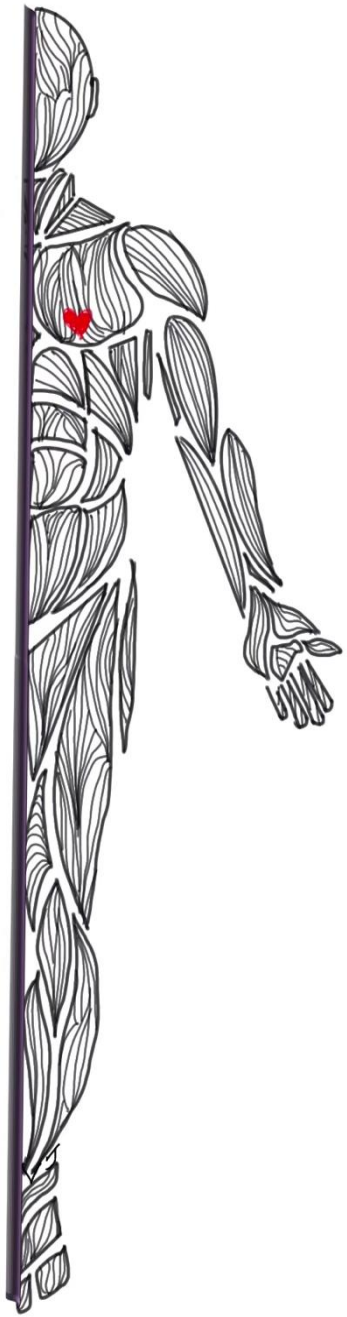
Medical Consult Handbook



Yayi Huang MD FRCPC

2022 Edition

UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

PREFACE

The Medical Consult service provides Internal Medicine consultations in the emergency department, non-medical inpatient units, and outpatient clinics. It necessitates competency in a wide variety of complex conditions with a unique emphasis on perioperative medicine. The Medical Consult Handbook is a compact resource based on common clinical scenarios designed to enhance the consultancy skills of trainees and provide quick on-the-go reference wherever needed.

The making of the 2022 edition of the handbook has truly been a multifaceted effort. Over 50 chapter editors, including residents, fellows, and faculty members, from across hospitals and disciplines contributed to this immense endeavour. Collectively, 25 sections were updated and 9 new chapters were created. A special thanks to Ian Downie, Samik Doshi, and Jennifer Korman for reviewing the handbook, and Vivien Jordan for the whimsical front cover illustration.

The Medical Consult Handbook has been fortunate to receive the support of the Mount Sinai Hospital Innovation in Education Award. This will help tremendously with the dissemination of this valuable content within the University of Toronto and beyond.

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PREVIOUS EDITIONS

1ST edition – combined SMH/MSH/UHN - May 2009
2nd edition – Sep 2009
3rd edition – Feb 2010
4th edition – Aug 2011
5th edition – Feb 2012
6th edition – Feb 2013
7th edition – Jan 2016
8th edition Jun 2017
SMH – Nov 2008, Oct 2007, June 2006, 2005
MSH/UHN – Sep 2008, Mar 2008, 2007, 2005

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1. Effective Consultation Skills

Author: Kevin Venus MD FRCPC

Introduction

The performance of medical consultations, in either hospital or ambulatory care settings, is a core role of general internists and subspecialists. Consultancy skills are "the ability to elicit a complete and pertinent history from a patient, combine this information with relevant findings on physical examination, and develop an effective, appropriate, timely and safe plan of investigation and treatment, in an organized fashion. A competent consultant must be able to communicate this information clearly and concisely to the referring physician, to the rest of the health care team, and to patients and their families".[1]

Reasons for Referral

One of the challenges of performing internal medicine consultation is that the consultant is approaching the clinical problem from a generalist's viewpoint. Internal medicine physicians are well suited to provide care/management suggestions for many dimensions of a patient's illness, in contrast to subspecialists who have a narrower scope of practice. This can lead to confusion about what the boundaries of the consultant's role are, or what the referring clinician desires.

Consultations may be requested for assistance in diagnosis and/or management, to obtain access to special tests, procedures, or other special services, or to arrange follow-up for patients with chronic conditions. Consultations may also be requested as a knee-jerk reaction to a new diagnosis, for medical-legal reason, to reconcile conflicting advice from other consultants, as a courtesy, or simply to share responsibility for ongoing care.[2]

Medical co-management/shared care is increasingly requested by surgeons, in which the consultant addresses all necessary medical aspects of the patient's care, writes/enters orders independently and conducts daily assessments.

The first essential step in the consultation process, therefore, is to clearly identify the specific question to address and/or service to be provided. Ongoing periodic direct contact between referring physicians and consultants in turn will improve not only communication, but also prevent misunderstandings, and significantly enhance implementation of recommendations.[2-4]

Consultation Responses

While the scope of consultation suggestion will depend on the clinical question raised, there are some key features of recommendations that are appreciated by referring clinicians and increase the likelihood of their being adopted.

These include:

1. Concise recommendations
2. Explanation of rationale behind decision-making
3. Contingency planning based on current recommendations
4. Description of the importance/urgency of the recommendations
5. A discussion of follow-up plan, both for the remainder of the patient's hospitalization and after discharge[5,6]

Patient Orders

Except in the event of a medical emergency, consultation services should always communicate directly with referring physicians to clarify specific roles and responsibilities, before directly entering patient orders. There has been a growing tendency for consultants to enter orders directly for further investigation and/or treatment on referred patients, to facilitate compliance, and to make sure that recommendations are implemented immediately. This practice has become particularly common with medical consultations on surgical patients, since surgeons may be unavailable for prolonged periods in the OR, and/or may simply prefer to have medical consultation services deal with medical problems directly.[7,8]

However, shared care approaches to management can potentially lead to misunderstanding and in turn risks about who is responsible for specific investigations and treatments, raising concerns about safety and liability. There remain wide discrepancies among physician groups, including family physicians, internists and different surgical specialties, about their expectations and preferences re: consultants writing orders on their patients.[5,7] As a result, consultation services should always document their specific recommendations for investigation and treatment in the consultation note, and whenever possible transmit this information directly to referring physicians.

Ideally, the division of responsibilities, including order entry, should be established at the time of the consultation. This is an important component of the initial discussion between referring clinician and consultant at the time of consultation.

Follow-up

The duration of in-hospital follow-up will vary for patients depending on their medical context, as well as the initial referral question. Consultants will determine at some point that their input is either redundant or does not benefit the patient any further and sign-off. When this occurs will vary, depending in part on the scope of clinical problem being addressed. The frequency of in-hospital follow-up will vary with individual practice and clinical context but should be communicated to the referring physician. As part of the consultation service, ambulatory follow-up should be offered and organized in situations that warrant it.

At the time a consultant signs-off, they should communicate any further recommendations, including when to re-refer the patient and give details about follow-up they have organized.

Specific Considerations for Perioperative Medical Consultations

Perioperative consultation constitutes the bulk of in-hospital internal medicine consultation requests. Consults can be requested immediately before or after surgery, or at any point during a patient's postoperative recovery.

A patient's *total perioperative risk* is subdivided into *intrinsic risk* and *modifiable risk*. The relative proportions of both of these parameters will depend on the patient's underlying medical conditions, urgency of the surgery and the planned surgical procedure. The ultimate goal of preoperative medical consultation is to reduce the amount of modifiable risk as much as possible.

Both referring physicians and consultants should avoid using terminology such as "medical clearance" or "optimization" as they can lead to internists, surgeons and patients have different views on what the total perioperative risk entails. "Medical clearance" is an inaccurate term as it can mistakenly convey that modifiable risk has been completely negated. "Optimization" is intuitively more appealing as it expresses an active process of decision-making, but since most preoperative interventions have not been conclusively shown to reduce postoperative adverse events, it can lead to false assurances. Importantly, neither of these terms explicitly communicate a risk estimate.[9,10]

While there are important shortcomings of risk estimation tools (i.e. RCRI), a comprehensive preoperative consultation should communicate what the patient's risk of postoperative adverse events (cardiac, pulmonary etc.) and if the tools used to develop the risk estimate likely resulted in an over- or underestimation. Clear communication with the

patient and referring surgeon is paramount to ensure informed shared decision-making.

Summary/Recommendations

To simplify these issues and recommendations, Goldman, Lee and Rudd published the "Ten Commandments for Effective Consultation" in the 1980's.[11] More recently, Salerno and colleagues produced a modified list of commandments, reflecting the evolving role of consultants and consultation services over the last two decades, as summarized below[5]:

Table 1 - Modified Ten Commandments for effective consultations

Commandment	Meaning
1. Determine your customer	Ask the requesting physician how you can best help them if a specific question is not obvious; they may want co-management.
2. Establish urgency	The consultant must determine whether the consultation is emergent, urgent, or elective.
3. Look for yourself	The consultants are most effective when they are willing to gather data on their own.
4. Be as brief as appropriate	The consultant need not repeat in full detail the data that were already recorded.
5. Be specific, thorough, and descend from thy ivory tower to help when requested	Leave as many specific recommendations as needed to answer the consult but ask the requesting physician if they need help with order writing.
6. Provide contingency plans and discuss their execution	Consultants should anticipate potential problems, document contingency plans, and provide a 24-h point of contact to help execute the plans if requested.
7. Thou may negotiate joint title to thy neighbor's turf	Consultants can and should co-manage any facet of patient care that the requesting physician desires, a frank discussion defining which specialty is responsible for what aspects of patient care is needed.
8. Teach with tact and pragmatism	Judgments on leaving references should be tailored to the requesting physician's specialty, level of training, and urgency of the consult.
9. Talk is essential	There is no substitute for direct personal contact with the primary physician.
10. Follow-up daily	Daily written follow-up is desirable; when the patient's problems are not active, the consultant should discuss signing-off with the requesting physician beforehand.

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Preoperative Consultation Template

Courtesy of Mirek Otremba MD FRCPC

MOUNT SINAI HOSPITAL
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Patient identification

Pre-operative medical consultation

Age _____ ☐ Male ☐ Female

Medical history

Cardiovascular

- ☐ Angina/CAD _____
- ☐ MI _____
- ☐ CABG _____
- ☐ PCI _____
- ☐ CHF _____
- ☐ Valvular ds _____
- ☐ Arrhythmia _____
- ☐ Hypertension _____
- ☐ PVD _____
- ☐ Other _____

Other

_____

Respiratory

- ☐ Asthma _____
- ☐ COPD _____
- ☐ Sleep apnea _____
- ☐ Other _____

Endocrine

- ☐ DM 1 ☐ DM 2 _____
- ☐ Hyperlipidemia _____
- ☐ Hyperthyroid _____
- ☐ Hypothyroid _____
- ☐ Steroid use _____
- ☐ Obesity _____
- ☐ Other _____

Renal

- ☐ CRF Cr= _____
- ☐ ESRD/HD/PD _____
- ☐ Other _____

GI

- ☐ Liver ds _____
- ☐ GERD _____
- ☐ Other _____

Neurologic

- ☐ Seizures _____
- ☐ TIA/CVA _____
- ☐ Other _____

Medications

- ☐ ASA _____ _____
- ☐ Clopidogrel _____ _____
- ☐ Warfarin _____ _____

_____ _____

_____ _____

_____ _____

_____ _____

Allergies

_____

_____

_____

_____

_____

_____

_____

Surgical History

_____

_____

_____

_____

_____

_____

_____

History of Present Illness

Patient activity level	METS
Sitting, light activity	1.5
Walking, 2 mins	2.5
Walking, 20 mins	3.0
Household tasks	3.5
Vacuuming	3.5
Raking lawn	4.0
1 fl stairs, walk 2 blocks	4.0
Gardening	4.4
Mowing lawn (power)	4.5
Social dancing	4.5
Jogging	7.0

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Patient identification

Pre-operative medical consultation

Family & Social History

	No	Yes	Details
Smoking:	☐	☐	
Alcohol:	☐	☐	
Drugs:	☐	☐	

Physical Exam

BP mmHg _____ Pulse _____ RR _____ SaO_2 % _____ Weight _____ BMI _____

ECG

ECHO/Stress/Cath

Labs

Surgery Specific Risk (AHA defn)
High > 5%
Emergent major operations
Aortic & other major vascular surgery
Peripheral vascular surgery
Intermediate 1 - 5%
Carotid endarterectomy
Head and Neck surgery
Intraperitoneal/intrathoracic surgery
Orthopedic surgery
Prostate surgery
Low < 1%
Endoscopic procedure
Superficial procedure
Cataract surgery
Breast surgery

Revised Cardiac Risk Index
1. High Risk Surgery (see below***)
2. Ischemic heart disease
3. CHF history
4. TIA/Stroke history
5. DM on insulin
6. Creatinine > 172 umol/L

***Unlike AHA, RCRI defines high risk surgery as suprainguinal vascular, intraperitoneal, or intrathoracic

Cardiac Risk	
# of risk factors	Event Rate (%)
0	3.9
1	6.0
2	10.1
3+	15.0

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Patient identification

Pre-operative medical consultation

Overall clinical summary

Dear Doctor _____

This is a _____ year-old going for _____ surgery on the date of _____

The surgery-specific probability of serious peri-operative cardiac complications is (%) _____

Perioperative (RCRI/Lee) cardiac risk is around _____ **%** **Low** ○ ○ ○ ○ ○ **High**

risk of cardiac complications.

Issues and related plan (full dictated note to follow)	
1. Testing required	
2. Cardiac optimization	
3. DM management	
4. Pulmonary management	
5. Endocarditis prophylaxis	
6. VTE prophylaxis & anticoagulant management	
7. Corticosteroid prophylaxis	
8. Medication management	

○ **Proceed with Surgery** ○ **Delay Surgery until patient optimized**

Follow up:

○ We'll **see patient again in clinic before** planned surgery
○ Please call the Medical Consult Resident **when patient is admitted**.
○ Please call the Medical Consult Resident **if you need assistance.**

Name _____ Signature _____ Staff _____

2. Anesthetic Record

Authors: Zaid Sweidan MDCM, Marcus Salvatori MD FRCPC

Introduction

All monitored physiologic variables should be charted at intervals appropriate to the clinical circumstances. Heart rate and blood pressure should be recorded at least every five minutes. Oxygen saturation must be monitored continuously and should be recorded at frequent intervals, at a minimum of every five minutes, for all patients. End-tidal carbon dioxide concentration must be monitored continuously and recorded at frequent intervals if the trachea is intubated or a supraglottic device is in situ. Reasons for deviation from these charting guidelines should be documented in the anesthetic record. Monitors, equipment, and techniques, as well as time, dose, and route of all drugs and intravenous fluids should be recorded. All other relevant intraoperative anesthesia care and events, including unexpected or adverse events, should be as well.

1. Preoperative Evaluation
    a. Specific focus on diseases as they relate to perioperative management.
    b. Focused cardiovascular and respiratory examination. Neurological if planned regional/neuraxial technique.
    c. Specific examination of the airway to identify need for special equipment.
    d. Discussion of risks/planned OR interventions. Consent for anesthesia is implied based on surgery, however, patients are often informed of specifics including invasive monitors, difficult airway management, regional nerve block techniques, perioperative pain management, and ICU care.
    e. Medication Management
        i. Regular medications are administered on the morning of surgery except ACEI/ARB (these may be associated with excessive hypotension following induction).
        ii. Anticoagulation is ideally held prior to most procedures (to minimize risk of blood loss and complications) and always held prior to procedures involving neuraxial anesthetic techniques. How long anticoagulation is held depends on agent (see Chapter 16).

