hyperglycaemic response in perioperative period
    - α - adrenergic inhibition of pancreatic β -cell secretion
    - Peripheral insulin resistance



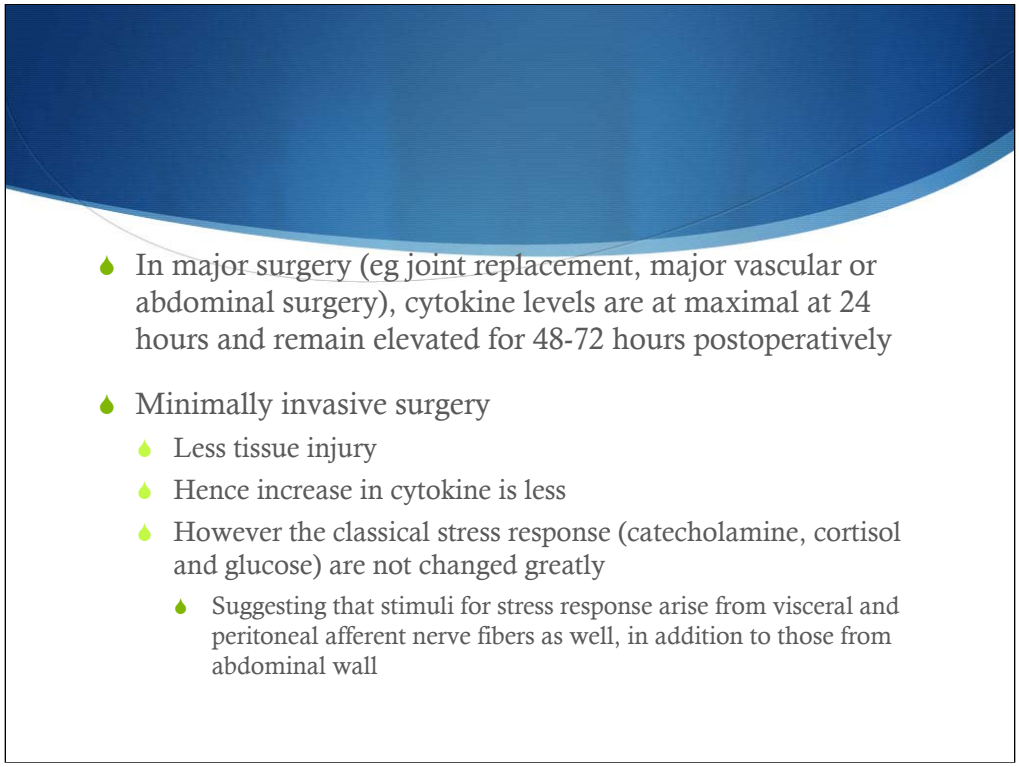
Increased catabolic hormones, relative lack of insulin and insulin resistance
Amino acid → directly catabolized for energy or via gluconeogenesis, fatty acid or ketone bodies
Led to interest in provision of nutrient supplement for major surgery
Glutamine: fuel for enterocyte/lymphocyte/nucleotide synthesis/(maintain gut mucosal integrity and cellular immune function, reduce bacterial/endotoxin translocation and reduce infective complication)/precursor for glutathione (anti-oxidant, may modifity cytokine response)/increase muscle mass. Metaanalysis 2003: RR for mortality and infective Cx is reduced
Arginine: not recommended for septic ICU patient due to increased NO via NOS → immunosuppression and increase mortality. But its beneficial effect on T-lymphocyte function has been shown to reduce infective Cx in elective general surgical patients

Retention of salt and water

- ADH
  - Promotes water retention
  - Increase in secretion may continue for 3-5 days
- Renin-aldosterone-angiotensin system activation
  - Result of sympathetic activation
  - Na+ and water reabsorption from renal tubules



Cytokine: produced by activated leucocyte, fibroblast, endothelial cells triggered locally as response to tissue injury → local effect of inflammation + initiate systemic changes of stress response eg IL-6 induce acute phase response. Cytokine can also stimulate pituitary ACTH secretion → increase cortisol release. Negative feedback exist btw cortisol and cytokine production.



Cytokine production reflects degree of trauma

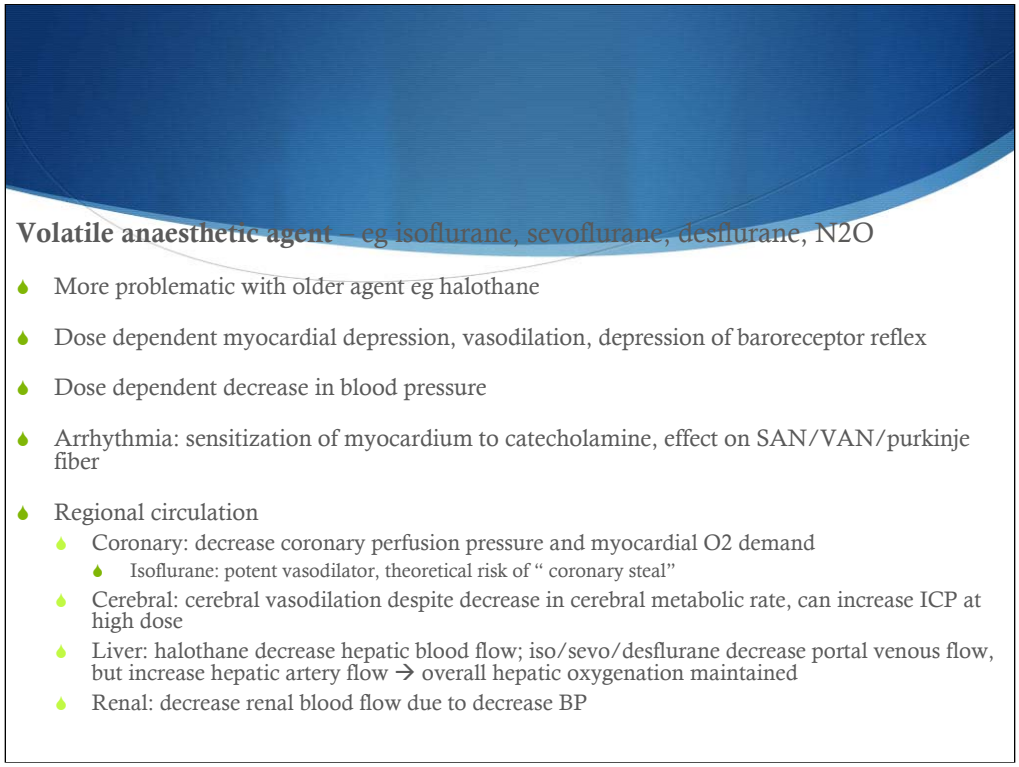
Effect of Anaesthesia

Commonly used anaesthetic agents

IV anaesthetic agent

- eg propofol, thiopentone, etomidate, benzodiazepam
- Varying degree of CVS effect
  - Myocardial depression
  - Vasodilation
  - Diminished baroreceptor reflex
  - Hypotension
    - Affect organ perfusion
- Accentuated by hypovolaemia, septic state, pre-existing cardiac disease
- Specific side effect
  - Etomidate: reversible adrenocortical suppression
  - Ketamine: activation of central SNS outflow, increase ICP, psychoactive

Except ketamine: increase SNS discharge



More problematic with older VA like halothane, newer agent genrally preserve CO, better less arrhythmia
Myo depression → E>H>I

- Respiratory effect
  - Dose –dependent depression in ventilation and response to hypercapnia/hypoxaemia
  - Decrease diaphragm and intercostal muscle tone → decrease functional residual capacity by ~20%
  - Bronchodilation
  - Upper airway irritation, larynospasm, decrease mucociliary action
  - Inhibit hypoxic pulmonary vasoconstriction

- Effect on muscles
  - Skeletal muscles
    - Potential trigger of malignant hyperthermia
  - Smooth muscles
    - Uterine relaxant

- N2O:
  - expansion of air-filled space eg pneumothorax
  - Inhibit HPV
  - pulmonary HT
  - Increase CBF and ICP
  - Increase homocysteine on prolonged exposure → theoretical risk of thrombosis
  - Bone marrow toxicity and megaloblastic anaemia on prolonged exposure

Analgesia

- Opioid
  - Sedation
  - Reduce sympathetic response to noxious stimuli
  - Bradycardia
  - Histamine-release for morphine and pethidine
  - Dose-dependent respiratory depression and blunting of hypoxaemic and hypercapnia response
  - Decrease gastric motility and LES tone
- NSAID
  - Renal impairment
  - Bronchospasm
  - ? Platelet inhibition
  - ? Effect on bone healing
  - ? Thrombosis for COX-II (prolonged use)

- Muscle relaxant
  - Suxamethonium
    - Increase K by 0.5mmol/L
    - hyperK associated with extrajunctional receptor (eg burn)
    - Bradycardia
    - Malignant hyperthermia
- Reversal agent
  - Neostigmine + atropine
    - Tachycardia

Cardiovascular disturbance during anaesthesia

- Induction
  - Hypertensive response to intubation
  - hypotension due to drugs and pre-existing conditions (eg hypovolaemia, sepsis, MI)
- IPPV
  - Reduce in venous return
  - Increase in RV afterload
  - Decrease in LV afterload
  - Effect on CO variable
- Reversal
  - Tachycardia, hypertension

Respiratory changes during anaesthesia

- Control
  - If spontaneously breathing → hypoventilation
  - Decreased sensitivity to hypoxia and hypercapnia
  - Apnoea after muscle relaxant
- Airway
  - Dry and cold gas from anaesthetic machine
  - Decreased mucociliary function
  - Sputum retention

- Gas exchange - overall increase in V/Q mismatch
  - Increased apparatus deadspace due to ETT/ connectors
  - Increased alveolar deadspace due to increased pulmonary vascular resistance from IPPV or decreased cardiac output
  - Increased anatomoical deadspace eg bronchodilation
  - Altered pattern of distribution of ventilation in IPPV (non-dependent part better ventilated than dependent part)
  - Decreased functional residual capacity
    - atelectasis of dependent lung
    - increased shunting
  - Inhibits pulmonary hypoxic vasoconstriction by volatile anaesthetic/N2O
- Loss of PEEP whenever during disconnection from circuit (eg during transfer to OT table, tracheostomy)

- Regional anaesthesia
  - Autonomic blockade associated with neuraxial block
    - Peripheral vasodilation, hypotension
      - Not suitable in fixed cardiac output state
    - If block involve cardiac sympathetic outflow (T2-4) → bradycardia

- Effect on stress response
  - Anaesthesia has little effect on cytokine response
    - because it cannot influence tissue trauma
  - But anaesthetic technique can attenuate stress response
    - Eg high dose opioid technique
    - Benzodiazepam
    - α2 agonist
    - Regional technique
      - Neural blockade with local anaesthetics

- Does attenuation of stress response translate to good outcome?
  - Individual studies show that provision of neural blockade as analgesia leads to improvement in physiological parameters in specific organ system
  - However its benefit in outcome is uncertain
- Potential benefit of regional analgesia
  - Decrease thromboembolic Cx (for lower limb and pelvic surgery)
  - Improved postop pulmonary function
  - Decreased cardiac complication
  - Decreased paralytic ileus (for thoracic epidural with LA)
- However, it is often not suitable in critically ill patients
  - Coagulopathic
  - Unstable haemodynamics
  - Emergency surgery

Cardiac risk assessment and optimization for non-cardiac surgery

Risk assessment tools

- Provide information on post-operative risk of a complication or death
- Assessment algorithm
  - Assist with risk stratification
  - Designed to guide need for further investigation before surgery
- Several risk assessment score developed over past 20 years
  - Eg Goldman, Detsky, Lee
- Other tools
  - Echocardiogram
  - Blood test eg BNP (Brain natriuretic peptide)

Original Cardiac Risk Index (Goldman)		Modified Cardiac Risk Index (Detsky)		Revised Cardiac Risk Index (Lee)
MI within 6 months Age >70	10 5	MI within 6 months MI >6 months Angina Class III Angina Class IV Unstable angina within 6 months Age>70	10 5 10 20 5 5	Prior or compensated CHF Hx of IHD IDDM Hx of CVA Creatinine >175 μ mol/L High risk surgery (intraperitoneal, intrathoracic, suprainguinal vascular surgery)
S3 gallop Raised JVP Aortic Stenosis Poor general condition	11 11 3 3	Pul edema within 1 week Pul edema ever Aortic stenosis Poor general condition	10 5 3 5	
Non-sinus rhythm >5 PVC/min	7 7	Non-sinus rhythm >5 PVC/min	5 5	
Emergency OT Thoracic Aortic or Upper abdominal surgery	4 3	Emergency OT	10	
TOTAL	53		120	

	Risk of postoperative CVS complication			
	Class I	Class II	Class III	Class IV
Goldman	0-5 points 0.9%	6-12 points 6.6%	13-25 points 13.8%	>26 points 77.8%
Detsky (for major surgery)	0-15 points 4.5%	16-30% 28.5%	>30 points 62.4%	
Lee	No risk factors **0.5%**	1 risk factors **1%**	2 risk factors **6.6%**	>2 risk factors **11%**

Compare these three indices and divide patients into different risk classes

- Goldman and Detsky scores
  - Not in widespread use
  - More tedious to use
- Lee Revised Cardiac Risk index (RCRI)
  - Designed to identify risk of postoperative cardiac complications after major non-cardiac surgery
  - Well validated
  - Simple to use
  - Incorporated into the AHA/ACC 2007 Guideline algorithm with regard to decision making about further cardiac investigation

Limitation of Lee RCRI

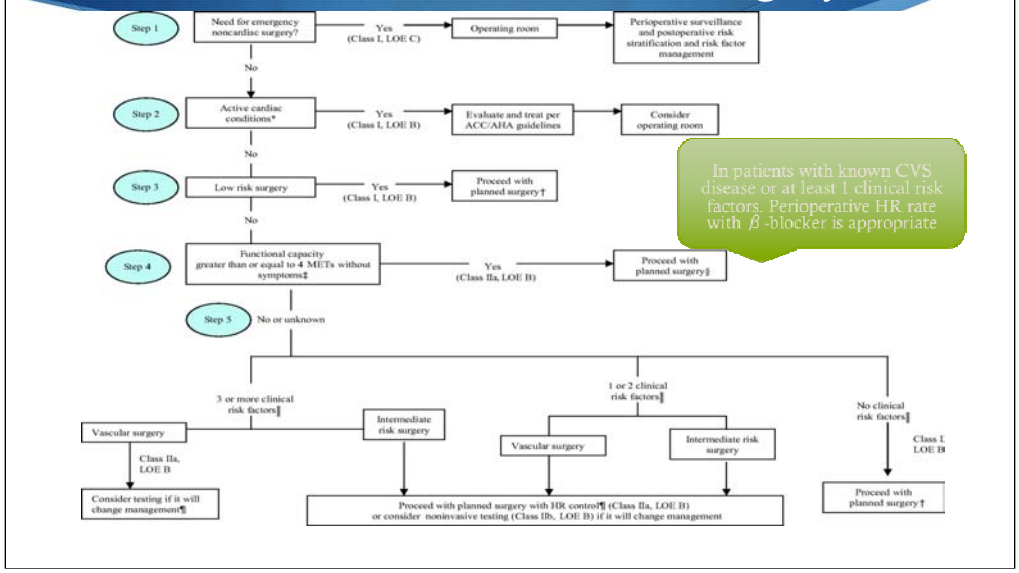
- Designed to estimate postoperative (not preoperative) risk
- Estimate risk of MI, heart block, cardiac arrest, VF or pulmonary edema postoperatively. It does not specifically measure risk of death
- Estimates the risk of these events occuring in the first 5 days postoperatively
- ? Assignment of one point per risk factor is too simplistic
  - Does not take into account degree of variation between individual factors

Attempts to refine RCRI

- Erasmus Cardiac Risk Index
  - Poldermans et al revise the RCRI to improve its predictive ability, by taking patient age and type of surgery into consideration
  - In a study in patients undergoing vascular surgery, risk factors and their odds ratio are:

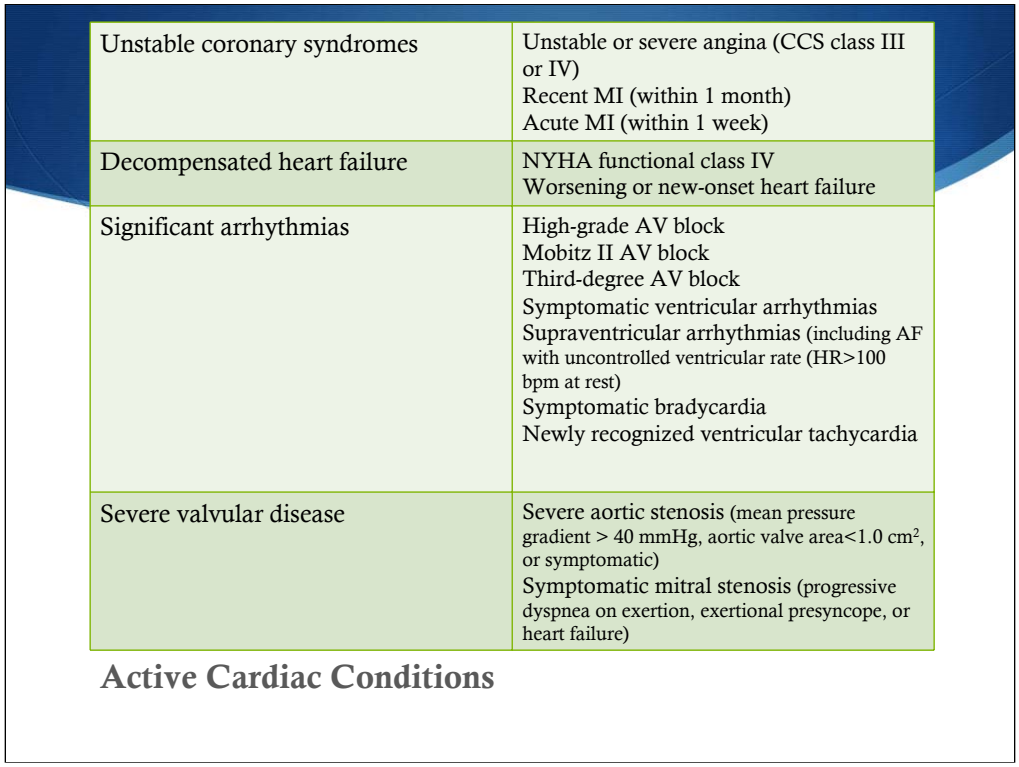
IHD	OR 3.5
CHF	OR 4
Renal impairment	OR 5.2
Stroke	OR 2.7
HT	OR 2
chronic lung disease	OR2
Ruptured AAA	OR 77
Elective AAA/TAA	OR 13
infra-inguinal vascular surgery	OR4
carotid surgery	OR 1
β -blocker	OR0.2
Statin therapy	OR 0.4

ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery



For patients >50 yrs old

Exclude the very high risk (active cardiac conditions) and low risk group (good functional status/low risk surgery), then use Lee's factor and surgery specific risk to stratify the "intermediate risk" group in terms of need for further cardiac testing



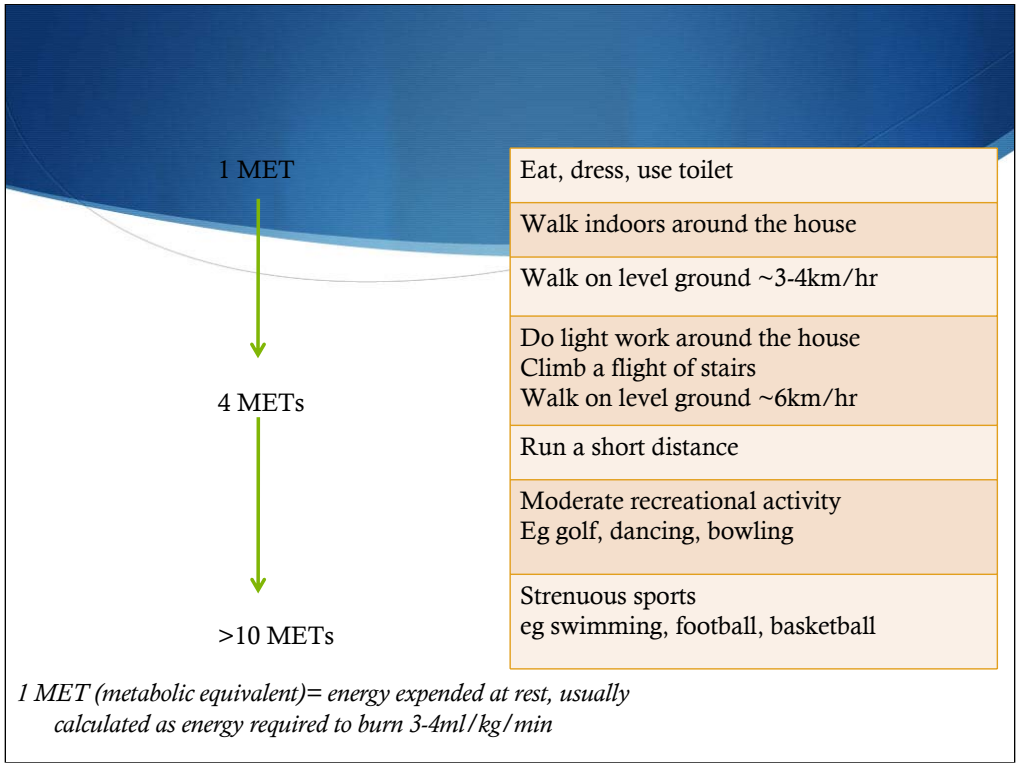
Active Cardiac Conditions

CCS III: marked limitation of normal activity, CCS IV: not able to carry out any physical activity without angina

Functional capacity testing

- A minimum aerobic capacity is required to survive the metabolic stress of the perioperative period
- Power generated by oxygen metabolism is the best measure of aerobic fitness
- The test should demand increasing power for at least 5 minutes

- Methods
  - Estimation from ADL – simple, but subjective
  - Exercise testing
    - Stair climb test
    - Incremental shuttle walk testing
    - Cardiopulmonary testing



1 MET (metabolic equivalent)= energy expended at rest, usually calculated as energy required to burn 3-4ml/kg/min

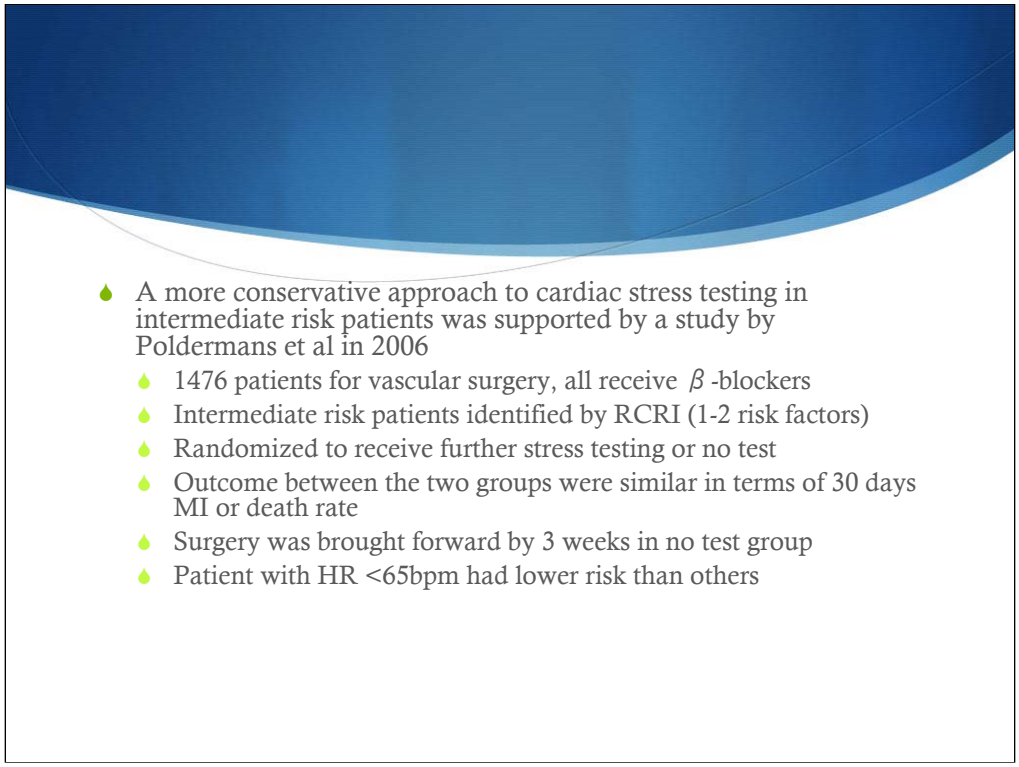
Vascular surgery (reported cardiac risk >5%)	Aortic & other major vascular surgery Peripheral vascular surgery
Intermediate risk surgery (reported cardiac risk 1-5%)	Intraperitoneal/Intrathoracic surgery Carotid endarterectomy Endovascular AAA repair Head and neck surgery Orthopaedic surgery Prostate surgery
Low risk surgery (reported cardiac risk <1%)	Endoscopic procedures Superficial procedures Cataract surgery Breast surgery Ambulatory surgery

Cardiac risk = cardiac death + non fatal MI

Factors to consider: duration, stress of OT, blood loss, fluid shift

Compared to the 2005 guideline

- "Major clinical predictors" are continued to be used to triage patient (active cardiac condition)
- Lee's RCRI are used to assess patients with intermediate risk (which are themselves similar to "intermediate clinical predictors")
- Assessment of functional status comes prior to assessment of clinical risk factors → pivotal role of assessment of functional status
- When functional status is poor or unknown + intermediate / high risk surgery, RCRI risk factors are used to determine need for further investigation
- Overall, the 2007 algorithm is more conservative in referral for further investigation than in 2005. Further testing is suggested for patients with multiple risk factors if the result will change management (eg coronary intervention)



Having said that, individualize decsion

- Non-invasive stress assessment
  - Treadmill
  - Dobutamine stress ECHO
  - Radionucleide myocardial perfusion imaging
    - Eg Thallium scan
  - CT coronary angiogram
- Management of positive test
  - Severe/global abnormality
    - consider coronary angiogram if revascularization is considered
  - Moderate abnormality → suggest some myocardium at risk
    - Usually appropriate to proceed without further coronary intervention
    - Risk factor reduction

- Other tests
  - TTE
    - Recommended for current or prior heart failure with worsening dyspnoea
    - Routine use not recommended
  - Brain Natriuretic peptide
    - Neuroendocrine hormone produced by LV secreted in response to wall stress
    - Correlates well with increasing clinical risk and predicive of inducible ischaemia on DSE
    - BNP <533pg/ml: 1.4% risk of cardiac event
    - BNP>533pg/ml: 42% risk