2. Intraoperative Care
    a. Documentation of monitors, patient positioning, access, and airway/ventilatory management.

i. Cormack Lehane grading scale on intubation:
    1. Grade 1 – full view of glottic opening.
    2. Grade 2 – only posterior portion of glottis/arytenoid cartilages.
    3. Grade 3 – only epiglottis. No glottis.
    4. Grade 4 – neither epiglottis nor glottis.

b. If invasive monitors placed/regional anesthesia used, expect a description of the technique and outcomes.
c. Documentation:
    i. Time proceeds horizontally with events charted vertically at the corresponding time.
    ii. Vitals are most commonly recorded at 5 minute intervals:
        1. Vitals are often an average/approximation because of considerable minute-to-minute variation
        2. Blood pressure management must balance end organ perfusion and operative requirements. Induced hypotension may be required to minimize bleeding for vascular anastomosis and small surgical spaces.
d. Ventilation:
    i. Principle causes of hypoxic brain damage and death during anesthesia are related to ventilation and/or oxygenation.
    ii. Expect documentation of ventilatory modes, gas exchange, and monitored parameters.
e. Fluid Administration:
    i. Shorthand description of fluid and volume.
    ii. Administration time noted by horizontal line/brackets.
f. Losses:
    i. Blood loss is an approximation. Losses through suction and weighed sponges are quantifiable - drapes and floor less so.
    ii. Intraoperative urine output does not reliably predict postoperative AKI.
        1. Urine output may be manipulated intraoperatively using diuretics. Common scenarios: e.g. priming of cardiopulmonary bypass machine, raised ICP, or prevention of TACO.

2. Surgical stress induces ADH release and reduces hourly rates.

3. Anesthetic agents
    a. Accomplished using a mixture of medications:
        i. Benzodiazepines for anxiolysis and amnesia.
        ii. Opioids for analgesia.
        iii. Propofol/Ketamine for induction.
        iv. Paralytic to improve intubation/surgical conditions.
    b. Maintenance of anesthesia is often accomplished using an inhaled anesthetic agent:
        i. Depth of anesthesia is recorded as either gas concentration or Minimum Alveolar Concentration (MAC).
            1. One MAC is the concentration of gas required to prevent movement in 50% of subjects exposed to a surgical stimulus. This allows comparison between gasses of different potency.
    c. Effects of Anesthesia Agents:
        i. Predominately vasodilation and myocardial depression
            1. Intravenous fluids and/or vasopressors/inotropes are used to restore blood pressure and cardiac output.

4. Cardiopulmonary Bypass (TGH and Sunnybrook only):
    a. Via venous cannulation of right atrium or SVC/IVC and arterial cannulation of aorta, the heart and lungs can be deflated to provide a still and 'bloodless' surgical field.
    b. Toronto centers generally use a non-pulsatile pump that delivers flow calculated to the patients BSA.
        i. As CPB takes over, the pulse pressure disappears, and a single blood pressure prevails.
        ii. Blood pressure is manipulated via SVR – minimal changes are made to flows.
    c. 'Prime' is the fluid mixture used to setup the pump prior to patient connection.
    d. Ultrafiltration and dialysis can be applied during CPB. This must be balanced against hemodynamic stability. Can also be used to prevent TACO.
    e. Temperature can be controlled actively if desired. Hypothermia provides organ protection by minimizing

oxygen consumption but increases likelihood of coagulopathy and infection.

f. Induces a state of vasoconstriction, pro inflammation, and activation/depletion of coagulation factors. Impaired platelet function is also a direct consequence.
g. Separation from CPB is often associated with vasoplegia, and direct acting vasoconstrictors may be necessary.
h. Duration of CPB is associated with increased complications: including, mortality, kidney injury, stroke, and bleeding.

5. Regional Anesthesia
    a. Bupivicaine 0.25% or Ropivicaine 0.2% are often used for postoperative analgesia.
        i. If used epidurally, local anesthesia produces dose dependent sympathectomy: two effects are vasodilation and faster return of bowel function.
        ii. Addition of opioids or epinephrine help prolong and deepen the block.
    b. Bupivicaine 0.5%, Ropivicaine >0.5%, or Lidocaine 2% are used for surgical anesthesia.
    c. Block height/effect can be assessed using cold temperature discrimination across dermatomes.

6. Postoperative
        i. The focus is on ABCs and surgical stability. Analgesia and postoperative nausea/vomiting should also be controlled.

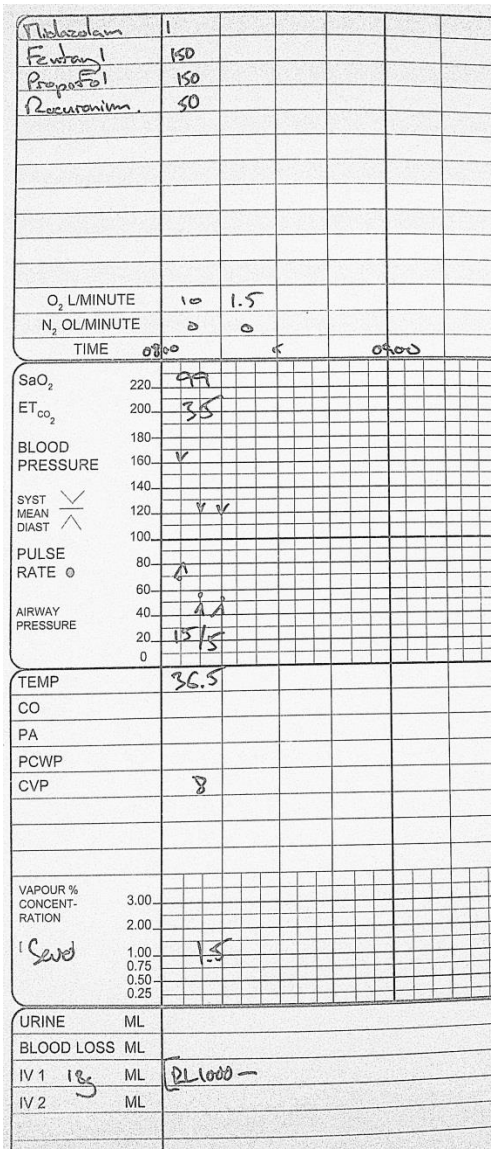

Figure 1 - Sample Anesthetic Record

In this example:

Midazolam 1mg was administered shortly after 0800, followed by Fentanyl 150ug, Propofol 150mg, and Rocuronium 50mg.

Fresh gas flows were initially 10 l/min but decreased to 1.5 l/min after intubation.

Saturation averaged 99% over 15 min.

End Tidal CO2 measured 35mmHg over 15 min.

At 0805: BP was 160/80 mmHg and HR was 70 bpm.

At 0810: BP was 120/45 and HR was 60 bpm.

Temperature was 36.5ºC; CVP was 8mmHg and Airway pressures were 15mmHg with a PEEP of 5mmHg.

The concentration of sevoflurane was 1.5% at approximately 0810.

Ringer's Lactate 1000mL started approximate 0800 and is still running.

ii.

3. Cardiac Risk Assessment

Authors: Kevin Singh MD MClSc FRCPC, Sherif Youssef MD FRCPC

Key Guideline: 2017 Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management of Patients Who Undergo Noncardiac Surgery[1]

Preoperative cardiac risk assessment **should be** conducted in patients undergoing elective non-cardiac surgery and requiring at least overnight admission who are:

- 45 years of age and older

OR

- 18-44 years of age with known significant cardiac disease, including:
  - Coronary Artery Disease
  - Cerebral Vascular Disease
  - Peripheral Arterial Disease
  - Congestive Heart Failure
  - Severe Pulmonary Hypertension
  - Severe obstructive cardiac disease (aortic stenosis, mitral stenosis, HOCM)

Preoperative cardiac risk assessment **should not be** conducted in patients undergoing emergent non-cardiac surgery.

Preoperative cardiac risk assessment **should be** conducted in patients undergoing urgent/semi-urgent surgery if there is an unstable cardiac condition or suspected obstructive cardiac disease.

Definitions:

Emergency surgery	Acute life- or limb-threatening condition, such as severe trauma or ruptured aortic aneurysm. Should be performed in hours.
Urgent surgery	Examples include hip fracture or bowel obstruction. Performed in hours to 1-2 days.
Semi-urgent surgery	Should be performed within 4—6 weeks. Examples include cancer surgery
Elective surgery	Could be delayed up to 1 year. Examples include knee or hip replacements

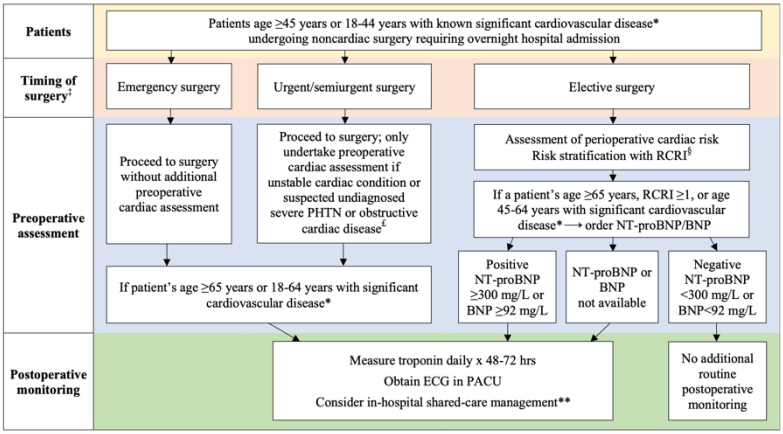

Figure 1 - 2017 CCS Perioperative Algorithm[1]

Preoperative cardiac risk stratification should be conducted using the **Revised Cardiac Risk Index**. Each factor listed below is worth 1 point, with the total score providing a cardiac risk estimate as per Table 1.

1. High-risk surgery
    a. Intraperitoneal, intrathoracic or suprainguinal vascular
2. History of ischemic heart disease
    a. any of: MI, positive stress test, current complaint of anginal chest pain, nitrate use, or Q waves on ECG
3. History of congestive heart failure
    a. Hx of CHF or any of pulmonary edema, history of PND, bilateral rales or S3 gallop or CXR showing vascular redistribution
4. History of cerebrovascular disease
5. Insulin therapy for diabetes
6. Preoperative serum creatinine > 177 µmol/L

Table 1 - Major cardiac risk estimates based on external validation studies of the RCRI. The major cardiac complications included myocardial infarction, cardiac arrest, and death.

# Risk factors	Risk estimate (%) with 95% CI Contemporary Studies (Troponin) Population event rate 7%
0	3.9 (2.8 – 5.4)
1	6.0 (4.9 – 7.4)
2	10.1 (8.1 – 12.6)
3+	15.0 (11.1 – 20.0)

The main benefit of the revised RCRI is its ease of use and its predictive ability with respect to death, myocardial infarction, and all-cause mortality. The risk estimates for these outcomes have been updated by the CCS to reflect the higher rates of cardiac outcomes observed in patients with lower RCRI scores (2 or less). The revised RCRI also performs similarly when compared to other cardiovascular risk indices measuring similar outcomes. However, the main limitation of the RCRI is that it does not capture or predict other clinical outcomes which may be important, such as heart failure, heart block, etc.

Predicting exercise capacity

Functional limitation due to cardiovascular disease is a major predictor of perioperative outcome.[2] It can be challenging to determine this clinically and there is limited evidence to support self-reported functional capacity. The 2017 CCS Guidelines do not make a recommendation on this topic.

Several questionnaires have been developed, like the VSAQ and DASI (Duke Activity Status Index). The VSAQ has further been used with a nomogram to predict performance on a treadmill. To determine predicted exercise METS, assess patient's activity level via the VASQ questionnaire (Table 2) and use the nomogram in Figure 2.

Table 2 - Veterans Specific Activity Questionnaire (VSAQ)

1 MET	Eating, getting dressed, working at a desk
2 METs	Taking a shower, shopping, cooking Walking down 8 steps
3 METs	Walking slowly on a flat surface for 1 or 2 blocks A moderate amount of work around the house, such as vacuuming, sweeping the floors, or carrying groceries
4 METs	Light yard work (ie, raking leaves, weeding, sweeping, or pushing a power mower), painting, or light carpentry
5 METs	Walking briskly Social dancing, washing the car
6 METs	Play 9 holes of golf carrying your own clubs. Heavy carpentry, mow lawn with push mower
7 METs	Carrying 60 pounds, perform heavy outdoor work (ie, digging, spading soil, etc) Walking uphill
8 METs	Carrying groceries upstairs, move heavy furniture
	Jog slowly on flat surface, climb stairs quickly
9 METs	Bicycling at a moderate pace, sawing wood, jumping rope (slowly)
10 METs	Brisk swimming, bicycle up a hill, jog 6 miles per hour

11 METs	Carry a heavy load (ie, a child or firewood) up 2 flights of stairs Cross-country ski, bicycling briskly, continuously
12 METs	Running briskly, continuously (level ground, 8 min per mile)
13 METs	Any competitive activity, including those that involve intermittent sprinting Running competitively, rowing competitively, bicycle riding

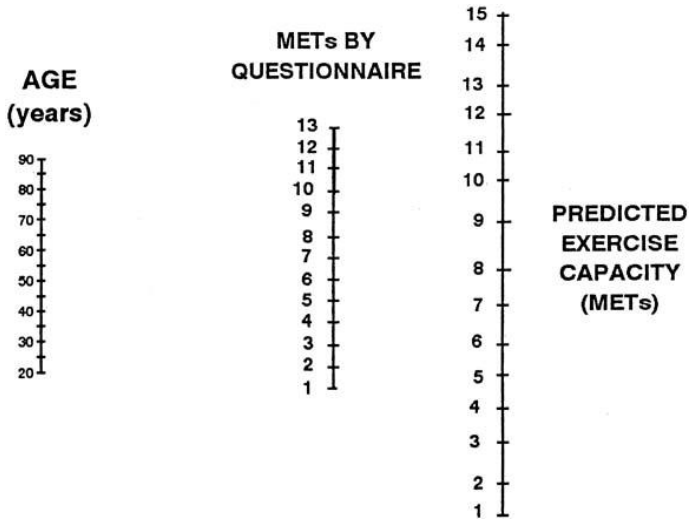

Figure 2 Nomogram to predict exercise capacity. With use of a straight edge, exercise capacity is predicted on the basis of age and response to specific activity questionnaire (VSAQ)[3]

Functional capacity -	Excellent	> 10 METS
	Good	7-10 METS
	Moderate	4-6 METS
	Poor	< 4 METS
	Unknown	

Preoperative Testing

NT-BNP/BNP should be measured before non-cardiac surgery in patients 65 years of age or older OR in patients aged 45-64 with significant cardiovascular disease (as above) or RCRI ≥ 1. BNP has significant prognostic value for postoperative cardiac events, as shown in Table 3.

Table 1 - Risk of Perioperative Death or MI at 30 days based on preoperative BNP levels. Adjusted OR = 3.4 (CCS 2016)

Test result	Risk Estimate (%)	95 % CI
NT-BNP < 300 ng/L BNP < 92 mg/L	4.9	3.9 – 6.1
NT-BNP ≥ 300 BNP ≥ 92	21.8	19.0 - 24.8

If the NT-BNP is not available OR if the NT-BNP is ≥ 300, obtain troponin and ECG daily X 48-72 hours postoperatively to monitor for myocardial injury after noncardiac surgery (MINS).

MINS is an umbrella term encompassing ischemic causes for troponin elevation within 30 days postoperatively. It includes both myocardial infarction and isolated troponin rise. MINS does NOT include troponin rise due to nonischemic causes, such as sepsis. MINS confers increased mortality as outlined in Table 4.

Table 4 - Peak Postoperative hsTnT and associated 30-day mortality. VISION study[4]

Peak hsTnT level (ng/L)	30 day mortality (%)	Odds Ratio
<5	0.1	1.0
5-13	0.5	3.7
14-19	1.1	9.1
20-64	3.0	23.6
65-999	9.1	70.3
1000+	29.6	227.0

VISION study[4] – Association of Postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing non-cardiac surgery.

Based on VISION substudies, the definition of MINS depends on the troponin assay used. These cutoffs are summarized in Table 5.

Table 5 – Troponin assay and definition of MINS

Assay	MINS hsTnI threshold
Abbott	≥ 60
Siemens	≥ 75
Any other assay (including TnT)	≥ 99th percentile URL

Cardiac imaging

- In the absence of an unstable cardiac condition (i.e. decompensated congestive heart failure) or suspected severe obstructive cardiac disease (i.e. severe aortic stenosis), routine echocardiography should **NOT** be ordered for preoperative risk assessment.

- In asymptomatic patients OR in patients with stable coronary artery disease, routine electrocardiograms should **NOT** be ordered for preoperative risk assessment.