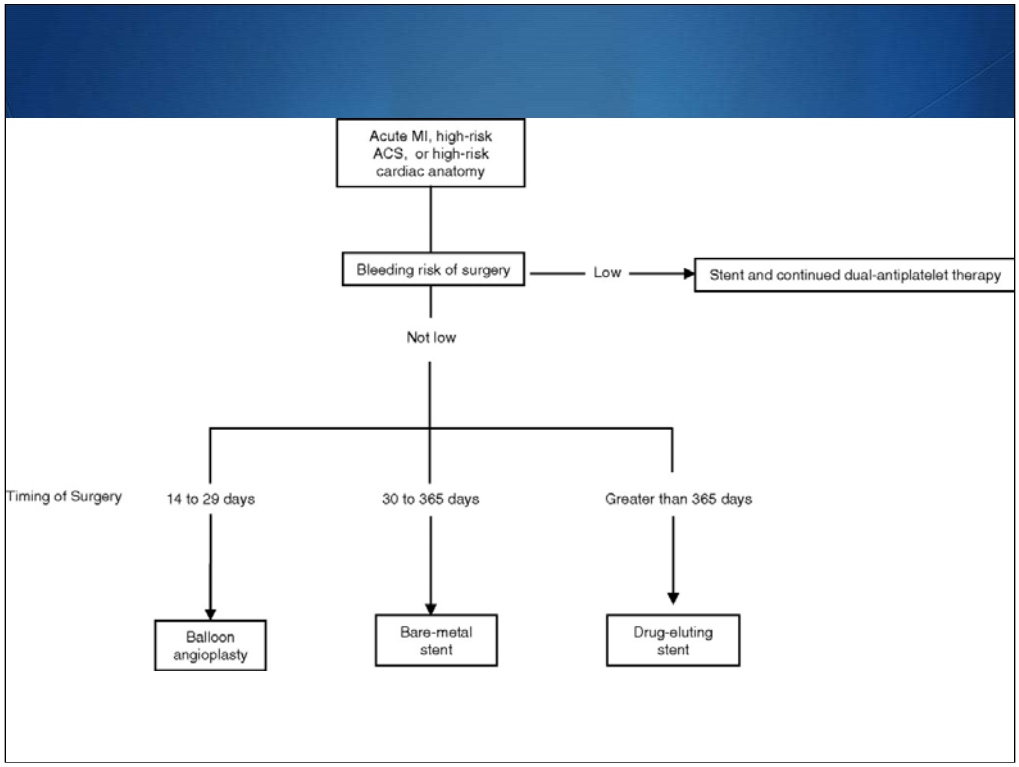
Risk reduction strategy- coronary intervention

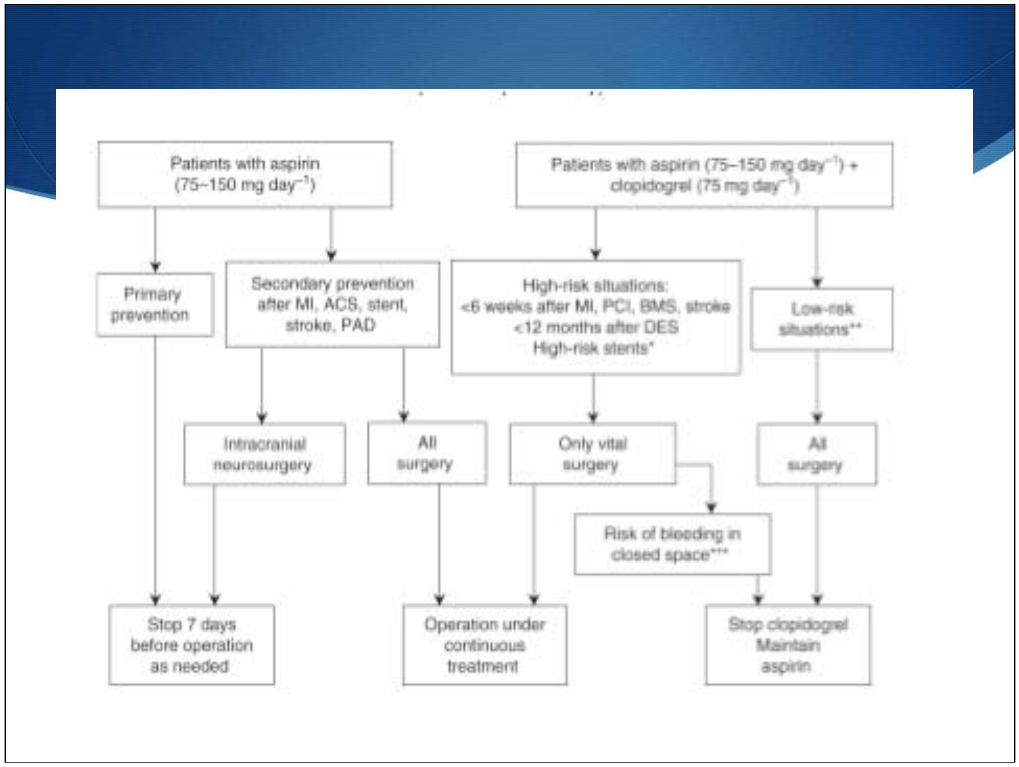
CABG prior to non-cardiac surgery

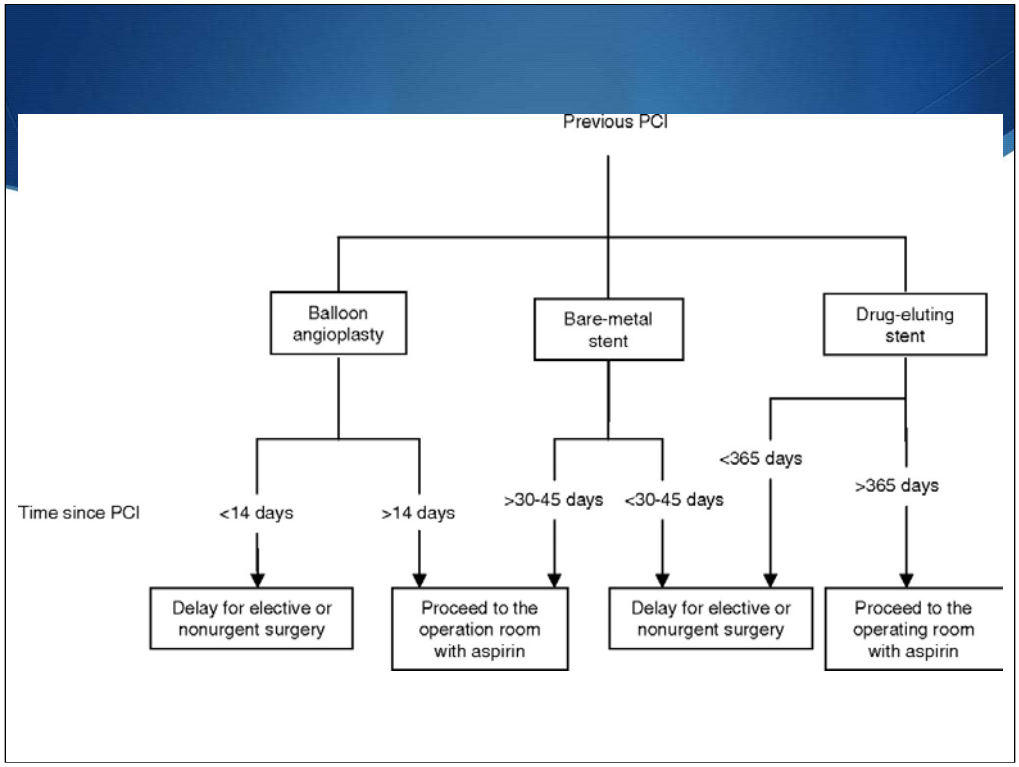
- Consider only if patient has lesion that justifies CABG in its own right
  - Left main disease (>50%)
  - Left main equivalent lesion (>70% in proxmal LAD and circumflex)
  - Severe triple vessel disease (>50% in 3 major coronary arteries), esp for patients who are symptomatic, has poor LV function
  - Severe 2 or 3 vessel disease (>70%) with involvement of proximal LAD
- Not indicated to "get the patient through" a non-cardiac surgery
- CARP study (2004):
  - patients with stable coronary disease for elective vascular surgery (excluded: severe LV impairment, severe AS, LMS>50%, unstable coronary symptoms), revascularization by CABG/PTCA did not improve outcome (MI, in-hospital and 2 year mortality)
- DECREASE V study (2007):
  - In patients with extensive stress-induced ischaemia scheduled for vascular surgery, revascularization did not improve survival (30 day/1 year). In this study, the patients have more significant coronary disease (75% have 3-vessel or LMS disease)

PCI prior to non-cardiac surgery

- Again, it is not indicated just to "get the patient through" a noncardiac surgery (NCS) if it is not indicated in its own right
- In fact, PCI performed shortly before NCS have potential problems:
  - NCS carries increased risk when undertaken within short time of PCI
    - A prospective analysis by Vicenzi et al of 103 patients having NCS within 12 months of PCI documented 44% complication rate with majority of these events being cardiac. This risk is especially high with PCI done <35 days before NCS
  - Need to maintain dual antiplatelet therapy, especially for drug-eluting stent (DES) means increased risk of surgical bleeding
    - With aspirin + clopidogrel → 30-50% increase in surgical blood loss, rate of RBC transfusion increased by ~30%. No increase in surgical mortality is observed (except for intracranial surgery).
  - If antiplatelet therapy is discontinued, there is risk of stent thrombosis
    - Rebound hypercoagubility + procoagulant effect associated with surgery
    - MI due to stent thrombosis carries high mortality 20-40%
    - Significantly increase perioperative cardiac death rate by 5-10x