- In asymptomatic patients OR in patients with stable coronary artery disease, routine exercise and pharmacologic stress tests should **NOT** be ordered for preoperative risk assessment.

- In asymptomatic patients OR in patients with stable coronary artery disease, routine coronary computed tomographic angiography (CCTA) should **NOT** be ordered for preoperative risk assessment.

- In asymptomatic patients OR in patients with stable coronary artery disease, routine coronary angiography should **NOT** be ordered for preoperative risk assessment.

When to consider delaying non-urgent surgery

The main purpose of the preoperative clinical assessment is to try to identify severe and unmanaged cardiovascular conditions that can immediately put patients at increased risk of death in the intraoperative/postoperative period.

The main conditions that need to be identified include obstructive cardiovascular lesions, unstable angina, acutely decompensated congestive heart failure, high-degree heart block, and pulmonary embolism.[5,8,9]

If there is clinical suspicion for obstructive cardiac lesions such as severe aortic stenosis or hypertrophic cardiomyopathy with obstruction or severe pulmonary hypertension, then consultation and communication with anaesthesiology is recommended as these patients may require urgent preoperative echocardiograms, and consideration for more invasive intraoperative hemodynamic monitoring (e.g. arterial line), and possibly postoperative monitoring in an intensive care level setting.[1]

Although most patients with optimized coronary artery disease/stable angina and stable congestive heart failure are at increased risk of postoperative complications, they can undergo elective and non-urgent surgery. However, it is prudent to try to identify patients with unstable angina or acutely decompensated congestive heart failure (i.e., pulmonary edema) as shock and hypoxaemia can significantly increase immediate intraoperative and operative mortality rates.[8,9]

In the case of suspected unstable angina, the patient, the surgeon, and the anaesthesiologist must be advised to delay non-urgent surgery until the patient's symptoms are stabilized. In some cases, patients may require urgent cardiology consultation and revascularization preoperatively, which would delay surgery. The duration of surgery delay will depend on the urgency of the surgery, coronary artery treatment modality (type of percutaneous intervention or pure medical management), and individual patient factors. The CCS 2018 antiplatelet guidelines provide general recommendations on the timing of antiplatelet therapy interruption preoperatively (see Chapter 5), however, the optimal management plan should be personalised based on individual patient considerations and shared decision-making with the patient, surgeon, and cardiologist/internist.[10]

In the case of suspected acutely decompensated congestive heart failure or pulmonary edema (i.e., if the patient is experiencing paroxysmal nocturnal dyspnoea, orthopnea, or oxygen desaturation when lying supine), surgery must be delayed, and the patient should be treated with diuretics until their symptoms resolve and euvolemia is achieved.[11]

High-degree and advanced heart block often necessitate delaying surgery until the patient's underlying condition is treated either with adjusting AV nodal blocking agents or pacing (temporary transvenous or permanent).

Postoperative MI Management

Management Principles

- Acute treatment = ASA (to prevent recurrent thromboembolism)
- Optimal medical treatment for risk factors (hypertension, diabetes, dyslipidemia)
- If the mechanism is suspected to be related to acute plaque rupture/type 1 ACS, then in consultation with cardiology and in discussion with the surgeon:
    - Consider second antiplatelet agent (to stabilize acutely ruptured plaque)
    - Consider anti-thrombotic agent for 48h – 72h (to prevent acute thrombosis)
    - Consider urgent revascularisation (to minimise myocardial infarction)

STEMI

- DAPT + Statin → Emergent inpatient revascularisation
- Cardiology consultation

Angina/NSTEMI

- DAPT + Statin → Urgent inpatient revascularisation
- Cardiology consultation

MINS

- ASA + Statin → Risk stratify

Most patients with MINS receive functional cardiac stress testing for further risk stratification. Beyond optimal medical management of major cardiovascular risk factors, however, the evidence supporting the use of functional cardiac stress testing in MINS patients is uncertain. If further cardiac stress testing is the chosen strategy, then testing can generally be done non-urgently in the outpatient setting for most patients.[6]

Cardiac catheterisation is rarely done upfront and is generally deferred until further cardiac stress testing is done. In the event of a positive cardiac stress test, then expert consultation with cardiology is recommended to decide on optimal management and revascularisation.[6]

New studies are examining the use of DOACs for the prevention of recurrent ischemia in the postoperative setting. The MANAGE trial showed that dabigatran 110 mg twice daily lowered the risk of major vascular complications (a composite of vascular mortality and non-fatal myocardial infarction, non-hemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic venous thromboembolism),

with no significant increase in major bleeding.[7] However, dabigatran's effect on preventing arterial vascular events such as MINS, as opposed to a composite of both venous and arterial vascular events in the postoperative setting, remains dubious, and its use in the postoperative setting is not currently commonly practiced.

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4. CARDIAC MEDICATIONS MANAGEMENT

Authors: Ciara Pendrith MD MSc, Anna Goulding MD FRCPC

Key Guideline: 2017 Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management of Patients Who Undergo Noncardiac Surgery[1]

Pre-existing Medications Before Non-Cardiac Surgery

ASA	• If recent stent or low bleeding risk, continue ASA • Otherwise hold at least 3 days before surgery (Thrombosis Canada 2021 recommends 5-7 days) • Restart postoperatively when bleeding risk has passed
P2Y12 inhibitor	• If recent stent and elective surgery delay OR hold Clopidogrel/Ticagrelor 5-7 days and Prasugrel 7-10 days (see Chapter 5) • If emergent surgery, no neuraxial anaesthesia • Restart antiplatelet after surgery as soon as it is deemed safe by the surgeon
Beta-blocker	• Continue perioperatively; if sBP is low prior to surgery then consider dose reduction or holding
ACE/ARB	• Hold at least 24 hours prior to surgery
Statin	• Continue perioperatively
Smoking	• Discuss and facilitate smoking cessation ideally ≥4 weeks prior to surgery

Initiation of Medications Before Non-Cardiac Surgery

ASA	• Do not start ASA for prevention of perioperative cardiac events
Beta-blocker	• Do not initiate within 24 hours of surgery; unless emergent surgery and otherwise indicated (i.e. arrhythmia)
CCB	• Do not start calcium-channel blockers for the prevention of perioperative cardiac events

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5. Coronary Artery Stents and Antiplatelets

Authors: Michael Ruiz MD MSc, John Janevski MD MSc FRCPC

Background

Coronary angioplasty, or percutaneous coronary intervention (PCI), has widely incorporated the use of stents to preserve coronary arterial patency. In patients undergoing PCI with stenting for ACS, dual antiplatelet therapy (DAPT) is ideally recommended for at least 1 year after the procedure. In patients undergoing PCI with stenting for stable angina, duration of therapy is dictated by the type of stent employed. In both cases, after this period of DAPT, lifelong aspirin is recommended.

The introduction of coronary artery stenting has led to improved outcomes compared to plain-old balloon angioplasty (POBA) alone. However, in-stent restenosis remains a significant concern. Bare metal stents (BMS) are associated with an in-stent restenosis rate of roughly 12% at one year, though this is based on older data. Drug eluting stents (DES) are associated with significantly lower rates of in-stent restenosis (5% at 5 years), and are now employed almost exclusively in PCI for both stable CAD and ACS. DES reduce in-stent restenosis by delivering anti-proliferative or immunosuppresive medications locally. As a consequence of this, DES take longer to endothelialize, resulting in persistence of exposed metal within the stented coronary segment, placing the patient at risk of stent thrombosis if DAPT is prematurely discontinued. DES therefore require a longer minimal duration of antiplatelet treatment than BMS.

Stent thrombosis, where an acute thrombus develops within a stent, resulting in myocardial infarction, is a rare complication of PCI. Stent thrombosis is estimated to occur at 30 days of stent placement in up to 2.5% of patients with BMS and 0.6% with DES with continuation of DAPT. If antiplatelet agents are interrupted before endothelialization has occurred, the risk of stent thrombosis increases several folds. The results can be catastrophic with case fatality rates ranging between 18-89% in various studies. In one study of 40 patients who underwent noncardiac surgery within 6 weeks of BMS implantation, 20% of patients died, most from myocardial infarction. All the patients that died had an antiplatelet agent withdrawn in the perioperative period.

The risk of stent thrombosis if antiplatelets are withdrawn prematurely must be balanced against the risk of bleeding if continued. Emergent surgery may not allow for planning of antiplatelet therapy, even if antiplatelet therapies are held on the day of the procedure, it may take several days for platelet function to normalize. Elective procedures will

allow for planning of antiplatelet management. Timing from stent insertion and type of stent are the most common factors used to inform decision making around antiplatelet management. If possible, aspirin is recommended to be continued in the perioperative period in a patient with a coronary stent. The second antiplatelet (i.e. clopidogrel, ticagrelor, prasugrel), may be interrupted to reduce bleeding risk. One month after BMS and three months after DES insertion is believed to allow sufficient time for endothelialization to reduce risk of stent thrombosis. If a decision is made to interrupt DAPT, clear instructions should be given on when to stop the second antiplatelet to allow recovery of platelet function. Consultation with the patient's cardiologist may help inform risk of interrupting DAPT. DAPT should be resumed postoperatively in consultation with the surgeon (i.e. when risk of bleeding is lower).

Assess the surgery-specific risk of bleeding

Table 1 – Surgery-specific and patient-specific risk factors associated with increased risk of perioperative bleeding

Risk category		Risk factors
Surgery-specific	Lower risk	Biopsies, endoscopy, anterior eye chamber, dental surgeries, minor orthopedic/ENT/general surgeries
	Moderate risk	Visceral, cardiovascular, urologic surgeries, major orthopedic/ENT/reconstructive surgeries
	Higher risk	Possible bleeding in a closed space, intracranial and spinal surgeries or interventions, posterior eye chamber
Patient-specific	Age >75, frailty, anemia with Hb <110, CKD (CrCl <40), low body weight (<60kg), hospitalization for bleeding in last year, previous stroke/ICH, need for OAC in addition to DAPT, regular NSAID/glucocorticoid use	

Assess the risk of stent thrombosis

1. Time period since PCI

Table 2 – Timing of elective noncardiac surgery and interruption of DAPT. Aspirin should be continued if possible and DAPT restarted as soon as possible after surgery.

Type of PCI	Time since PCI
Bare metal stent (BMS)	**After 1 month**
Drug eluting stent (DES)	**After 3 months**

2. Other risks for DES thrombosis
    a. Advanced age
    b. Index PCI for acute coronary syndrome
    c. Diabetes
    d. CHF
    e. Renal failure
    f. Prior stent thrombosis
    g. Angiographic factors (long stents, multiple lesions, overlapping stents, ostial or bifurcating lesions, small vessels, suboptimal stent results – mal-opposition; stent fracture)

Consider risk of bleeding when continuing antiplatelet agents perioperatively

1. ASA:
    a. Continuing ASA perioperatively was associated with 1.5 fold increase risk of bleeding in one meta-analysis of 41 studies. There was no increase in complications, mortality, or surgical outcomes.
    b. Possible exceptions:
        i. Intracranial neurosurgery
        ii. Posterior chamber eye surgery
        iii. Prostate surgery

2. Dual antiplatelet therapy:
    a. Very limited evidence available
    b. Retrospective study of 550 patients who underwent noncardiac surgery after PCI found an increase in risk of bleeding for dual antiplatelet therapy vs. single (21% vs. 4%).
    c. Prospective cohort study of 847 patients who underwent noncardiac surgery found that continuation of DAPT in the perioperative setting was associated with increased bleeding (RR=6.55) without any difference in cardiac outcomes, though only one fourth of patients had a stent within one year.

Conclusions

1. Elective and non-urgent surgery should be delayed until at least 1 month after BMS insertion, and at least 3 months after DES insertion. Discontinuation of DAPT before the recommended treatment duration should, where possible, be carried out in consultation with the patient's cardiologist.

2. Premature withdrawal of antiplatelet medications in patients with recent stent insertion can result in thrombosis with potentially catastrophic results
3. ASA should be continued in most cases in patients with stents, and in some cases dual antiplatelet therapy may be considered
4. In patients undergoing PCI who are treated with a BMS or DES and who require elective noncardiac surgery, it is suggest withholding clopidogrel and ticagrelor for 5-7 days preoperatively, and prasugrel for 7-10 days preoperatively
5. In patients undergoing PCI who are treated with a BMS or DES and who have undergone noncardiac surgery, it is suggested to restart maintenance-dose DAPT after surgery, as soon as it is deemed safe by the surgeon.
6. When urgency dictates that the surgery must be performed sooner than recommended, a decision regarding antiplatelet therapy must be made on a case-by-case basis, taking into account the surgical bleeding risk and patient's risk of thrombosis, and in consultation with the surgeon, cardiologist, and anesthetist.

Abbreviations

P2Y12 inhibitor = thienopyridines (e.g. clopidogrel)
ACS = acute coronary syndrome
BMS = bare metal stent
DES = drug-eluting stent

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6. CONGESTIVE HEART FAILURE

Authors: Vicki Ning Wang MD FRCPC, Juan Duero Posada MD FRCPC

Epidemiology

- Diagnosed in > 90,000 Canadians every year
- Increasing prevalence in aging population with hypertension, diabetes mellitus and coronary artery disease (CAD)

Etiology

1. Ischemic cardiomyopathy (significant CAD)
2. Non-ischemic cardiomyopathy
    a. Idiopathic dilated cardiomyopathy
    b. Hypertensive cardiomyopathy
    c. Valvular heart disease
    d. Tachyarrhythmia
    e. Toxins (i.e. alcohol, amphetamines, chemotherapy)
    f. Inflammatory/Infectious (i.e. myocarditis, sarcoidosis)
    g. Hypertrophic cardiomyopathy
    h. Infiltrative cardiomyopathies (i.e. amyloidosis, Fabry's)

Perioperative Risk (death prior to discharge or 30-day mortality)

- Major non-cardiac surgery: risk-adjusted operative mortality 11.7% in HF, 6.6% in CAD and 6.2% in controls[1]

Goals of Preoperative Assessment

- Identify patients with known or suspected HF
- Assess stability: stable chronic HF vs. decompensated (new onset or acute) HF
- Identify high-risk patients
    - Acute decompensated HF
    - Advanced HF: severe symptoms limiting activities of daily limiting, intolerance to or down-titration of HF medications, hyponatremia, tachycardia, hypotension, ventricular arrhythmia +/- ICD shocks, recent HF hospitalization, renal dysfunction, elevated brain-natriuretic peptide (BNP)

Preoperative Assessment

1. History
    a. Symptoms of HF: exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, kamtopnea/bendopnea (dyspnea while bending over), fluid retention (abdominal bloating, peripheral edema), fatigue

b. Previous history of HF, myocardial infarction, CAD
c. Functional status (New York Heart Association Class III symptoms 71% sensitive and 47% specific for serious postoperative complications[2]

2. Physical Exam
    a. S3 heart sound (ventricular filling gallop)
    b. S4 heart sound
    c. Elevated jugular venous pressure
    d. Lower extremity edema
    e. Auscultation for rales/wheezes
    f. Auscultation for a murmur (i.e. aortic stenosis, mitral regurgitation)
    g. Displaced apical impulse on palpation

Adapted from Wang et al., 2005[3]

Investigations

- Chest X-ray
    - Evaluating for cardiomegaly, pulmonary venous congestion, interstitial edema, pleural effusions
- 12-lead ECG
    - Assess for atrial fibrillation, ischemic ST-T changes, Q-waves
- Transthoracic echocardiogram
    - Assess biventricular size and function, valvular disease, elevation of pulmonary pressures (right ventricular systolic pressure), presence of wall motion abnormalities
- Brain-natriuretic peptide level
    - When HF suspected or disease severity uncertain (trend from baseline)
    - Additionally, as per CCS Perioperative guidelines if elective surgery in patient $\geq$ 65 years, Revised Cardiac Risk Index (RCRI) $\geq$ 1 or age 45-64 years with significant cardiovascular disease (see Chapter 3)