Acute MI, high-risk ACS, or high-risk cardiac anatomy
Bleeding risk of surgery
Low
Stent and continued dual-antiplatelet therapy
Not low
Timing of Surgery
14 to 29 days
30 to 365 days
Greater than 365 days
Balloon angioplasty
Bare-metal stent
Drug-eluting stent


Patients with aspirin (75–150 mg day⁻¹)
Patients with aspirin (75–150 mg day⁻¹) + clopidogrel (75 mg day⁻¹)
Primary prevention
Secondary prevention after MI, ACS, stent, stroke, PAD
High-risk situations: <6 weeks after MI, PCI, BMS, stroke <12 months after DES High-risk stents*
Low-risk situations**
Intracranial neurosurgery
All surgery
Only vital surgery
All surgery
Risk of bleeding in closed space***
Stop 7 days before operation as needed
Operation under continuous treatment
Stop clopidogrel Maintain aspirin


Previous PCI
Balloon angioplasty
Bare-metal stent
Drug-eluting stent
Time since PCI
<14 days
>14 days
>30-45 days
<30-45 days
<365 days
>365 days
Delay for elective or nonurgent surgery
Proceed to the operation room with aspirin
Delay for elective or nonurgent surgery
Proceed to the operating room with aspirin

Risk reduction strategy- pharmacological β blocker

- **Proposed mechanism of protective effect**
  - Dec HR, contractility and wall tension
    - Dec myocardial O2 consumption
    - Dec shear stress at vulnerable plaque
  - Anti-arrhythmic effect
  - Dec activation of renin/aldosterone/angiotensin
  - Shift in energy substrate use from fatty acid to more energy efficient glucose
  - Anti-inflammatory effect promoting plaque stabilization
  - Remodelling of LV
  - Redistribution of coronary blood flow to myocardium at risk

β -blocker- Pros

- Mangano (1996)
  - 200 patients with risk factors for IHD, elective NCS
  - Atenolol (immediately prior to surgery+post op x 7 days) vs placebo
  - Reduction in cardiac events 6-8 months after surgery
  - However
    - In-hospital cardiac event/mortality is not improved
    - Control group contains patients who have abrupt cessation of β Blocker, which may have been a confounding factor

- DECREASE I trial, Poldermans (1999)
  - High risk patients (inducible ischaemia on DSE in one or more region)
  - High risk surgery -- aortic or peripheral vascular surgery
  - Low dose bisoprolol for at least 7 days preop + for 30 days postop, titrate to HR <70-80bpm vs placebo
  - Found 10x decrease in cardiac event (MI/death) in the beta blocker group ($p<0.001$) (34% vs 3.4%)

β -blocker- Cons

- POISE trial (2008)
  - 8351 patients with or at risk of IHD, scheduled for NCS
  - Randomized to metoprolol CR (fixed dose 100mg daily 2-4hours before OT + 200mg postop x 30 days) vs placebo
  - Not titrate to HR, withheld if HR <50, SBP <100
  - Result
    - Reduced cardiac death (5.8% vs 6.9%, p<0.04) and non-fatal MI (4.2% vs 5.7%, p<0.002)
    - Dec onset of new AF and need for coronary revascularization
    - More death in β B group (3.1% vs 2.3%, p<0.003)
    - More stroke in β B group (1% vs 0.5%, p<0.005)
  - For every 1000 patients on metoprolol CR
    - Prevents: 15 MI, 3 cardiac revascularization, 7 new AF
    - Extra: 8 deaths, 5 disabling stroke, 53 hypotension, 42 bradycardia
    - Hypotension is associated with increased mortality

- Criticism of POISE study
  - Dose regimen (metoprolol 100-200mg daily) is too large
  - Timing of starting may be too late (immediately pre-op)
    - Some potential benefit eg plaque stabilization require time to develop

AHA guideline (2007)

- Class I (ie should be given)
  - Patients currently taking beta-blocker
  - Patients to undergo vascular surgery + finding of myocardial ischaemia on preop testing
- Class IIa (ie probably recommended)
  - Patients to undergo vascular surgery + no previous preop testing or IHD identified but no ischaemia on testing or >1 clinical risk factor
  - patients to undergo intermediate risk surgery + >1 clinical risk factors or IHD identified preop
- Class IIb (ie usefulness not certain)
  - patients with single clinical risk factors for vascular/intermediate surgery
  - Patients with no clinical risk factors for vascular surgery

- Class III (ie harmful)
  - Contraindication to beta-blocker
- The AHA guideline was published before POISE study result was available
- Limitation in literature on perioperative beta-blocker
  - Few examined titration of therapy to effect (eg HR endpoint)
  - Optimal type and dose of beta-blocker not clear
  - Care-delivery system in the perioperative setting is not adequately studied (eg how, when, by whom, followup)
  - Studies on intermediate and low risk population lacking

Statin

- **Proposed mechanism of protective effect**
  - Improved lipid profile
    - Decrease circulating LDL-cholesterol
    - Decrease atherogenesis
  - Anti-inflammatory effect
  - Plaque stabilization
  - Anti-oxidant
  - Modulation of endovascular dysfunction
  - Effect on arterial smooth muscle proliferation
  - Prevent platelet activation

- A large meta-analysis (223010 patients) found preoperative statin therapy
  - Associated with 38% reduction in mortality after cardiac surgery
  - 59% reduction in mortality after vascular surgery
  - 44% reduction in mortality for non-cardiac surgery
- Combination of statin + beta-blocker seems to confer the largest risk reduction

Others

- α 2 agonist
  - Clonidine (given perioperatively to patients at risk of IHD was found to significantly reduce incidence of perioperative myocardial ischaemia and postoperative death (up to 2 years)
    - 0.2mg po + patch night before surgery
    - 0.2mg po on day of surgery
    - Patch remained on patient for 4 days
- Aspirin
  - Benefit in perioperative use in reducing cardiac risk is not clear
- Calcium channel blocker and TNG
  - Inconclusive result

- Anaesthetic preconditioning (APC)
  - Preconditioning = phenomenon whereby exposure to a physical or pharmacological stimulus reduces subsequent injury from ischaemia
  - Involves exposure of myocardium to halogenated volatile agent in order to attentuate subsequent injury due to ischaemia and reperfusion
    - Maximum effect seen at 1.5-2 MAC
    - As low as 0.25MAC may be protective
  - All currently used volatile anaesthetic are cardioprotective
    - Not related to beneficial effect on myocardial O2 balance due to its negative inotropy and chronotropy effect
    - This property extends to ischaemic tissue
  - Postulated mechanism
    - Triggering of intracellular signalling pathway leading to opening of mitrochondrial K_{ATP} channels

- Other drugs found to have pre-conditioning properties
  - Eg Morphine, Noradrenaline, adenosine, nicorandil
  - Morphine have synergistic effect with volatile agents

- In a recent meta-analysis involving ~3000 patients undergoing CABG, APC is found to be associated with
  - significantly lower troponin I
  - Reduced inotrope requirement
  - Reduced hospital length of stay
  - Did not reduce periop MI/death

When can patient be operated on after a recent MI ?

- First 6 weeks within an episode MI is of greatest risk
  - Heart takes 4-6 weeks for healing and remodelling
  - During this high risk period, vulnerable to arrhythmia and stunning
  - Haemodynamic stress and hypercoagulability associated with surgery → increase risk of extention of infarct and precipitate other cardiac complication
- Between 6 weeks to 3 months
  - Period of intermediate risk
- Factors to consider
  - Urgency of surgery
  - Size of infarct
  - Ongoing symptoms and complications
  - Functional status

When to give IE prophylaxis?

Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
Previous IE
Congenital heart disease (CHD) • Unrepaired cyanotic CHD, including palliative shunts and conduits • Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure • Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
Cardiac transplantation recipients who develop cardiac valvulopathy

Endothelization of prosthetic material occurs within 6 months after procedure

- Change in guideline based on
  - Risk of acquiring IE is much more likely during daily activities than during a specific surgical procedure
  - Even if prophylaxis is 100% effective, only an extremely small number of cases of IE can be prevented
  - Prophylaxis is reasonable in the presence of these cardiac conditions for
    - Dental procedure
    - Respiratory tract procedure
    - Infected skin/musculoskeletal
  - Not recommended for GU or GI procedure

Optimization of respiratory system

Preoperative Factors Associated with Increased Risk of Postoperative Respiratory Failure

History
Age >70 years
Smoking history with chronic obstructive pulmonary disease
Cardiac dysfunction
Neuromuscular disease
Poor functional status/dyspnea with light exertion
Physical Findings
Increased baseline work of breathing
Preoperative wheezing (not controlled by bronchodilators)
Lower extremity edema/jugular venous distention (suggestive of right-side heart dysfunction)
Obesity
Cachexia
Laboratory
P_{CO_2} >45 mmHg
P_{O_2} <50 mmHg
ppoFEV_1 <40% predicted
ppoDLco <40% predicted
RV/TLC >30%
VO_2max <15 mL/kg/min

ppo, Predicted postoperative; *DLCO,* diffusion capacity for carbon monoxide; *FEV_1,* forced expiratory volume in one second; *RV,* residual volume; *TLC,* total lung capacity; *VO_2max,* maximum oxygen consumption.

Smoking:

- increases: airway irritability, secretions , closing volume
- decreases: mucociliary transport

Cessation of smoking:

2 days -- decreased carboxyHb, decrease intraop myocardial ischaemia

4 weeks: -- decreased wound complication

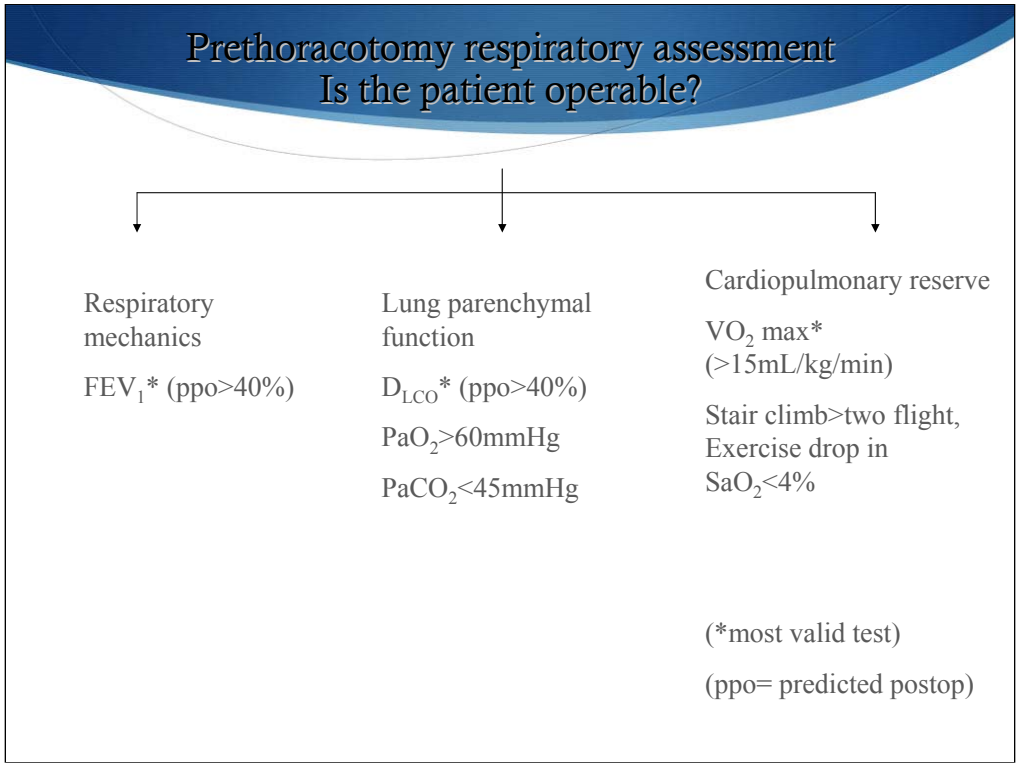
6-8 weeks -- decreased postop pulmonary complications

2-3 months -- improve ciliary function, CV, decreased sputum production

Probability for Preoperative Interventions to Reduce the Risk of Pulmonary Complications

Risk Factor	Intervention	Probability
Smoking	Cessation >8 weeks	++++
	Cessation <8 weeks	+
Exacerbation of COPD or asthma	Steroids, bronchodilators and delay elective surgery	++++
	Antibiotics indicated by sputum	+++
Stable COPD or asthma	Physiotherapy	++++
	Bronchodilators	+++
	Rehabilitation	++
Obesity	Physiotherapy	++++
	Weight loss	++
Malnutrition	Oral nutrition program	++

Physiotherapy → vibration / percussion, loosen secretion and allow to cough out, incentive spirometry
Bronchodilator in stable COPD/asthma→ especially beneficial in those with lots of sputum. Can also decrease atelectasis and its undesirable effect postop



VO2 max: maximum O2 consumption
Resectable tumour → is it operable??

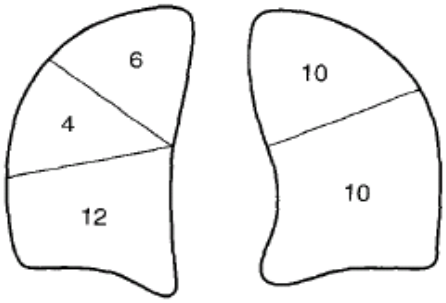


FIGURE 1-3 The number of subsegments of each lobe is used to calculate the predicted postoperative (ppo) pulmonary function. For example, after a right lower lobectomy, a patient with a preoperative FEV_1 (or DLCO) at 70% of normal would be expected to have a $ppoFEV_1$ = 70% × (1-29/100) = 50%. (From Slinger PD, Johnston MR: *J Cardiothorac Vasc Anesth* 14:202, 2000.)

Increased risk of Desaturation during One-lung Ventilation

- High percentage of ventilation or perfusion to the operative lung on preoperative V/Q scan
- Poor PaO_2 during two-lung ventilation, particularly in the lateral position intraoperatively
- Supine position during one-lung ventilation
- Right-sided thoracotomy
- Normal preoperative spirometry (FEV_1 or FVC) or restrictive lung disease
  - Auto-PEEP to dependent lung in obstructive lung disease

Postthoracotomy anaesthetic management

Predicted postoperative FEV_1

>40%	30%-40%	<30%
Extubate in operating room	Consider extubation based on: Exercise tolerance D_{LCO} V/Qscan Associated diseases	Staged weaning from mechanical ventilation Consider extubation if >20% plus: Thoracic epidural analgesia

Perioperative renal protection

Perioperative ARF

- Accounts for 20-25% of hospital-acquired renal failure
- Often associated with MODS, infection, prolonged ICU and hospital stay, progression to chronic renal failure, and increased mortality
- Full recovery from ARF in surgical setting only ~15%
- Vascular and cardiac surgeries are at particular risk of developing ARF
  - 1.1% cardiac surgical patients develop ARF requiring dialysis
  - ARF = independent predictor of mortality in post cardiac surgery and AAA repair
- ARF related to major surgery in patients with significant comorbidities common results in poor outcome

- Ischaemia or toxin mediated acute tubular necrosis (ATN) is the primary cause of perioperative acute renal failure
- Kidney is sensitive to effect of hypotension
- Heterogeneous pattern of flow and O2 requirement
  - Cortex: 90% of blood flow, 20% of O2 extraction
  - Medulla 10% of blood flow, 80% of O2 extraction
- Outer medulla susceptible to hypoxic injury
  - Thick ascending limb of Loop of Henle
  - Rate of active salt and water reabsorption is the main determinant of O2 requirement
- A combination of microvascular, tubular injury and ischaemia-reperfusion injury contributes to ATN

- Nephrotoxins
  - NSAID, ACE-I, IV contrast, aminoglycoside, beta-lactam antibiotics, amphotericin B, cyclosporin
- Cardiac and vascular surgery
  - Renal hypoperfusion outside limit of autoregulatory range (MAP 75-160mmHg) eg, during cardiopulmonary bypass, aortic cross-clamping
  - SIRS related cell-mediated cytotoxic injury
  - Renal embolic injury: eg aortic atheroma, thrombus, air, lipid tissue
  - Prolonged surgery produces hemolysis – haem derivatives cause renal tubular injury
  - Large dose of contrast associated with endovascular aortic repair

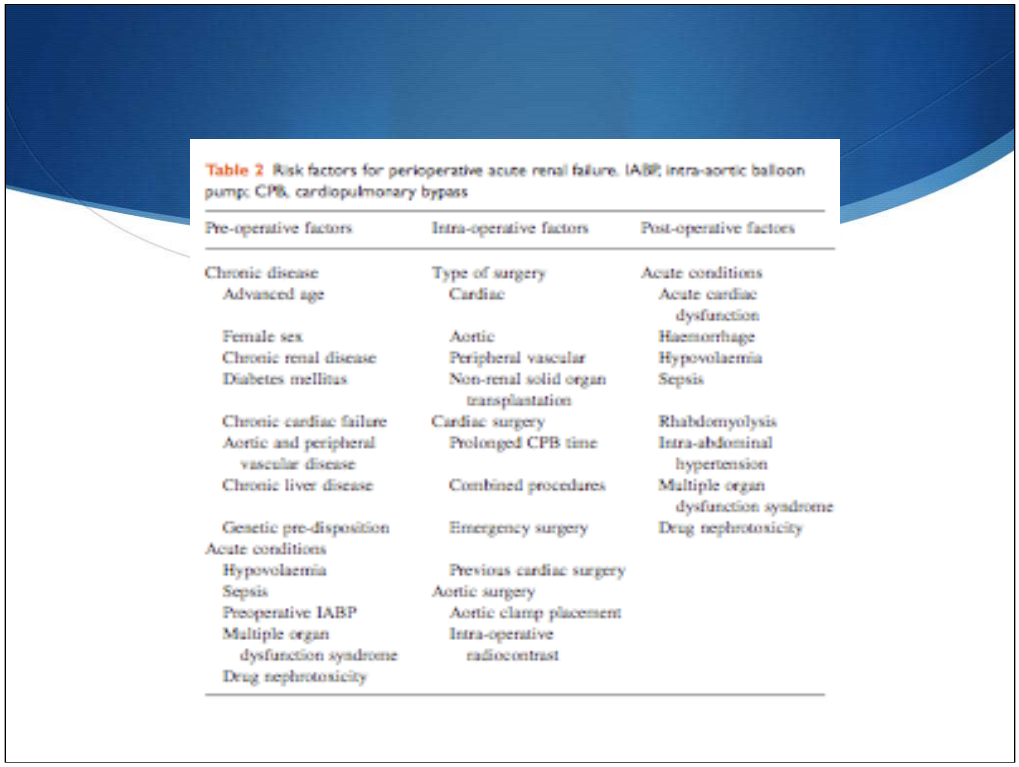


Table 2 Risk factors for perioperative acute renal failure. IABP, intra-aortic balloon pump; CPB, cardiopulmonary bypass