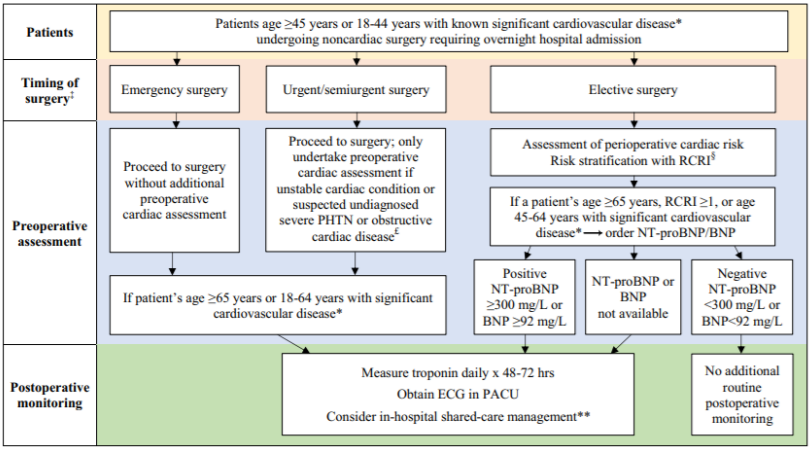

Figure 1 – 2017 CCS Perioperative Algorithm[4]

Management

- Identify etiology of HF
- Improve symptoms, optimize volume status
- Ensure evaluation and optimization of contributing factors to increased perioperative mortality:
    - Myocardial ischemia – assess risk through non-invasive ischemia testing and/or coronary angiogram if **active** signs/symptoms of ischemia
    - Hypertension – optimization of pre-op and post-op blood pressure including adequate pain management
    - Severe valvular disease - assess if valve requires intervention prior to operation
    - Atrial fibrillation – rate and/or rhythm control
    - Renal dysfunction
    - Diabetes mellitus
- For patients who are on stable HF medical therapy
    - Discuss with primary cardiologist withholding or reducing vasodilators (i.e. ACE-inhibitors, ARBs, ARNIs, hydralazine/ISDN) if low or borderline blood pressure to avoid hypotension during induction
    - Do not withhold beta-blocker perioperatively
- For emergency surgeries in high risk HF patients: consultation with specialist team (i.e. Cardiology, Advanced HF)
- If stable, compensated HF:
    - Proceed with urgent or elective surgeries

- If new onset HFrEF or decompensated HF:
    - If urgent surgery required, consult with anesthesia regarding close intra-operative hemodynamic monitoring and specialist team assessment
    - If elective surgery, postpone surgery and allow for stabilization and medical/or optimization

Intra-operative considerations

- ECG monitoring for atrial/ventricular arrhythmias and ischemia
- Maintenance of euvolemia
    - Maintenance of adequate preload to support cardiac output and myocardial perfusion
- May require inotropic agents (i.e. milrinone, dobutamine), vasodilators (i.e. nitroprusside, nitroglycerin) for management of hypertension, volume overload; vasopressors to be used with caution (will increase afterload)

Postoperative considerations

- Close monitoring in ICU setting for:
    - Myocardial ischemia
    - Arrhythmias
    - Respiratory status
    - Renal function
    - Evidence of acute HF decompensation
    - Judicious fluid management to avoid or detect decompensation early
- Once hemodynamically stable, re-introduction of HF therapies:
    - Resume afterload reduction (i.e. ACE-inhibitors, ARB, hydralazine/ISDN) early
    - Beta-blocker re-initiation (if withheld postoperatively) based upon stability and volume status, often last to be introduced unless issues surrounding rate control in atrial arrhythmia

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7. ARRHYTHMIAS

Authors: Armin Abadeh MD, Jeremy Kobulnik MD FRCPC

Epidemiology

- Incidence varies from 16-62% with intermittent ECG monitoring.
- Affects 70.2% of patients that receive general anaesthesia across all surgical procedures and >90% of patients undergoing cardiac surgery.

Contributing Factors

- Several factors can contribute to perioperative arrhythmia (Table 1). These factors should be identified in the preoperative period or recognized and managed during the intraoperative period.

Table 1 – Common contributing factors for perioperative cardiac arrhythmias

Contributing Factors
• Pre-existing ECG abnormalities (e.g. atrial fibrillation, PVCs, QT prolongation) • Medications/Medication withdrawal (e.g. beta blockers, anticholinergic agents, vasoconstrictors, opioids, QT-prolonging meds) • Myocardial ischemia/heart failure • Metabolic/respiratory abnormalities (hypoxemia, hypo/hypercarbia, and acid-base disturbances) • Electrolyte abnormalities (hypo/hyperkalemia, hypo/hypermagnesemia, hypo/hypercalcemia) • Intravascular volume depletion, anemia • Procedure-specific factors (e.g. intrathoracic and intravascular procedures)

Diagnosis

- ECG monitoring recommended for all patients receiving anesthetic agents for sedation, regional anesthesia, or general anesthesia.
- Use stable waveforms from the pulse oximeter, intra-arterial catheter, and/or central venous catheter to help distinguish artifact from a true arrhythmia.
- If a tachyarrhythmia or bradyarrhythmia develops that cannot be readily diagnosed, a 12-lead ECG should be obtained as soon as feasible.

Bradyarrhythmias

All perioperative bradycardia may be vagally mediated and transient related to postoperative symptoms. As an initial step, these symptoms should be treated.

- Sinus bradycardia
    - Hemodynamically stable: no immediate treatment.
    - Hemodynamically unstable: Atropine IV at the dose of 1 mg every 3 to 5 minutes. Do not administer more than 3 mg total (ACLS algorithm).
- AV block
    - First degree AV block: no immediate treatment.
    - Second degree AV block: may require pacing if bradycardia is severe or if hemodynamic unstable.
    - Third degree AV block: may require pacing, especially if QRS complex is wide or if there is hemodynamic instability.

Supraventricular/Narrow Complex Tachyarrhythmias

- Sinus tachycardia
    - Treat underlying cause (inadequate anesthesia and/or analgesia, hypovolemia, anemia, PE, etc.).
    - If evidence of ischemia, consider low dose beta blocker (assuming the absence of hypotension or heart failure). Please refer to Table 2.
- Atrial fibrillation or flutter (see Chapter 7)
    - Hemodynamically stable: Similar to sinus tachycardia: Underlying cause should be treated. If ventricular rate is inappropriately high for the clinical context, consider IV beta blockers or calcium channel blockers (refer to Table 2) to control heart rate rather than with immediate cardioversion, assuming no heart failure or hypotension.
    - Hemodynamically unstable: immediate synchronized cardioversion with sedation if patient is conscious.
- Narrow complex regular tachycardias: consider vagal maneuvers or adenosine. Calcium channel blockers and beta blockers may also be used.
- If hemodynamically unstable: synchronized cardioversion with sedation, if patient is conscious.

Table 2 – Common medications, doses, adverse effects and precautions to consider for acute management of supraventricular/narrow complex tachyarrhythmias

Class	Agent	Initial Dose	Follow-up Dose	Adverse Effects / Precautions
Beta-blockers	Metoprolol	2.5–5.0mg IV bolus over 2 min	Oral therapy: Initial: 12.5-25mg bid Target: 100-200mg bid	**Potential adverse effects:** hypotension, worsening HF, bronchospasm, bradycardia. **Precautions with:** AV block greater than first degree or SA node dysfunction (in absence of pacemaker), decompensated systolic HF, hypotension, and cardiogenic shock
Calcium Channel Blocker	Diltiazem	0.25mg/kg IV bolus over 2 min	Oral therapy: Initial: IR 30 mg q6h-q8h or ER 120mg daily Target: IR 120mg q6h or ER 360mg daily	**Potential adverse effects:** hypotension, worsening HF in patients with pre-existing ventricular dysfunction, bradycardia, abnormal liver function studies, acute hepatic injury (rare). **Precautions with:** AV block greater than first degree or SA node dysfunction (in absence of pacemaker), WPW with AF/atrial flutter, hypotension, decompensated systolic HF/LV dysfunction, drugs with SA and/or AV nodal-blocking properties, and hepatic or renal dysfunction
	Verapamil	5–10mg (0.075–0.15-mg/kg) IV bolus over 2 min	Oral therapy: Initial: IR 80mg tid or SR 120-240mg daily Target: IR 120mg tid or SR 360mg daily	
Nucleoside	Adenosine	6mg rapid IV bolus (injected into IV as proximal or as close to the heart as possible), administered over 1–2 seconds, followed by rapid saline flush	No oral option If no result within 1–2 min, 12mg rapid IV bolus; can repeat 12mg dose one time. The safe use of 18mg bolus doses has been reported	**Potential adverse effects:** Transient AV block, flushing, chest pain, hypotension, or dyspnea, AF can be initiated or cause decompensation in the presence of pre-excitation. **Precautions with:** AV block greater than first degree or SA node dysfunction (in absence of pacemaker), reactive airway disease, concomitant use of verapamil or digoxin, and WPW

Ventricular/Wide Complex Tachyarrhythmias

- Pulseless VF or VT: immediate defibrillation and follow ACLS algorithm.
- Hemodynamically stable sustained ventricular tachycardia:
    - Pharmacologic Cardioversion:
        - There is no consensus on the choice of initial antiarrhythmic medication. Amiodarone, lidocaine, or procainamide are some of the drugs that can be used.
        - In a non-cardiac arrest situation, amiodarone is typically given as a 150mg IV bolus followed by an infusion rate of 900 mg over 24 hours. Typically, it requires cardiac monitoring.
        - Factors such as time required to administer, and association with hypotension should be considered. If VT terminates during drug infusion, it can usually be discontinued at that point. If patient is experiencing frequent recurrent episodes, consider continuing the infusion while initiating oral antiarrhythmic drug therapy.
    - Electrical Cardioversion:
        - Intravenous analgesics or sedatives (for procedural sedation) should be cautiously administered (close blood pressure monitoring).
        - If the QRS complex and T wave can be distinguished, synchronized cardioversion with least 100 joules using either a biphasic or monophasic defibrillator can be attempted. If the initial shock is unsuccessful, subsequent shocks should be delivered at escalating energy levels.
- Torsades de pointes (TdP)
    - Pulseless patient: immediate defibrillation and follow ACLS algorithm.
    - Hemodynamically unstable: attempt synchronized cardioversion.
    - Hemodynamically stable: start with magnesium sulfate 2 g as a slow IV bolus
- Frequent premature ventricular contractions (PVCs), non-sustained VT, and ventricular paced rhythms are not immediately life-threatening and usually do not require immediate interventions.

Postoperative Considerations

- Patients to be continually monitored via ECG if undergoing procedures that pose an intermediate to high risk for the development of an arrhythmia or if the patient is known to have structural heart disease or a history of arrhythmias.
- Obtain a cardiology consultation for patients with:
    - Suspected myocardial ischemia
    - Persistent or clinically significant arrhythmia (e.g., new onset of AF, second or third degree AV block, VT). Importantly, anticoagulation for atrial fibrillation will be required for some but not all patients.
    - If pharmacologic or other treatment (e.g., infusion of an antiarrhythmic agent, pacing, cardioversion) was necessary during the intraoperative period.

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8. Atrial Fibrillation

Authors: Carol Graham MD, Kevin Venus MD FRCPC

Epidemiology

- The wide range in reported rates can be partly explained by inconsistent definitions, postoperative monitoring practices and the wide range of surgical procedures and patient comorbidities that occur in non-cardiac surgeries[1]
- The incidence of postoperative atrial fibrillation (POAF) correlates significantly with the site of surgery and degree of invasiveness[1]:
    - Non-cardiac thoracic surgery – ranges between 2-4% based on international database registries[2]
    - Non-thoracic non-cardiac surgery- highly variable from prevalence 0.5-3%[2]
        - Orthopaedic 1.7%
        - ENT 6%
        - Colorectal 13%[1]
- Re-analysis of the VISION cohort has shown that POAF complicates 1/100 major noncardiac surgeries[2]
    - 2 events per 1000 patients after low-risk surgery
    - 32 events per 1000 patients after major thoracic surgery
- Typically occurs on postoperative day 2 with >70% of cases arising within the first 4 days postoperatively.[3]

Postulated Mechanisms

There is currently a lack of certainty about whether patients who are diagnosed with POAF have experienced a removable trigger for AF or if the surgery has unmasked their baseline predisposition to developing chronic AF.

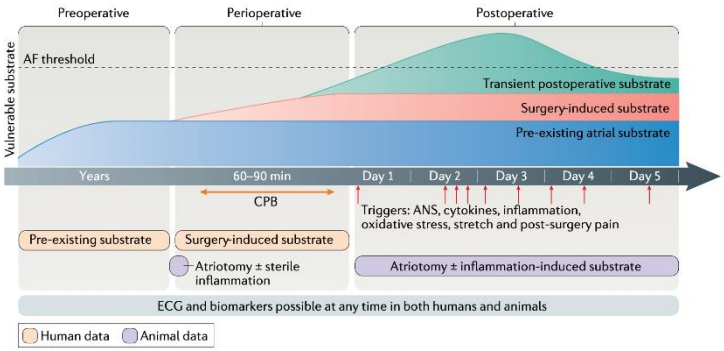

Figure 1 – Proposed mechanism of POAF[1]

Table 1 - Risk factors for postoperative atrial fibrillations [4-7]

Patient Factors	Surgery/Anaesthetic Factors
• Age • Prior stroke/TIA • CHF • Diabetes • Hypertension • CKD • Elevated BNP	• Site of surgery (thoracic, vascular, orthopaedic) • Emergent procedure • Combined general/regional anaesthesia • Use of inotropes/intraoperative hypotension

Prevention

- Paucity of data overall compared to cardiac surgery population
- A systematic review and meta-analysis provide some insight, but 21 studies examined mostly focused on thoracic surgery patients, and mix of active and placebo comparators and heterogenous follow-up timelines/case definitions make it difficult to draw firm conclusions.[8]
    - Amiodarone- only studied in patients undergoing thoracic surgery, (RR 0.42,CI 0.26-0.67; ARR 17%, NNT 5.88)
    - Calcium channel blockers- trend toward significant (RR 0.55, CI 030-1.01)
- Beta blockers- Cochrane systematic review showed significant reduction POAF (RR 0.41, CI 0.21-0.79) with increased rates of bradycardia and hypotension.[9]
- Withdrawal of preoperative beta-blockers also seems to increase rates of POAF.[10]
    - Canadian Cardiovascular Society recommends that patients who have been receiving beta-blocker prior to surgery, have it continued postoperatively (Strong, High-Quality Evidence).[10]

Prognosis

- Initial episodes of POAF are typically self-limited and most revert to sinus rhythm (exact durations unclear due to lack of standardized telemetry protocols).[3]
- The rate of recurrence of AF after non-cardiac surgery is unclear but may approximate that of cardiac surgery patients with POAF (40-60% at 1 year).[5,11]
- The frequently transient nature of POAF has led clinicians to believe that it was less impactful for future stroke/cardiac risk, however this is now being challenged.
    - POAF after non-cardiac surgery has higher 1 year risk of stroke that after cardiac surgery (HR 2.0, CI 1.7-2.3 vs. 1.3, CI 1.1-1.6).[12]

    - Single documented episodes of subclinical AF 6 minutes in length is sufficient to increase stroke risk (not perioperative data).[13]
- Patients who develop POAF have a similar stroke risk to those with non-valvular atrial fibrillation.[14]
- Patients with POAF have higher rates of mortality, stroke, MI compared to those without (see Figure 2).

Table 3 **Adverse clinical outcomes associated with perioperative atrial fibrillation**

Outcomes	Unadjusted HR (95% CI)		Adjusted HR (95% CI)	
	(*N* = 18 117)	*P*-value	(*N* = 17 996)[a]	*P*-value
Total stroke	4.17 (2.47–7.06)	<0.001	3.43 (2.00–5.90)	<0.001
All-cause mortality	3.59 (2.89–4.47)	<0.001	2.51 (2.01–3.14)	<0.001
Vascular mortality	3.46 (2.45–4.90)	<0.001	2.74 (1.92–3.90)	<0.001
Myocardial infraction	6.28 (4.85–8.12)	<0.001	5.10 (3.91–6.64)	<0.001
Composite of vascular mortality, myocardial infarction, or stroke	4.90 (3.94–6.08)	<0.001	3.93 (3.14–4.91)	<0.001

CI, confidence interval; HR, hazard ratio.
[a]Adjusted for age, sex, history of hypertension, diabetes, smoking, heart failure, coronary artery disease, peripheral artery disease, or stroke, type of surgery, undergoing urgent/emergency surgery, and randomized treatment assignments.

Figure 2 – Adverse outcomes associated with POAF[4]

Anticoagulation

- At present there are no completed randomized controlled trials that have assessed stroke prophylaxis in postoperative atrial fibrillation (the ASPIRE trial currently underway is hoping to address this knowledge gap).
    - Retrospective database studies have conflicting results.[6]
- It is reasonable to use the $CHADS_2$ score to aid in clinical judgement to determine who would likely benefit from anticoagulation, while balancing the bleeding risk in the postoperative period.
- The duration of atrial fibrillation that warrants anticoagulation is unclear. Increased stroke risk is seen after 6 minutes in patients with implanted devices and in over 24 hours of atrial fibrillation for patients monitored with telemetry, but these studies did not include patients with postoperative atrial fibrillation.
- Commencement of anticoagulation should be a collaborative decision between the medical and surgical team.
- Canadian Cardiovascular Society recommends that patients with POAF who are prescribed anticoagulation should continue it at least 6 weeks postoperatively.[10]

Post Discharge Follow up

- Post discharge follow up is recommended for all patients who develop postoperative atrial fibrillation by the CCS.[10]

- Further testing such as echocardiogram and extended Holter monitoring can usually be completed in the outpatient setting for risk stratification and to identify those with ongoing paroxysmal atrial fibrillation.

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9. AORTIC STENOSIS

Authors: Sameer Kushwaha MD, Caroline Chessex MD FRCPC

Epidemiology

- Most common form of valvular heart disease in the elderly
- Affects 1-2% of people >65 years old, 3-8% of people >75 years old
- 50% of AS stenosis patients >50 years old will also have CAD

Etiology

- Age < 70 years old: Bicuspid aortic valve
- Age > 70 years old: Calcific degeneration, rheumatic (less common)

Natural History

- Aortic valve area decreases ~0.1cm^2 per year
- Once symptoms develop (angina, syncope, dyspnea), the average survival is 2-3 years without valve replacement

Table 1 – Severity of aortic stenosis by echocardiographic findings[9]

	Valve Area (cm^2)	Mean Gradient (mmHg)	Peak Jet Velocity (m/sec)
Normal	3-4	<5	<2
Mild	>1.5	<20	2.0-2.9
Moderate	1-1.5	20-39	3.0-3.9
Severe	≤1.0	≥40	≥4

Preoperative Considerations

- Presence or absence of symptoms
- Severity of valvular disease
- Risk of surgery/intervention
- Response of left/right ventricle to overload caused by valvular disease
- Pulmonary artery systolic pressure (estimated by RVSP)

Perioperative Risk

- Relative risk of perioperative cardiac events is 3-7 compared to patients without AS.
- Risk is increased with: high risk surgery (OR 7.3), symptomatic severe AS (OR 2.7), co-existing moderate-severe MR (OR 9.8) or pre-existing CAD (OR 2.7).
- Rate of cardiac complications in those with undiagnosed severe AS undergoing non-cardiac surgery is approximately 10-30%.

- Acquired von Willebrand syndrome (AVWS) in AS may increase the risk of bleeding.

Pathophysiology of Risk from Severe AS

- Fixed outflow tract obstruction of the left ventricle:
    - Results in fixed cardiac output (HR x SV).
    - Since (Blood pressure = cardiac output x peripheral vascular resistance), decreases in PVR can result in significant hypotension.
- Left ventricular hypertrophy, leads to:
    - Decreased LV compliance (increasing dependence on atrial kick, preload and ventricular filling time).
    - Decreased coronary reserve and increased myocardial oxygen demand (increasing susceptibility to ischemia).
- Multiple perioperative factors can cause hypotension/ischemia leading to hemodynamic compromise, which precipitates a cycle of progressively worsening hypotension/ischemia, including:
    - Decreased preload (fasting, fluid shifts, bleeding).
    - Decreased ventricular filling time/loss of atrial kick (tachycardia, atrial fibrillation).
    - Decreased peripheral vascular resistance (anesthesia/epidural effects).

Preoperative Assessment

History

- Symptoms of severe AS (angina, syncope, dyspnea)
- Symptoms of CAD

Physical Exam

- Crescendo-decrescendo (diamond shaped) systolic murmur
- Late peaking (increased severity as peak approaches S2)
- Murmur loudest at the RUSB with radiation to the clavicle/carotid (highly sensitive)
- Quiet S2 ± paradoxical splitting
- Weak and delayed carotid upstroke (pulsus parvus et tardus)
- Apical-carotid or brachial-radial delay

Investigations

- 12-lead ECG
- Transthoracic Echo (can assess severity and etiology of AS, LV function, presence of wall motion abnormalities), if known or suspected moderate or greater severity valvular disease
    - If no change in clinical status, TTE within the past 12 months is acceptable

    - Important metrics: Severity of stenosis, systolic/diastolic function, LV size and structure, RV size and function, PA systolic pressure (estimated by RVSP), other concurrent valvular diseases
- Dobutamine stress echocardiogram: consider if low-flow low-gradient severe AS suspected (symptomatic with AVA $\leq$1.0, and peak jet velocity <4.0 m/s and mean gradient <40 mmHg and LVEF <50%).
- Exercise stress test: consider if asymptomatic severe AS, to verify absence of symptoms (AVOID exercise stress test if already known symptomatic severe AS).
- If symptomatic or other concurrent cardiovascular diseases are suspected (e.g. CAD, pulmonary hypertension, peripheral arterial disease) additional investigations may be needed to fully ascertain risk and determine if other procedures needed before non-cardiac surgery.

Management

- Maintain sinus rhythm, appropriate rate control.
- Optimize volume status and avoid hypotension and tachycardia.
- Endocarditis prophylaxis is NOT required (unless otherwise indicated).
- There is no role for B-blockade in isolated AS.
- Patients with severe valvular heart disease should be assessed by Evaluation by Heart Team (Cardiology, Cardiac Anesthesiology, Cardiac Surgery) in cooperation with the operating surgeon before non-cardiac surgery.
- Intraoperative hemodynamics
    - Hemodynamic changes with anesthesia and surgery can be poorly tolerated with moderate or greater AS.
    - General anesthetics well tolerated; agents should be chosen to maintain sinus rhythm and normotension.
    - Phenylephrine can be used if no significant CAD.
    - Hypertension – short acting CCBs are preferred.
    - Epidural/spinal anesthetic can be modified to minimize large changes in blood pressure (high dilution anesthetics).

Symptomatic patients

- Key message: If a patient meets the standard criteria for valve intervention, elective surgeries should be deferred until the valve is repaired (Class 1 recommendation, LOE: C).
- Severe valvular disease + low risk surgery:
    - Consultation with cardiac anesthesiologist
    - Non-invasive monitoring

- Severe valvular disease + medium or high-risk surgery
    - Shared decision making about whether to proceed with surgery
    - Invasive hemodynamic (e.g. right heart catheterization) and TEE monitoring intraoperatively and postoperatively
    - ICU admission postoperatively

Asymptomatic patients

- If asymptomatic but severe:
    - Ensure valve assessed within past year
    - Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe aortic stenosis (AHA 2014: Class IIa, LOE: B).
    - In general, risk-benefit ratio currently favors undergoing surgery with hemodynamic monitoring and optimization, instead of prophylactic aortic valve replacement (limited evidence available).
- Moderate or greater AS with normal LV systolic function – reasonable to perform elective non-cardiac surgery (Class 2a recommendation, LOE: B).
    - Increased risk if severe CAD is present – consider coronary CT angiogram if clinically suspected.
- Mild-Moderate AS: Safe to go to OR without further interventions.

Percutaneous valve interventions

- Transcatheter aortic valve implantation (TAVI)
    - There is little data on TAVI use preoperatively for people undergoing non-cardiac surgery.
    - Likely a reasonable approach to minimize delay to semi-urgent non-cardiac surgeries.
- Balloon aortic valvuloplasty
    - May be considered as a temporizing option if surgical aortic valve replacement (SAVR) is preferred modality and patient is unstable with prohibitive surgical risk for SAVR.

AHA/ACC 2020 Guideline Recommendations

All patients with severe valvular disease being considered for intervention should be evaluated by a multidisciplinary team with consultation at a Comprehensive Valve Centre (AHA 2020).

Class I

1. In patients with clinical suspected moderate or greater degrees of valvular stenosis or regurgitation who are undergoing non-cardiac surgery, preoperative echocardiography is recommended if there has been either 1) no prior echocardiography within 1 year or 2) a significant change in clinical status or physical examination since last evaluation (Class 1 recommendation, LOE: C).
2. For adults who meet standard indications for valvular intervention (replacement and repair) on the basis of symptoms and severity of stenosis or regurgitation, valvular intervention before elective noncardiac surgery should be performed to reduce perioperative risk if possible, depending on the urgency and risk of the non-cardiac procedure *(LOE: C)*.

Class IIa

1. Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe aortic stenosis (LOE: B).

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10. MITRAL STENOSIS

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Key points

- Rheumatic fever and mitral annular calcification (MAC) are the two most common etiologies leading to mitral stenosis (MS).
- The natural history and management of these two etiologies are different. Although balloon mitral valvulotomy (BMV) is an option in the perioperative management of rheumatic MS, it is not available for MS due to MAC.
- Stenosis severity grading is more complex with MS due to MAC.
- Stenotic pathologies are generally less well tolerated than regurgitant diseases in a perioperative setting.
- Heart rate control is very important in these patients.

Epidemiology

- Prevalence of moderate or severe MS in industrialized countries: 0.1- 0.3%.
- Prevalence of moderate or severe MS in low human development index countries where rheumatic heart disease is more common: up to 0.8%.

Etiology

- Rheumatic fever
- MAC (degenerative MS)
- Congenital
- Carcinoid
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Mucopolysaccharidosis
- Fabry
- Whipple
- Methysergide
- Radiation therapy
- Myxoma (may mimic mitral stenosis)
- Thrombus (may mimic mitral stenosis)
- Large vegetation (may mimic mitral stenosis)

Natural History

- Valve area decreases by 0.09 cm^2/year.
- Mean gradient increases by 1 mmHg / year (large variation between patients).
- The natural history of MS is highly variable, especially for rheumatic MS.

Severity Grading Severity Grading

Table 1 – Stage of MS (ACC/AHA 2020)

Stage	Definition	Valve anatomy	Valve hemodynamics	Hemodynamic consequences	Symptoms
A	At risk of MS	Mild valve doming during diastole*	Normal transmitral flow velocity	None	None
B	Progressive MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets* Planimetered mitral valve area >1.5 cm^2	Increased transmitral flow Velocities Mitral valve area >1.5 cm^2 Diastolic pressure halftime <150 ms	Mild to moderate LA enlargement Normal pulmonary pressure at rest	None
C	Asymptomatic severe MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets* Planimetered mitral valve area ≤1.5 cm^2	Mitral valve area ≤1.5 cm^2 Diastolic pressure halftime ≥150 ms	Severe LA enlargement Elevated PASP >50 mm Hg	None
D	Symptomatic severe MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets* Planimetered mitral valve area ≤1.5 cm^2	Mitral valve area ≤1.5 cm^2 Diastolic pressure halftime ≥150 ms	Severe LA enlargement Elevated PASP >50 mm Hg	Decreased exercise tolerance Exertional dyspnea

*Applicable only to rheumatic MS

Perioperative Risk

- Rheumatic MS:
    - There is little data available in the current literature to assess the effect of rheumatic MS on non-cardiac surgery, mainly due to the wide availability of balloon miral valvotomy (BMV).
    - However, pregnancy in low human development index countries where diagnosis and access to BMV is limited, maternal mortality for medically managed decompensated MS is 47%. In industrialized countries with access to BMV, maternal mortality from moderate and severe MS is between 1-3%.
    - Untreated significant MS in asymptomatic patients undergoing noncardiac surgery can significantly impact intervention morbidity and mortality. Although there are no definitive data, the absence of symptoms, atrial fibrillation (AF), and pulmonary hypertension,

probably signifies a lower risk cohort for noncardiac surgical interventions. Prognosis is poor in patients with untreated symptomatic MS.

- Calcific MS:
    - No study has examined the impact of calcific MS in the perioperative setting. Most expert opinions are extrapolated from rheumatic MS data. Note that stenosis severity grading in patients with calcific disease is more challenging. For the same gradient, the degree of stenosis can be very different between rheumatic and calcific MS, and so, the impact of elevated gradients secondary to calcification remains unclear.

Pathophysiology of Risk

- Severe MS results in:
    - Impaired left ventricular (LV) filling due to obstruction of left atrial (LA) outflow
    - LA pressure, pulmonary artery pressure (PAP), and pulmonary artery wedge pressure are increased
    - Patients with chronic MS typically have increased pulmonary vascular resistance (PVR) and pulmonary hypertension
    - Increase risk of perioperative AF

Contributing Perioperative Factors

- Decreased or increased pre-load:
    - Fasting patient
    - Fluids shifts/bleeding
    - Fluid resuscitation
- Decreased atrial kick/ventricular filling time:
    - Tachycardia/arrhythmias
- Risk of hypoventilation, subsequent hypercapnia/hypoxemia, increase PVR and secondary right ventricular (RV) failure
    - Anesthetic effects
    - Epidural

Preoperative Assessment

- History
    - Symptoms of severe MS (dyspnea, tiredness, poor exercise tolerance, orthopnea, paroxysmal nocturnal dyspnea)
    - Symptoms of pulmonary hypertension (peripheral edema, hemoptysis)

    - Symptoms of AF (palpitations)
    - Symptoms of peripheral embolism
    - Other (recurrent laryngeal nerve compression by dilated LA – Ortner's syndrome)
- Physical Exam
    - Mitral facies
    - Jugular vein distension with a prominent a wave
    - Increased S1 (when leaflets still pliable)
    - Opening snap (may be absent with extensive leaflet calcification)
    - Diastolic rumble
    - Signs of pulmonary hypertension

Physical Exam Bottom Line

- If a diastolic murmur suggestive of MS is heard at the apex, an opening snap close to S2 (or a long diastolic murmur) is suggestive of severe MS.

Investigations

- 2D Echo → assess severity and etiology of MS, LV function, RV function, pulmonary pressure, and concomitant valvulopathies ***(ACC/AHA Class 1 recommendation)***
- Optional: Stress echocardiogram → assess the hemodynamic consequences of MS with exercise/stress, and confirm the symptom status
- Optional: Invasive catheterization → assess valve hemodynamics and confirm severity
- ECG or 48-hour Holter monitoring to identify atrial fibrillation
- The role of BNP in the perioperative setting in MS patients remains unclear. BNP has been associated with valve disease severity and prognosis and has been used to distinguish dyspnea of cardiac versus noncardiac etiology. BNP is included in some perioperative guidelines to assess the risk of perioperative myocardial infarction, but its usefulness specifically in valvular heart disease patients is unknown.

Management

Preoperative management:

Rheumatic MS:

If symptomatic with valvular area <1.5 cm^2 (moderate or severe MS):

- Consider BMV before noncardiac surgery ***(ACC/AHA Class 1 recommendation).***
- If not suitable, consider valve surgery before the noncardiac surgery.
- If BMV and valve surgery are not an option, proceed with noncardiac surgery with strict monitoring if the noncardiac procedure is absolutely needed.

If asymptomatic with valvular area <1.5 cm^2 (moderate or severe MS), assess for the presence of red flags at rest (i.e. sPAP>50mmHg) or with exercise (i.e. symptoms, mean gradient >15 mmHg, sPAP>60 mmHg).

- If red flags present, consider BMV or valve surgery prior to the noncardiac surgery depending on the urgency and risk of the noncardiac procedure. If not possible, proceed with noncardiac surgery with strict monitoring.
- If no red flags, proceed with noncardiac surgery with strict monitoring ***(ACC/AHA Class 2a recommendation).***

Calcific MS:

If symptomatic with valvular area <1.5 cm^2 (moderate or severe MS):

- BMV is usually not an option. Valve surgery before the noncardiac surgery can be considered.
- If valve surgery is not an option, proceed with noncardiac surgery with strict monitoring if the noncardiac procedure is absolutely needed.