Pre-operative factors	Intra-operative factors	Post-operative factors
Chronic disease	Type of surgery	Acute conditions
Advanced age	Cardiac	Acute cardiac dysfunction
Female sex	Aortic	Haemorrhage
Chronic renal disease	Peripheral vascular	Hypovolaemia
Diabetes mellitus	Non-renal solid organ transplantation	Sepsis
Chronic cardiac failure	Cardiac surgery	Rhabdomyolysis
Aortic and peripheral vascular disease	Prolonged CPB time	Intra-abdominal hypertension
Chronic liver disease	Combined procedures	Multiple organ dysfunction syndrome
Genetic pre-disposition	Emergency surgery	Drug nephrotoxicity
Acute conditions	Previous cardiac surgery	
Hypovolaemia	Aortic surgery	
Sepsis	Aortic clamp placement	
Preoperative IABP	Intra-operative radiocontrast	
Multiple organ dysfunction syndrome		
Drug nephrotoxicity		

Nephrotoxin: bilirubin, myoglobin,Hb, and drugs (including anaesthetic agent halothane)

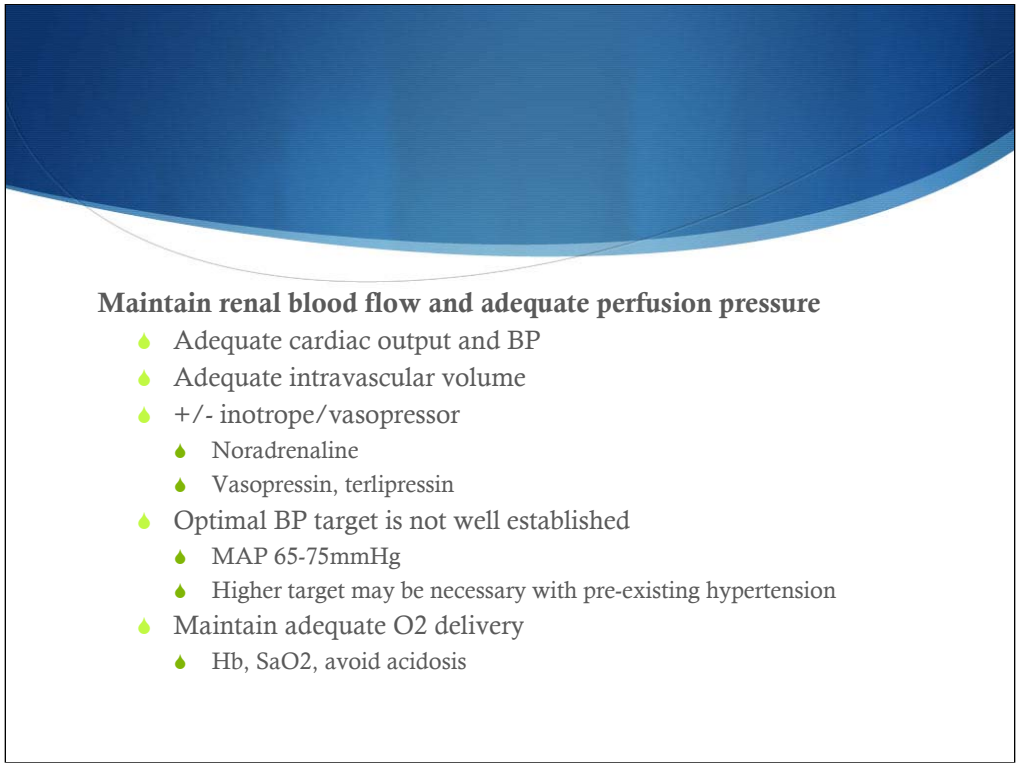
Prevention: Non-pharmacological

- Intravascular volume expansion
- Maintenance of renal blood flow and renal perfusion pressure
- Avoid nephrotoxic drugs
- Glycaemic control
- Prompt treatment of postoperative complications

Intravascular volume expansion

- Role of crystalloid vs colloid remains unclear
- Renal effect of different colloids have not been fully elucidated
  - Albumin and Gelatin appears to be safe in those with normal renal function
  - HES in setting of established renal impairment is not clear
    - Higher incidence of ARF associated with HES (vs LR) in critically ill septic patients demonstrated in one study
- Isotonic IV fluid expansion for prevention of contrast-induced nephropathy is beneficial
  - However ideal composition and optimal rate of infusion has not been determined
  - Use lowest possible volume of non-ionic, iso-osmolar contrast

- One example of protocol for endovascular AAA repair
  - N-acetycysteine 600mg BD x 2 days (starting on the day before OT)
  - NS 1ml/kg/hr after fasting
  - Dilute 8.4% NaHCO3 into 0.9% (ie 154mmol/L) with D5, give 3ml/kg/hr 1 hr before contrast, then 1ml/kg/hr for 6 hours afterwards



Noradr: no evidence that it compromises renal/hepatic/GI blood flow

Avoid nephrotoxic drug

- Eg NSAID, aprotinin
- Once daily aminoglycoside
- Lipid formulation of amphotericin B

Glycaemic control

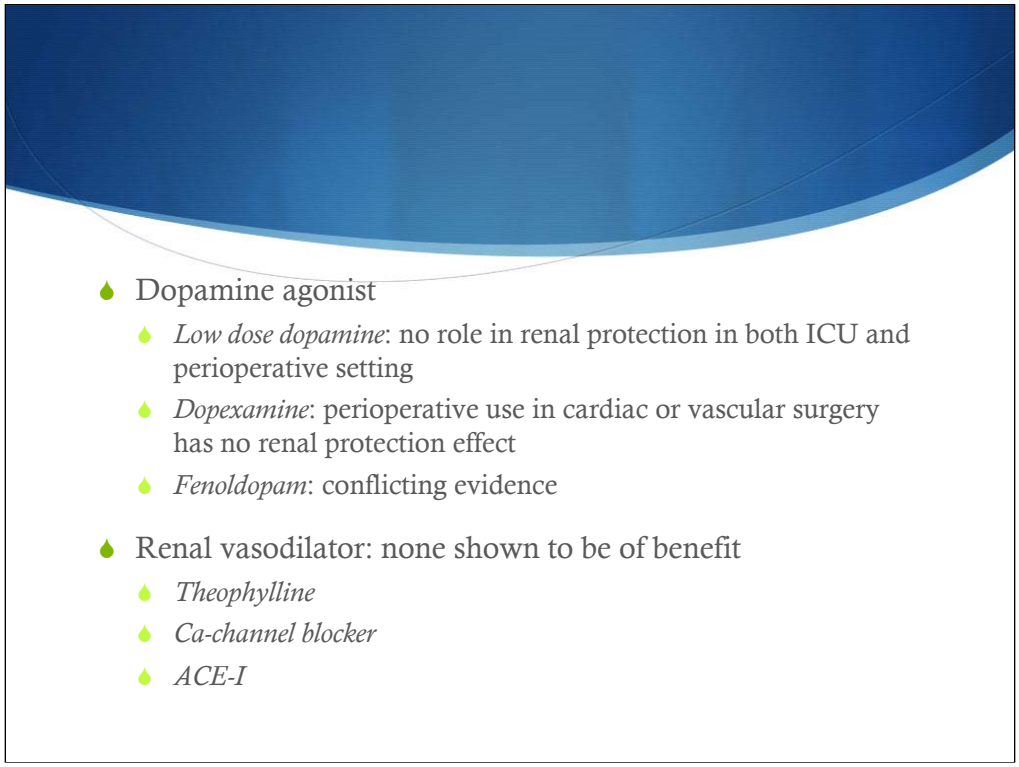
- Perioperative hyperglycaemia during cardiac and vascular surgery is associated with increased renal morbidity and overall mortality

Treatment of postoperative complication

- Acute cardiac dysfunction, hemorrhage
- Sepsis
- Rhabdomyolysis
- IAH

Prevention: pharmacological

- Postulated pathophysiology of ATN suggests that perioperative intervention that optimize renal O2 delivery may prevent ARF
- However despite extensive investigation, few, if any, drug interventions have been demonstrated to provide clinical benefit
- A 2005 Cochrane database review of 37 RCTs (1227 patients) concluded that there is no evidence that pharmacological interventions are effective in protecting renal function during surgery



Dopamine theoretically: dopaminergic renal vasodilation, beta mediated inc cardiac output, alpha mediated inc renal perfusion pressure
Dopexamine: synthetic dopamine analogue with beta adr and dopaminergic effect
Fenolopam: selective DA-1 , inc renal blood flow