If asymptomatic with valvular area <1.5 cm^2 (moderate or severe MS), assess for the presence of red flags at rest (sPAP>50mmHg) or with exercise (symptoms, mean gradient >15 mmHg, sPAP>60 mmHg).

- If red flags present, consider valve surgery prior to the noncardiac surgery. If not possible, proceed with noncardiac surgery with strict monitoring.
- If no red flags, proceed with noncardiac surgery with strict monitoring.

Regardless of severity and etiology:

- Endocarditis prophylaxis NOT required (unless otherwise indicated)

Perioperative optimization:

- **Heart rate: Maintain heart rate between 50-70 bpm with B-blockade**
- **Heart rhythm: Maintain sinus rhythm with cardioversion and/or antiarrhythmics**
- Preload: Maintain adequate intravascular volume
- Afterload: Control blood pressure (SBP>100 mmHg, MAP>70 mmHg)
- Contractility: Avoid drugs with negative inotropic effect (ex: high dose of propofol or volatile inhalation anesthetic agents)
- PVR: Avoid hypoxemia, hypercarbia, and metabolic acidosis

Postoperative management:

- Monitor for arrhythmias
- Anticoagulation is indicated if atrial fibrillation is present (regardless of CHADS2 score)
- In patients with rheumatic heart disease, secondary prevention of rheumatic fever is indicated (10 years after last episode or until patient is 40 years of age - whichever is longer), usually with penicillin (see ACC/AHA 2020 guidelines for specific treatment regimens)

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12. RESPIRATORY ASSESSMENT

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Introduction

- This section does not pertain to primary cardiac or pulmonary surgeries given their unique risk factor and management principles. It also does not discuss treatment of respiratory complications after they arise.
- Unlike perioperative cardiac risk assessment, there are minimal consensus group guidelines to help direct general care. One of the most commonly referenced is by the American College of Physicians in 2006[1]. There is a recent guideline for the preoperative evaluation of adults undergoing non-cardiac surgery by the European Society of Anaesthesiology, although the respiratory section is limited in scope[2]
- Despite less attention compared to perioperative cardiac risk stratification, rates of perioperative pulmonary complications (PPCs) occur in similar frequency to cardiac complications and associated with higher length-of-stay and cost[3]
- Commonly-studied PPCs include[4]:
    - respiratory failure
    - respiratory infection
    - pleural effusion
    - atelectasis
    - pneumothorax
    - bronchospasm treated with bronchodilators
    - aspiration pneumonitis

Risk Assessment

- Unlike cardiac complications, the risk of PPCs is correlated more with the type of surgery than patient-associated risk factors. Therefore, even in relatively healthy patients, there may still be a significant risk of PPCs depending on the planned surgery[3].

<u>Surgical Procedure Associated Risk Factors</u>

Of all risk factors (both surgical and patient-related), the specific surgical site is the most important risk factor for PPCs (Table 1).[5] Other surgical risk factors include:

- Emergency surgery
- Prolonged surgery (greater than 2.5-4 hours)
- Use of general anesthesia
- Perioperative transfusion

Table 1 - OR of perioperative pulmonary complications (PPCs) at different surgical sites

Surgical Site	OR (95% Confidence Interval)
Aortic	6.9 (2.74–17.36)
Thoracic	4.2 (2.89–6.23)
Any abdominal	3.1 (2.54–3.77)
Upper abdominal	3.0 (2.40–3.63)
Neurosurgery	2.5 (1.84–3.47)
H&N	2..1 (1.82–2.68)
Vascular	2.1 (0.81–5.42)

Patient Associated Risk Factors[2,3]

- Advanced age (independent of co-morbidity)
- ASA class > II (as surrogate for co-morbidity)
- CHF
- Functional dependence
- COPD
- Weight loss
- Impaired sensorium
- Cigarette use
- Alcohol use
- Abnormal findings on chest examination
- Obstructive sleep apnea (newer finding)
- Pulmonary hypertension (newer finding)

A high STOP-BANG score for OSA has been associated retrospectively with higher rates of postoperative complication.[6] Severe sleep apnea has also been associated with an increased risk of 30-day of postoperative cardiovascular complications[7], though there are no standardized screening recommendations. It should be noted that neither well-controlled asthma nor obesity are associated with PPCs. Interestingly, weight loss or low BMI denotes higher risk of PPCs.

Risk Scores/Calculators

There are several risk scores that can aid prediction of perioperative pulmonary complications (PPCs) and facilitate discussions of risk with patients. Outlined below are the best studied/most common risks scores and their associated benefits and downsides[8]:

Table 2 – Respiratory risk scores and their characteristics

Risk Score/Calculator	Complications Measured	Benefits	Downside	
ARISCAT (2010)	Overall PPCs	Externally validated Only requires easily accessible data	Inclusion of minor PPCs in total risk calculation, which may not be important to patients	
Arozullah respiratory failure index	Postoperative respiratory failure (mechanical ventilation for ≥48 hours)	Externally validated Predicts a patient-relevant outcome	Requires computer to use given complexity	
Gupta calculator for postoperative respiratory failure (2011)	Postoperative respiratory failure (mechanical ventilation for ≥48 hours or unplanned intubation/reintubation)	Externally validated Predicts a patient-relevant outcome	Requires computer to use given complexity	
Gupta calculator for postoperative pneumonia (2013)	Postoperative Pneumonia	Externally validated	Requires computer to use given complexity	

Preoperative Investigations

Pulmonary Function Test (PFTs)

For non-thoracic surgery, PFTs are not routinely indicated as they do not add significant risk prediction when used in combination with the other risk factor assessments described above.

If a patient is thought to have either undiagnosed or progressive obstructive lung disease however, PFTs may be helpful for management of their chronic illness.

Chest Radiograph

The chest radiograph only rarely provides unexpected information that influences preoperative management, above and beyond what can be determined from a history and physical examination. In a meta-analysis of routine perioperative chest radiographs, 10% of the radiographs had abnormal findings, and results were unexpected in only 1.3%. Furthermore, these findings were significant enough to change management in only 0.1%.[9]

Bloodwork

There are no bloodwork screening tests to help predict PPC. An elevated BUN (>7.5 mM) and decreased albumin (<35 g/L) have both been shown to correlate with PPC.[5]

Strategies to Reduce Postoperative Pulmonary Complications

PPC risk reduction strategies can be divided into preoperative, intraoperative, and postoperative interventions. The role of the internist is primarily allocated to the pre- and postoperative sections, although it may be helpful to understand the intraoperative strategies when discussing cases with surgeons and anesthesiologists. The evidence for these interventions in general is limited.[10]

<u>Preoperative Interventions</u>

Treat underlying chronic pulmonary conditions and or infections as per non-operative standards of care

Optimizing management of chronic pulmonary conditions such as COPD and asthma should be done similarly to as if the patient was not planned

for surgery. Likewise, if the patient has a respiratory infection, they should be treated as per standard of care. Furthermore, if symptomatic sleep apnea or pulmonary hypertension was discovered on examination, it may be reasonable to delay elective surgery for further investigations and initiation of treatment. These decisions should consider patient preference and the surgical team's opinion.

Smoking Cessation

There has been previous concern that stopping smoking less than eight weeks prior to surgery may paradoxically increase the risk given PPCs given previous prospective studies. It was theorized that alterations in the pulmonary system after smoking cessation such as increased sputum production may have been a cause. More recent meta-analyses (although having mixed results) either show no change in PPCs with recent cessation[11] or a continuous decrease in PPC with longer duration of cessation.[12] From a perioperative standpoint, smoking cessation either has neutral or positive effects, however given the considerable long-term health benefits of smoking cessation, it should be encouraged.

Correcting Malnutrition

In a prospective study of patients, undergoing cardiac or abdominal surgery, patients with malnutrition (based on BMI and biochemical testing) had increased muscle weakness, decreased chest wall expansion and postoperative respiratory complications.[13] Although to our knowledge there is no trial of nutritional optimization preoperatively, given the low risk of harm, it may be reasonable to attempt to improve nutrition prior to surgery via counselling or dietician referral.

Inspiratory Muscle Training

A Cochrane review found that inspiratory muscle training prior to surgery decreased risk of PPCs based on low to moderate evidence.[14] These training programs may or may not be available locally.

Intraoperative Interventions

These interventions are primarily managed by the surgeon and anesthesiology physicians involved. Those with the best evidence are underlined.[10]

Interventions include:

- Anesthesiology-guided
    - Using neuraxial (spinal or epidural) anesthesia instead of general anaesthesia
        - Despite the associated increased risk of PPCs, a recent RCT in NEJM comparing spinal anesthesia vs. general anaesthesia for patients undergoing hip fracture surgery did not find a difference in recovery of ambulation or survival.[15] The study was not powered to detect differences in PPCs but the lack of difference in mortality suggests that even if pulmonary complications did occur, in general they did not lead to death or delay ambulation.
    - Using short acting neuromuscular blockade over longer acting agents
    - Lung protective ventilation
    - Goal-directed hemodynamic therapy
- Surgery-guided:
    - Choose surgical plan that minimizes time under general anesthesia
    - Change surgery or procedure to a lower risk type or manage non-surgically

Postoperative interventions

A recent meta-analysis of perioperative interventions for PPCs found the following interventions listed below had benefit, although all had low quality evidence. Given the low-quality evidence, none of these interventions are routinely administered in current local clinical practice:

- Prophylactic non-invasive ventilation
- Prophylactic mucolytics
- Enhanced recovery pathways (bundled intervention programs)
- Content of the enhanced recovery pathways varied from trial to trial, but all patients received a combination of at least three of the following elements: early ambulation, early feeding, protocolized analgesia, early removal of nasogastric tubes, and urinary catheters.
- Respiratory therapy

Interestingly, despite the 2006 ACP guideline advocating for postoperative lung expansion techniques like deep breathing exercises or incentive spirometry a more recent meta-analysis found moderate quality evidence that did not support routine use.[10]

Other research has shown that routine use of nasogastric tubes for decompression increases risk of PPCs and therefore be avoided unless required due to clinical circumstances.[16]

Other postoperative considerations

- Chronic therapies for underlying pulmonary conditions (COPD, asthma, OSA, pulmonary hypertension) should be re-initiated when possible.
- Early mobilization and pain management may be beneficial and unlikely to be harmful

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13. HEMATOLOGIC DISORDERS

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Consider hematological risk assessment in the following circumstances:

- History of bleeding disorder or excessive bleeding
- Prolonged PT or aPTT, thrombocytopenia or platelet function defect
- Surgery with an increased risk of bleeding and insufficient number of red blood cells available
- History of sickle cell disease
- Patient refusing red blood cell transfusion for religious or cultural reasons

1. Hemostasis and Coagulation

Table 1 - Etiologies for prolonged coagulation assays

Prolonged PT/INR with normal aPTT	Prolonged aPTT with normal PT/INR	Prolonged PT/INR and aPTT
• Acquired factor VII deficiency: early warfarin therapy, early vitamin K deficiency, early liver disease • Drugs: direct Xa inhibitors (e.g. rivaroxaban, apixaban, edoxaban) • Congenital deficiency of factor VII • Specific inhibitors to factor VII (exceptionally rare) • Caution: PT/INR can be normal with mild single factor deficiencies due to reagent sensitivity.	• Congenital deficiency of factors VIII, IX, XI, XII • Therapeutic unfractionated heparin exposure • Antiphospholipid antibodies • Specific inhibitors e.g. factor VIII inhibitor • Caution: aPTT can be normal with mild single factor deficiencies and often normal in von Willebrand disease. Hemophilia A and B: x linked (males predominant; female carriers can be symptomatic), aPTT if factor 8 and factor 9 < 30%	• Thrombin inhibitors: heparin, direct thrombin inhibitors (e.g. dabigatran), direct Xa inhibitors (e.g. apixaban, rivaroxaban, edoxaban) • Liver disease • Supratherapeutic warfarin effect • Severe vitamin K deficiency • Consumption: massive hemorrhage, DIC • Congenital deficiency

Table 2 - Appropriate use of PT/INR and aPTT

Use of PT/INR	Use of aPTT
• Warfarin therapy • Liver disease • Risk factors for vitamin K deficiency: malnutrition, malabsorption, cholestasis, prolonged antibiotics	• Planned for IV heparin exposure intraoperatively (e.g. cardiac or vascular surgery) • Suspected hemophilia A/B • Factor XI deficiency • Severe von Willebrand disease • Suspected factor inhibitor • Suspected antiphospholipid syndrome
Choosing wisely: do not order in following circumstances	
• Routine blood work • Routine preoperatively screen in low risk non-cardiovascular surgery patient • No personal or family history of bleeding	

2. Assessment of Perioperative Bleeding Risk

Guidelines regarding screening:

- Due to poor sensitivity and specificity of coagulation testing (i.e. normal PT and PTT does not rule out the presence of a bleeding disorder), it is not recommended to use coagulation studies to screening for bleeding disorders in unselected patients prior to surgery.[1]
    - PT and aPTT had a sensitivity of 1.0-2.1% for ruling out bleeding disorders.[2]
- For bleeding risk assessment, the patient history is the most important tool in determining pre-test probability of a bleeding disorder, and guidelines recommend it be done preoperatively.[1,3]
- The questions should include personal and family bleeding history, particularly prior bleeding challenges, comorbidities that may increase bleeding risk (Table 3), type of surgery planned, and detailed history of medications.
    - Bleed risk assessment tools (such as ISTH or MCMDM-1 has been validated for bleeding disorders)
    - Please see bleeding risk assessment tool validated for perioperative setting: Koscielny J, Ziemer S, Radtke H, et al. Clin Appl Thrombosis/Hemostasis 2004; 10(3):195–204

Table 3 - Conditions with increased risk of bleeding

Hepatic insufficiency Renal failure (bleeding due to platelet dysfunction) Clotting factor deficiency or inhibitor Platelet deficiency or defect Drug-induced clotting deficiency (ASA, GPIIb/IIIa inhibitors, anticoagulants)

3. Hemostatic defects

Issues with Primary Hemostasis: Thrombocytopenia

Investigations suggested preoperatively when platelet count is < 100 (Table 4).

Table 4 – Investigations for various etiologies of thrombocytopenia

Causes of thrombocytopenia	Mechanism	Investigations
Pseudothrombocytopenia	Due to platelet clumping	Collect specimen in citrate tube
Decreased Production	Nutritional deficiency, bone marrow suppression or invasion: myelodysplasia, toxins/infection, leukemia	Blood smear, B12, RBC folate, TSH, viral workup (HIV, EBV, HCV), SPEP+IFE, ±bone marrow
Increased Destruction/ Consumption	*Immune-mediated:* ITP, HIT, drug-induced ITP, posttransfusion, malignancies, viral infections, autoimmune diseases	ANA, Coombs, anticardiolipin antibodies, lupus anticoagulant, HIV, Hep C, EBV, CMV, H. Pylori ±bone marrow, HIT assay (if applicable)
	Non-immune : TTP/HUS, sepsis, malaria, DIC, HELLP	INR, PTT, Fibrinogen, D dimer, bilirubin, LDH, haptoglobin, blood smear, renal function
Sequestration	Enlarged Spleen	Abdominal U/S

Specific thrombocytopenia etiologies

Disseminated intravascular coagulation (DIC)

- Clinical suspicion for DIC with underlying condition known to be associated with DIC (Table 5) AND thrombocytopenia/prolonged coagulation tests (INR/PT, aPTT) and hypofibrinogenemia
- Calculate DIC score using ISTH algorithm
    - Score ≥ 5 has sensitivity of 93% and specificity of 98% for diagnosis of DIC
    - Severity of this score also strong predictor of mortality in sepsis
- Treatment
    - Treat underlying condition
    - Overt thrombosis: therapeutic anticoagulation
    - Active bleeding or need for procedures: transfusion targets below
        - Platelet > 30-50
        - Cryoprecipitate or fibrinogen concentrate to maintain fibrinogen ≥ 1.5 g/l
        - Vitamin K if suspicion of deficiency

Table 5 - Conditions commonly associated with DIC

Condition	Examples	Consequence
Severe infectious diseases	Sepsis, malaria, hemorrhagic fevers	Thrombosis may contribute to organ failure
Malignancy	Solid tumors (e.g., adenocarcinomas) Acute promyelocytic leukemia or monocytic leukemia	Thrombosis Severe thrombocytopenia and factor deficiency may lead to bleeding
Trauma	Multitrauma, brain injury, burns	Primary feature is acute bleeding, followed by thrombosis
Obstetrical complications	Placental rupture, amniotic fluid embolism	Bleeding and thrombotic complications
Vascular malformations	Kasabach-Merrit syndrome Giant hemangiomas	Bleeding

	Large aortic aneurysms	
Severe immunologic reactions	Transfusion reaction	
Heat stroke		Thrombosis more common than bleeding
Post-cardiopulmonary resuscitation		Thrombosis more common than bleeding

Adapted from "How I treat disseminated intravascular coagulation")[4]

Heparin induced thrombocytopenia (HIT)

- Typically occurs following heparin exposure (usually cardiovascular or vascular surgery): usually ≥ 5 days after exposure with thrombocytopenia and thrombosis.
- If HIT suspected: stop heparin from all sources (including lines, flushes) and calculate 4T score.
- If 4T score low probability: can resume heparin.
- If 4T score intermediate or high probability:
    - Consult Hematology.
    - Send confirmatory testing (serotonin release assay)
    - Prophylaxis for thrombotic complications or treatment of thrombotic complications with fondaparinux, argatroban or direct oral anticoagulants, in discussion with Hematology

Issues with Primary Hemostasis: von Willebrand factor

von Willebrand disease (vWD)[5]

- Epidemiology
    - The most common inherited bleeding disorder, affecting up to 1% of the population.
- Pathophysiology
    - Causes defective platelet adhesion and aggregation.
- Symptoms
    - Most commonly causes mucosal bleeding (i.e. dental procedures), menorrhagia, and rarely gastrointestinal bleeding from angiodysplasia
    - Rarely can present with deep tissue bleeding (ie. type 3 vWD).

- Types
    - Type 1 (quantitative deficiency of von Willebrand factor):
        - It is the most common
        - Usually causes mild bleeding
    - Type 2 (qualitative defect of VWF):
        - Variable bleeding
    - Type 3: (absence of VWF):
        - Behaves like hemophilia A due to low factor VIII
- Diagnosis
    - Screening: von Willebrand factor antigen, von Willebrand factor platelet binding activity (vWF–ristocetin cofactor activity assay), and factor VIII activity
    - Subtype classification requires specialized testing
- Prevention preoperatively
    - Avoid trauma, avoid antiplatelet agents, increase VWF levels prior to surgery/procedure
- Treatment during bleeding episodes requires normalizing von Willebrand factor and factor VIII levels (with desmopressin or exogenous vWF)
- Management principles for bleeding
    - Call Hematology or hemophilia treatment center (St. Michael's hospital)
    - General hemostatic measures
        - Local hemostatic control
        - Tranexamic acid 25 mg/kg PO q8hours (usually dose 1-1.5 g/dose) or 10mg/kg IV for mucosal bleeding
    - Treatment of bleed depends on subtype and severity of bleed
        - Type 1:
            - If known responder: DDAVP 0.3 mcg IV or SC (20 mcg dose cap in Canada)
            - If known non-responder or unclear: vWF/FVIII concentrate (Humate-P or Wilate)
        - Type 2 and type 3:
            - usually require VWF/FVIII concentrate: dose depends of VWF activity level desired

Issues with secondary Hemostasis: Factor Deficiency

Hemophilia[6]

- X linked FVIII deficiency (hemophilia A) or FIX deficiency (hemophilia B)
    - Female carriers may be symptomatic
    - Severity depends on baseline FVIII or FIX level
        - Severe < 0.01 IU/ml (<1%)
        - Moderate 0.01-0.04 (1-4%)
        - Mild >0.05-0.40 (5-40%)
- Clinical presentation
    - Classically joint, tissue, muscle bleeds, excessive post op bleeding
- Prevention preoperatively
    - Avoid trauma, avoid antiplatelet/NSAIDS, prophylactic factor replacement therapy
- Management principles for bleeding
    - Call hematology or hemophilia treatment center (St. Michael's hospital)
    - 1. General hemostatic measures
        - Local hemostasis
        - Tranexamic acid 25 mg/kg PO q8hours q8hours (usually dose 1-1.5 g/dose) or 10mg/kg IV for mucosal bleeding
    - 2. Treat bleeding: factor replacement
        - 1/kg U factor VIII increases patient level by ~ 2% → dose for severe hemophilia A = 50 U/kg
        - 1/kg U factor IX increases patient level by ~ 1% → dose for severe hemophilia B = 100 U/kg
        - DDAVP 0.3 mcg/kg iv or SC (20 mcg dose cap in Canada) can be used for mild Hemophilia A
- Management of inhibitors
    - Approximately 30% of patients with severe hemophilia A develop inhibitors to replacement factor VIII
    - Note: acquired factor VIII inhibitors = acquired hemophilia A
    - Management using bypassing agents:
        - recombinant factor VIIa
        - FEIBA (Factor Eight Bypassing Agent – FII, VII, FIX, FX and activated FVII)
        - Obizur (recombinant porcine FVIII) (not widely available)

Perioperative Management of Patients with Cirrhosis

Bleeding risk assessment

- Laboratory markers of coagulation exhibit marked changes with liver disease progression.
- Despite increased INR and thrombocytopenia, global hemostatic assays suggest a hypercoagulable state.
    - PT/INR does not adequate reflect state of coagulation in cirrhosis, with a lack of association between PT/INR and procedural bleeding risk.
- Thrombocytopenia occurs in 80% of patients with cirrhosis; however, also does not correlated with bleeding.
- The majority of bleeding complications in patients with cirrhosis are gastrointestinal secondary to portal hypertension; hence, bleeding history predating onset of cirrhosis may be more helpful for identifying underlying inherited bleeding disorder.

Table 6 - Bleeding risk by procedure

	Low bleeding risk	High bleeding risk
Endoscopic	• Diagnostic procedures Endoscopic variceal ligation Trans-esophageal echocardiogram	• Bronchoscopy with biopsy Colonoscopy with • polypectomy Endoscopic retrograde • cholangiopancreatography with sphincterotomy
Percutaneous	• Paracentesis • Thoracocentesis	• Percutaneous liver biopsy Tunnelled ascitic/pleural drain placement Cranial/spinal surgery
Vascular	• Peripheral/central venous catheterization • Transjugular liver biopsy	• Transjugular intrahepatic portosystemic shunt • Transcatheter arterial chemoembolization
Other	• Dental procedures including extractions • Skin biopsy	• Intraocular procedures

Adapted from "Periprocedural management of abnormal coagulation parameters and thrombocytopenia in patients with cirrhosis: Guidance from the SSC of the ISTH"[4]

Management:

- There is no recommendation for use of fresh frozen plasma (FFP) for prophylactic correction of abnormal coagulation parameters in the periprocedural setting in the absence of warfarin use.
    - FFP has higher risk of transfusion related acute lung injury, and the additional volume may also increase risk of transfusion associated circulatory overload; notably, extra volume can increase portal pressures and paradoxically increase bleeding risk.
- Similarly, there is no recommendation for PCC or rFVIIa.
- Vitamin K 10 mg can be administered given low side effect profile.
- There is no recommendation for prophylactic platelet transfusions, with exception of platelet transfusion within one hour of surgery for very high-risk surgeries (such as neurosurgery).
    - Caveat: although guidelines do not recommend prophylactic transfusion, discussion should be had with the surgical team as it may be reasonable to transfuse platelet if < 20.
- Management strategy should be focused on mitigating modifiable risk factors of bleeding such as antithrombotic medications and renal dysfunction.

4. Anticoagulant Reversal

General principles

1. Stop all anticoagulant medication and resuscitate as indicated
2. Provide local hemostasis if applicable
3. Obtain STAT CBC, PT/INR, PTT, creatinine and calculate CrCl (requires accurate weight), DOAC level if accessible/appropriate
4. Identify which anticoagulant the patient is taking
5. Identify the time of last dose
6. Determine likely drug presence and expected eliminant rate based on above information (time of last dose, HL, CrCl)
7. Review concomitant medications (antiplatelets, NSAIDs)
8. Evaluate seriousness of bleed
9. Decide on whether reversal is indicated: usually reserved for major, life-threatening into critical organ
10. Consider tranexamic acid: may exacerbate prothrombotic effect when given with other prothrombotic products
11. Multidisciplinary care: endoscopy, surgery, procedural interventions

Table 7 - Anticoagulant characteristics and reversal strategy

Anticoagulant	Mechanism of action	Half life	Reversal Strategy
Argatroban	Parenteral direct thrombin inhibitor	7-54 minutes	Monitor with PTT TXA 1 g IV over 10 min FEIBA 50 iu/kg x 1 **or** PCC 50 iu/kg
Low molecular weight heparin (dalteparin, tinzaparin, enoxaparin)	Subcutaneous injection of indirect anticoagulant that inactivates factor II and factor Xa via antithrombin	3-4.5 hours	Incomplete neutralization by protamine (~60% anti-xa neutralized) Dose: 1 mg per 100 units anti-Xa (tinzaparin or dalteparin) or 1 mg protamine per 1 mg enoxaparin
Unfractionated heparin	Parenteral indirect anticoagulant (activating antithrombin) resulting in inactivation of factor IIa, Xa, IXa, XIa, and XIIa	60-90 minutes in healthy adults	Monitor with PTT Protamine: dose based on amount received **in the last 4 hours** and time of last dose if received IV Dose: 1 mg per 100 IU of UFH (max dose 50 mg) Time since heparin administration / Protamine dose per 100 units of heparin administered 0 - 29 minutes / 1 mg 30 - 59 minutes / 0.5 -- 0.75 mg 60 - 119 minutes / 0.375 - 0.5 mg Greater than 2 hours / 0.25 - 0.375 mg Alternatively, an empiric dose of protamine 25-50 mg may be given

Anticoagulant	Mechanism of action	Half life	Reversal Strategy
Apixaban, Rivaroxaban	Direct anti-Xa inhibitors	Rivaroxaban 9-13 hours Apixaban 8-15 hours	Drug level (anti-Xa level) > 30 ng/ml indicate presence of DOAC PCC 50 IU/kg or 2000 IU IV x 1
Edoxaban	Direct anti-xa inhibitor	10-14 hours	Drug level (anti-Xa level) > 30 ng/ml indicate presence of DOAC PCC 50 IU/kg or 2000 IU IV x 1
Dabigatran	Direct thrombin (FII) inhibitor	12-17 hours	Order stat dabigatran level (dilute thrombin time), creatinine. Idarucizumab: 5g IV (two consecutive boluses of 2.5 g 15 minutes apart) If not available: FEIBA 50 IU/kg bolus or PCC 50 IU/kg
Warfarin	Vitamin K antagonist inhibits the activation of FII, FVII, FIX, FX, protein C and S	36-42 hours	No bleeding: • INR > 9-10: hold, vitamin K 2.5-5 mg PO • INR > 4.5-9: hold, decrease dose Non-life- threatening bleed: Vitamin K 5-10 mg IV, supportive Life-threatening bleed: • Vitamin K 10 mg IV • PCC based on INR • INR 1.5-3: 1000U • INR 3-5: 2000U • INR> 5: 3000U

Important notes for PCCs:

- Contain vitamin K dependent factors (FII, VII, IX, X, Protein C and S) and a small amount of heparin
- CONTRAINDICATED if HISTORY OF HIT POSITIVITY
- Increase risk of thrombosis

Important notes for DOAC levels: “safe” DOAC level based on expert opinion reviewing PK data

- <30 ng/mL for high risk surgery
- >50 ng/mL with serious bleeding = consider reversal
- >200 ng/mL: concentration associated with periprocedural bleeding

5. Antiplatelet reversal

Antiplatelet reversal

- PATCH trial randomized patients on antiplatelets to platelet transfusion vs no platelet transfusion: showed harm in platelet transfusion arm (with worse mortality); transfusion NOT recommended if no surgical intervention planned.
- Consider platelet transfusion if neurosurgery planned as these patients were excluded.
- Consider tranexamic acid: meta-analysis of 7 trials using TXA to reduce surgical bleeding related to antiplatelet monotherapy or DAPT showed reduction in blood loss, re-operation, blood/platelet transfusion.
- Consider DDAVP: small studies of DDAVP shown affect in aspirin and bleeding.

6. Transfusion

Table 8 - Red blood cell transfusion target

Patient	Hgb threshold	Transfusion approach
Young patients with severe iron or B12 deficiency anemia (fatigue and pallor)	any	IV iron
Young patient with reversible asymptomatic anemia (postpartum, recovering trauma)	<50	1 unit
Average patient without symptoms or cardiac history	<70	1 unit
Cardiac history without symptoms	<70-80	1 unit
Hemodynamic symptoms (tachycardia, presyncope)	<90	1 unit
MI with only fatigue and pallor (	<80	1 unit SLOW
Slow bleeding and asymptomatic anemia	<70	1-2 units
Rapid hemorrhage (stabbing, gunshot, varices)	keep 60-110	As many as needed, use uncross matched

Table 9 - Platelet transfusion target

Platelet count	Clinical setting	Transfusion approach
<10	Prophylactic	1 adult dose
<20	Procedures not associated with significant blood loss (e.g. central line placement)	1 adult dose
<30-50	Patients on anticoagulants that cannot be stopped*	1 adult dose
<50	major elective surgery requiring epidural anaesthesia, LP, significant bleeding, c-section	1 adult dose immediately prior to procedure
<100	CNS surgery, ICH, TBI	1 adult dose
Any	Platelet dysfunction and marked bleeding: aspirin, post cardiopulmonary bypass, antiplatelet agents (except if no neurosurgical intervention while on antiplatelets in ICH)	1 adult dose
Thrombosis within 30 days • Transfusion platelet > 50 to allow full dose anticoagulation Thrombosis beyond 30 days[7] • Platelets > 50: reasonable • Platelets 25-50: 50% dose reduction of LMWH • Platelets < 25: hold anticoagulation		

Fresh frozen plasma

- Indications: significant bleeding with INR >1.8 or *significant procedure* with INR >1.8 (Choosing Wisely)
- Dose is 15 ml/kg = approximately 3-5U per adult patient (Typically 4)

7. Blood conservation

Alternatives to Red blood cell Transfusion in the Patient with Anemia[8]

- Transfusion of red blood cells and other blood products may be refused by individual patients due to cultural or religious reasons (Jehovah's Witnesses).
    - It is important to obtain precise products that would be accepted and not accepted by patients
    - Generally, the following will NOT be accepted:
        - Whole blood, packed red blood cells, plasma, platelets, WBCs, autologous products
    - Generally, the following will be accepted

        - Autologous salvaged blood, albumin, cryoprecipitate, hemostatic agents, desmopressin, crystalloid or colloid solutions
- It is therefore imperative that hematological risk assessment be done in these patients, preferably at least 2 weeks prior to planned surgery, and that use of other blood-sparing strategies be considered if the risk of bleeding is high.

Blood Sparing Strategies include (where available):

- Preoperative strategies to increase red blood cell mass:
    - Erythropoietin 150-300 IU/kg SC 6 doses in 3 weeks or 600 IU/kg 3 doses in 7-10 days[1]
    - Iron 100-300mg/day, Folic Acid 5mg/day, vitamin B12 1000mg/day
- Preoperative autologous blood donation:
    - The patient's whole blood is collected weeks prior to surgery, stored, and then reused if needed perioperatively or postoperatively. This practice may not be acceptable to all Jehovah's Witnesses and should be addressed individually.
- Acute normovolemic hemodilution:
    - The patient's whole blood is collected on induction of anesthesia while simultaneously infusing colloid or crystalloid. The patient's blood can then be re-infused as needed as a continuous circuit during surgery or postoperatively.
- Intraoperative cell salvage:
    - This practice involves suctioning blood from the operative field with heparinized saline, following by filtering and centrifuge so that the patients individual red blood cells can be reinfused.
- Intraoperative controlled hypotensive anesthesia:
    - d deliberately lowering systolic blood pressure to 80-90, mean arterial pressure of 50-65 or a 30% reduction in baseline mean arterial pressure in order to decrease cardiac output and subsequent blood loss.
- Intraoperative hypothermia or hyperoxic ventilation
- Use of Hemostatic agents (antifibrinolytics)
- Hemoglobin based oxygen carriers

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14. LIVER DISEASE

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Perioperative assessment goals are to identify patients with liver disease using clinical history and examination, estimate perioperative risk, optimize modifiable risk factors to improve morbidity and mortality outcomes, and determine if the risk is too high to recommend surgery.