- Diuretics
  - Increases urine output by decreasing tubular reabsorption (loop diuretic) or as osmotic diuretic (mannitol)
  - Increase tubular flow maintains patency and prevents obstruction and back-leak
  - Mannitol: free radical scavenging
  - Evidence for use of diuretic in surgical and ICU patients are scarce
    - Recent metaanalysis in 2007 including 5 RCTs (555 patients) did not demonstrate increased mortality in patients with ARF
    - Perioperative use of diuretic not shown to offer renal protection in cardiac surgery

Mannitol

- Used commonly in renal transplantation to decrease risk of allograft ARF
- Usually given before reperfusion of graft kidney to promote graft function, Dose: 12.5g-50g
- RCT in 1987 demonstrate that mannitol decrease postop ATN significantly
- Proposed mechanism
  - O2 free radical scavenger following reperfusion of allograft
  - Flushes out debris and prevent tubular cast
  - Intra-renal vasodilation
  - Preferential increase renal blood flow to renal medulla
- Side effects:
  - Rarely assoc with hyperK
  - High dose may be associated with hyperosmolar ATN (rare)

- N-acetylcysteine
  - Antioxidant
  - Substantial evidence to support prophylactic use in prevention of contrast nephropathy
  - In high risk patients in ICU or perioperative setting, not shown to have renal protective effect
- Natriuretic peptides
  - Natriuretic and diuretic effect by increasing glomerular perfusion pressure and filtration
  - Conflicting result on prevention of ARF

- Surgery-specific risk
  - Limit CPB and aortic cross-clamp time
  - CPB technique
    - eg maintain adequate flow and perfusion pressure
    - Avoid excessive hemodilution
    - Use of haemofiltration or leucodepletion during CPB

- Management of dialysis
  - HD: arrange before OT, alert with dysequilibrium syndrome
  - PD: continue before time of OT, drain PD fluid before OT
  - Recheck electrolyte after dialysis
- General optimization
  - fluid, electrolyte, acid base status
  - Hb
    - anaemia generally well tolerated with Hct>25%
    - Transfuse during dialysis if indicated
  - Platelet dysfunction
    - Partially corrected by dialysis
    - Consider ddAVP (IV 0.3mcg/kg in 50ml NS over 30mins)
  - Stress ulcer and aspiration prophylaxis

Glycaemic optimization

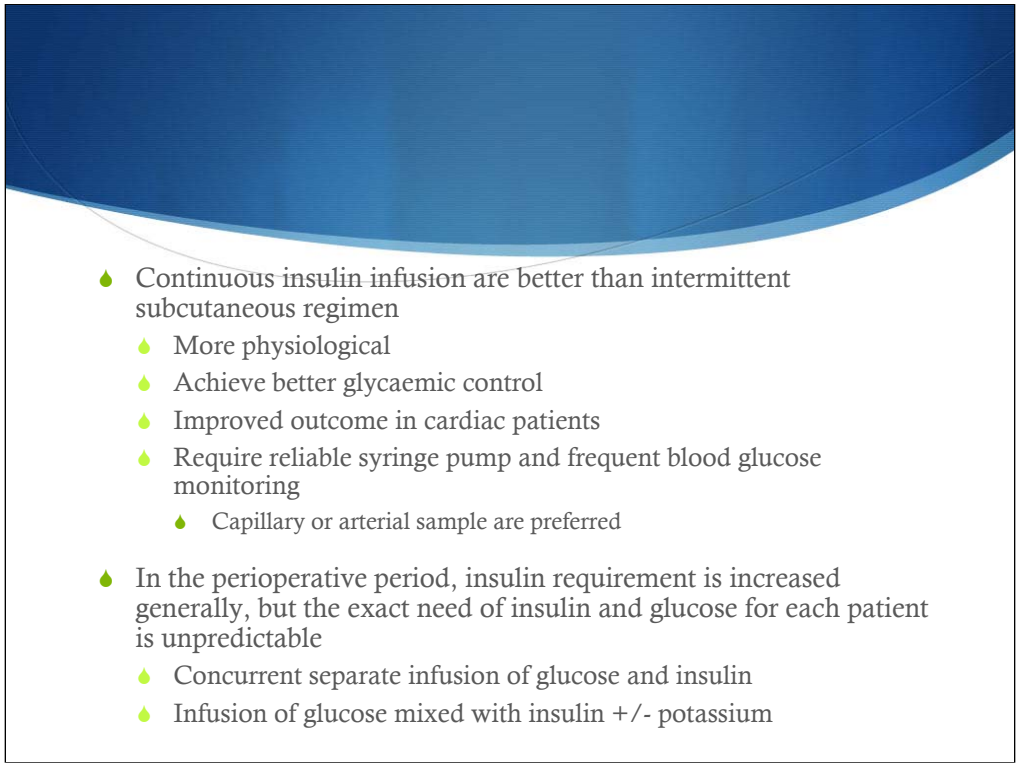
Diabetes

- DM are associated with micro- and macrovascular Cx
- Over-represented in surgical population
- Literature data predominantly on type 2 DM

- Perioperative problems posed by surgery in DM patients
  - Catabolism associated with stress response leads to hyperglycaemia and insulin resistance
  - Interruption of oral intake: fasting, GI surgery, post op gastric stasis
  - Altered consciousness may mask symptoms of hypoglycaemia
  - Circulatory disturbance associated with surgery and anaesthesia may alter the absorption of subcutaneous insulin

Infection: more related to perioperative glycaemic control rather than pre op HbA1c.

- Biguanide therapy (eg metformin) is reported to precipitate lactic acidosis
  - More likely in postoperative setting, elderly, associated renal and hepatic failure
  - Metformin should be stopped before elective surgery and insulin therapy started if required
  - For those presenting for emergency surgery, monitor for any metabolic derangement
- Sulphonylurea (eg diamicron) have potassium channel-blocking effect which may interfere with myocardial ischaemic preconditioning
  - In patients undergoing angioplasty, those receiving sulphonylurea have greater mortality and morbidity than those receiving insulin
  - Seems reasonable to convert to insulin several days before cardiac or other major surgery where myocardial perfusion may be compromised



Concurrent sep infusion: provide better control and more acceptable to nursing staff, but risk of discontinuing one infusion accidentally
Infusion of premixed: inherent safety

- Glycaemic target? -- Optimal target remains unclear
  - In cardiothoracic surgical patients (DM or non-DM), intensive perioperative glycaemic monitor + administration of insulin infusion to achieve glycaemic target of 4.5-6.1mmol/L is associated with better outcomes in terms of morbidity and mortality
    - Eg decreased incidence of mediastinitis
    - Improved white cell function → less infection
  - For other surgeries the risk of prolonged perioperative hyperglycaemia are less well established
    - Potential risk: wound infection, impaired wound healing, graft rejection

- Study by van den Berghe (2001) showed a tight glycaemic target of 4.4-6.1mmol/L has an improved outcome in ICU patients (predominantly postop cardiothoracic) (vs conventional target of <12mmol/dL)
- However recently, NICE-SUGAR study (2009) showed intensive glucose control (4.5-6mmol/dL) is associated with increased mortality in ICU patients (medical + surgical ICU), and increased risk of severe hypoglycaemia

Perioperative steroid replacement

- Appropriate cortisol surge after surgery is thought to be protective
  - anti-inflammatory
  - prevents hypotension
- Loss of this surge may precipitate intraoperative and postoperative haemodynamic stability
- Adults secretes
  - 75-150mg /day cortisol in response to major surgery
  - 50mg /day for minor surgery
- Concern that patients on long term steroid have suppressed hypothalamic-pituitary-adrenal axis causing insufficient cortisol secretion
- In a review of perioperative haemodynamic instability <1% f cases are attributed to glucocorticoid insufficiency

- For patients on long term steroid >10mg prednisolone daily within last 3 months, physiological replacement regimen is recommended
  - Alternative would be to perform preop testing
- It is not advisable to prescribe supraphysiological amounts of steroid to this group of patients
  - Current evidence suggest that physiological amounts are sufficient
  - Side effect of excessive steroid
    - Impaired wound healing
    - Hyperglycaemia
    - Immunosuppression
    - Hypertension, fluid overload
    - Psychosis

PATIENTS WHOSE HAVE RECEIVED A REGULAR DAILY DOSE OF MORE THAN 10MG PREDNISOLONE OR EQUIVALENT IN THE LAST THREE MONTHS	
Minor Surgery *(hernias, hands)*	25mg Hydrocortisone at induction
Moderate Surgery *(hysterectomy)*	Usual pre-op steroids + 25mg Hydrocortisone at induction +100mg hydrocortisone/day
Major Surgery *(major trauma, prolonged surgery, or surgery where there is delayed oral intake)*	Usual pre-op steroids + 25mg Hydrocortisone at induction +100mg hydrocortisone/day for 2-3 days Resume normal oral therapy when gastrointestinal function has returned
ALL OTHER PATIENTS - no additional steroids required.	

- The regimen is based on physiological requirement of stressed controls in human studies
- Physiological substitution regimen in adrenal insufficient patient results in circulating cortisol values greater than that in normal patients
  - Sufficient to prevent intraop hemodynamic instability