Assessment of surgical risk includes assessing liver disease severity, the urgency of surgery, and co-morbidities. Surgical risk assessment is less relevant if immediate surgery is required to prevent mortality.

Major Causes of Perioperative Mortality in Liver Disease

- Hemorrhage
- Sepsis
- Liver failure/ hepatic encephalopathy
- Hepatorenal syndrome
- Respiratory failure

Predictors of Perioperative Mortality

Risk of surgery in liver disease is dependent on the type of surgery, nature and severity of liver disease, and comorbidities. The risk is increased compared to patients without liver disease in the following situations[1]:

- Type of surgery
    - Emergency
    - Abdominal, especially laparotomy, cholecystectomy, gastric resection or colectomy
    - Cardiac
    - Hepatic resection (eg. HCC resection)
    - Vascular procedures with large volume blood loss
- Nature of liver disease
    - Acute hepatitis, obstructive jaundice and advanced cirrhosis associated with higher risk than mild chronic hepatitis
- Severity of liver dysfunction
    - Child-Pugh class C>B>A
        - Ascites
        - Encephalopathy
        - Elevated INR
        - Hypoalbuminemia

    - Jaundice
    - MELD score
    - Portal hypertension, eg. Esophageal varices
    - Infection
    - Anemia
    - Malnutrition
    - Hypoxemia
- Comorbidities
    - Chronic kidney disease
    - Hepatorenal syndrome
    - Lung disease
    - Ischemic heart disease
    - diabetes mellitus

Table 1 - Contraindications to Elective Surgery in Patients With Liver Disease[1]

Acute viral hepatitis
Acute alcoholic hepatitis
Fulminant hepatic failure
Severe chronic hepatitis
Child-Pugh class C cirrhosis
Severe coagulopathy (INR> 3.0 despite vitamin K) replacement; platelet count < 50,000/mm^3)
Severe Extrahepatic complications (Acute renal failure, CHF, Hypoxemia)

Estimating Surgical Risk

Three surgical risk assessment tools applicable to clinical practice will be reviewed: Child-Pugh Score, VOCAL-Penn Score and the Mayo Risk score.

Surgical mortality rates in patients with cirrhosis correlate with the Child-Pugh Class, and were derived from retrospective studies of patients with alcoholic and non-alcoholic cirrhosis undergoing abdominal surgery, elective or emergent[2].

1. Child-Pugh Score

Table 2 - Child-Pugh score calculation

Variable\Points	1	2	3
Ascites	0	Slight	Moderate
Albumin (g/L)	> 35	28 - 35	< 28
Encephalopathy	0	Grade 1-2	Grade 3-4

INR	< 1.7	1.7 – 2.3	> 2.3
Bilirubin (µmol/L)	< 34	34 – 51	> 51
Class A 5-6	(well-compensated)		
Class B 7-9	(functional compromise)		
Class C 10-15	(decompensated)		

Table 3 - Surgical mortality with respect to Child-Pugh class[3]

Child-Pugh Class	Mortality
A	**10%**
B	**30%**
C	**80%**

2. VOCAL-Penn Score[4]

The Veterans Outcomes and Costs Associated with Liver Disease (VOCAL)-Penn score can risk stratify cirrhotic patients undergoing surgery according to mortality risk at postoperative 30, 90, and 180 days. This calculator was derived from a large cohort of patients with mainly Child Pugh class A cirrhosis and a MELD score ≤9 who had various surgical procedures (abdominal, vascular, abdominal wall, cardiac, and orthopedic surgery but not hepatic surgery)[3]. This calculator also incorporates: type and urgency of surgery, age, albumin, platelet count, total bilirubin, presence of fatty liver disease, ASA class, and body mass index (BMI).

The VOCAL-Penn risk calculator can be found at:
https://www.vocalpennscore.com/

3. Mayo Risk Score[5]

The Mayo risk score includes the MELD score plus the American Society of Anesthesiologists (ASA) class and age. It is based on the patient's age, ASA class, international normalized ratio (INR), bilirubin, and creatinine. It can estimate the 7 day, 30 day, 90 day, 1 year, and 5 year mortality rates post-surgery.

The Mayo risk calculator can be found at:
https://www.mayoclinic.org/medical-professionals/transplant-medicine/calculators/postoperative-mortality-risk-in-patients-with-cirrhosis/itt-20434721

Preoperative Liver Assessment[6]

- ☐ Emergent or Elective
  - If surgery is potentially life-saving, proceed with surgery with adequate informed consent. Consider non-surgical alternative like ongoing medical therapy or interventional radiologic procedures or palliative care as appropriate.
- ☐ Characterize liver disease
  - Determine cause and chronicity of liver disease.
    - ➢ If acute viral or alcoholic hepatitis or severe drug-induced injury, postpone surgery until liver function improves.
    - ➢ If chronic but mild liver disease, proceed with surgery.
    - ➢ If there is evidence of cirrhosis or non-cirrhotic portal hypertension, continue with liver assessment.
- ☐ Identify significant comorbid conditions
  - Focus on presence of diabetes, chronic kidney disease, and cardiovascular disease.
  - If moderate or severe malnutrition is present, optimize nutrition by oral, enteral, or even parenteral means before surgery.
- ☐ Perform liver imaging
  - MRI or CT are preferred to evaluate for liver appearance, vessel patency, hepatocellular carcinoma, and evidence of portal hypertension (e.g. intra-abdominal varices, spleen size).
  - Ultrasound with Doppler is sufficient if there is contraindication to CT or MRI such as acute kidney injury.
- ☐ Obtain history of prior hepatic decompensation
  - Ascites: if yes, consider future impact on wound healing with postoperative recurrence
  - Encephalopathy: if yes, adjust planned sedation and analgesia, monitor for regular bowel movements. Do not restrict dietary protein, give dietary protein 1.2-1.5 g/kg daily.
  - Variceal bleeding: if yes, perform upper endoscopy and initiate variceal hemorrhage prophylaxis
- ☐ Evaluate for current hepatic decompensation
  - Ascites: if yes, perform diagnostic paracentesis to evaluate for SBP
    - ➢ If moderate or severe, perform LVP before surgery.
    - ➢ If diuretic resistant and MELD<15, consider preoperative TIPS, but not routinely recommended.
    - ➢ Give 2 g sodium diet, 35-45 kcal/g daily
  - Encephalopathy: if yes, optimize lactulose to achieve 2-4 bowel movements per day (even if NGT needed) and give rifaximin
    - ➢ Do not restrict dietary protein, give 1.2-1.5 g/kg protein daily.
    - ➢ Order aspiration precautions.
  - Variceal bleeding: if yes, perform upper endoscopy and initial variceal hemorrhage prophylaxis.
  - Hypoxemia or CHF: if yes, consider hepatopulmonary syndrome or portopulmonary hypertension
    - ➢ Perform ABG, contrast-enhanced echocardiography
- ☐ Estimate liver function and the likelihood of portal hypertension
  - Check serum total bilirubin, albumin, INR, creatinine, platelets, hepatic venous pressure gradient, if available especially with partial hepatectomy.
- ☐ Calculate CTP, MELD, and modified MELD for surgery at several time points (all cirrhotics are ≥ ASA class III)
  - If Child C or MELD>12 or high risk, consider alternative to surgery or transfer to liver transplant center
  - If Child C or MELD>12 or high risk, consider completing liver transplant evaluation before surgery
- ☐ Evaluate coagulopathy and anemia
  - Give subcutaneous vitamin K supplementation leading up to surgery.
  - Give DDAVP/desmopressin if renal insufficiency present.
  - In absence of hemorrhage, do not transfuse platelets if count ≥50 x 10^3 μL or cryoprecipitate if fibrinogen >50 mg/dL
  - Avoid over-transfusion to correct anemia (use hemoglobin goal 7 g/dL) to avoid increasing portal pressures
- ☐ Review medications
  - Avoid hepatotoxic medications like herbal supplements and acetaminophen >2-3 g/day.
  - Avoid nephrotoxic medications like NSAIDs (ie. ketorolac, ibuprofen) or aminoglycosides (ie. gentamicin)
  - Avoid all benzodiazepines for anxiety/insomnia and narcotics or administer those with short half-lives
  - Monitor and correct for electrolyte and acid-base disturbances that may precipitate encephalopathy
  - Avoid prophylactic antibiotics with greater risks of drug-induced liver injury like amoxicillin-clavulanate (augmentin), nitrofurantoin, TMP/SMX (Bactrim), ciprofloxacin, and levofloxacin

Figure 1 – Comprehensive preoperative liver assessment (Adapted from Im et al. 2014)

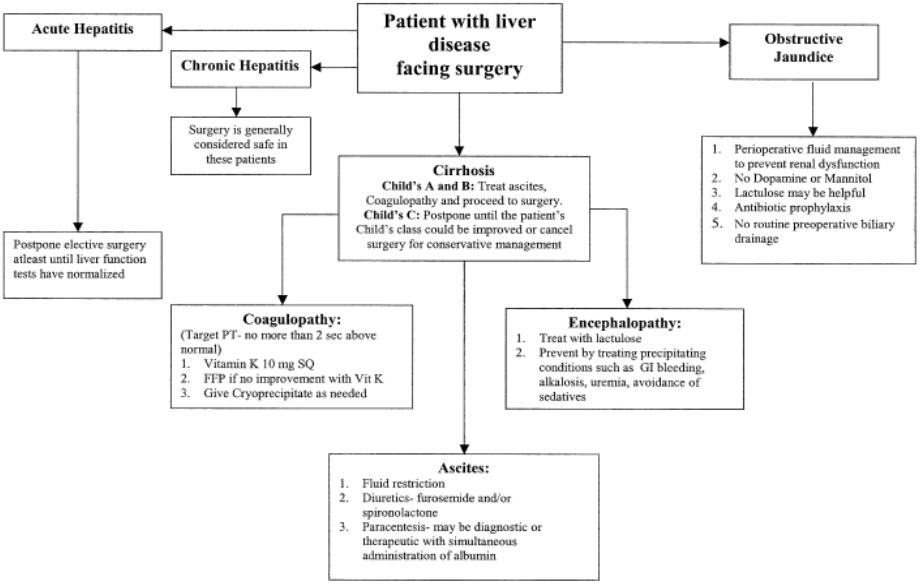

Figure 2 – Algorithm for Perioperative Management of Liver Disease

Obstructive Jaundice[1,7,8]

- Mortality rates range from 8% to 28% and increase with the following:
    - Hematocrit < 30%
    - Serum bilirubin > 11 mg/dL
    - Malignant cause of biliary obstruction
    - Azotemia
    - Hypoalbuminemia
    - Cholangitis
- Perioperative broad-spectrum antibiotics reduce postoperative infections but not mortality
- Preoperative percutaneous drainage does not improve morbidity or mortality
- Endoscopic biliary drainage does not improve surgical mortality in malignant biliary obstruction, but does have lower mortality and morbidity rates in acute stone–related cholangitis compared to surgical decompression

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15. KIDNEY DISEASE

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Acute kidney injury overview

Definition (KDIGO 2012 Guideline[1])

An Acute Kidney Injury is defined as the following occurring perioperatively

- Absolute increase in creatinine of ≥26.5µmol/L in 48 hrs
- Relative increase in creatinine of ≥50% over the last 7 days
- Urine output <0.5ml/kg/hr x 6 hours

Table 1 - AKI Staging (KDIGO 2012 Guideline)

Stage	Serum creatinine	Urine output
1	1.5-1.9 x baseline, OR ≥26.5 µmol/L increase	<0.5 mL/kg/hr for 6-12 hrs
2	2.0-2.9 x baseline, OR	<0.5 mL/kg/hr for ≥12 hrs
3	3.0 x baseline, OR ≥353.6 µmol/L Cr, OR Initiation of renal replacement therapy, OR eGFR< 35 IF <18 years old	<0.3 mL/kg/hr for ≥24 hrs, OR anuria for ≥12 hrs

Epidemiology of Perioperative AKI

The incidence of perioperative AKI varies by type of surgery. Some common examples are listed below:

- Major non-cardiac surgery (1%)[2,3]
- Cardiac surgery (1-5%)[3]
- Gastric bypass surgery (8.5%)[4]
- Liver transplant (one-third require renal replacement therapy)[5]
- Aortic aneurysm (thoracoabdominal or abdominal) (10-100%, with many needing dialysis after)[3,6]

Perioperative AKI is associated with increased:

- Re-admissions to hospital, and resultant health care costs.[7]
- Progressive CKD[8], including potential need for RRT.
- Poor long-term survival.[8-10]

Table 2 - Risk factors for perioperative AKI[11]

Preoperative (patient related)	Intraoperative (Surgery related)
• Age • Female • BMI • Hypertension • CKD Insulin requiring DM • COPD • Peripheral vascular disease • CHF • Sepsis • Ascites	**Non Cardiac Surgery:** • Duration of surgery • Intraperitoneal surgery • Abdominal aorta aneurysm repair • Intraoperative hypotension • Intraabdominal hypertension • Transplant of solid non renal organs • Transfusion of PRBC • Nephrotoxic agents (Antibiotics, NSAIDs) **Cardiac Surgery:** • Length of cardiopulmonary bypass • Cross-Clamp time • Hemodilution • Use of IABP • Type or cardiac surgical procedure

Preoperative Assessment
The preoperative kidney assessment can be split into seven domains:

1. Predicting AKI risk
    - Several surgery-specific criteria have been proposed to predict the incidence of postoperative AKI (assuming stable preoperative kidney function, either CKD or normal). See http://perioperativerisk.com or below for a list.

Table 3 - AKI risk score for general surgery developed & validated by Kheterpal et al.[2]

Risk Factor	Points
Age≥56 years	1
Male	1
Active CHF	1
Ascites	1
Hypertension	1
Emergency surgery	1
Intraperitoneal surgery	1
Renal insufficiency with Cr > 120 µmol/L baseline	1
Diabetes mellitus on oral therapy or insulin	1

Table 4 - AKI incidence within 30 days postop

Risk class	Approx. AKI incidence
I (0-2 risk factors)	0.2%
II (3 risk factors)	0.8%
III (4 risk factors)	2%
IV (5 risk factors)	3.6%
V (6+ risk factors)	9.5%

Cardiac surgery – Thakar et al. developed & validated a score to predict risk of AKI needing dialysis after open-heart surgery[12]; see www.perioperativerisk.com.

Orthopaedic surgery – Bell et al. developed an orthopaedic surgery specific risk score[13]; see www.perioperativerisk.com

Liver resection – Slankamenac et al.[14]; see calculator on www.perioperativerisk.com.

Lung transplantation – Grimm et al.[15]; see calculator on www.perioperativerisk.com.

2. Preventing AKI

- Optimize volume status[16]
  - Keep mean arterial pressure > 65.
  - Use balanced crystalloid fluid (Ringer's lactate) Normal saline can cause hyperchloremic metabolic acidosis and exacerbate hyperkalemia.[17]
  - Over-hydration: Also to be avoided (especially in patients with CKD).

- Avoiding nephrotoxic medications (not an exhaustive list)
  - NSAIDs
  - ACE-inhibitors/Angiotensin Receptor Blockers (stop at least 24 hours prior to surgery). Restart after 48-72 hours if kidney function is stable[18]
  - Antimicrobials: Vancomycin, Aminoglycosides, and Amphotericin B are common culprits. Suggest using an alternate if equally effective.
  - Monitor levels of medications (e.g. Aminoglycosides, Vancomycin) to avoid supra-therapeutic levels[1,16] Dose Amphotericin B and Aminoglycosides once daily if possible.

3. Optimizing blood-work/fluids for patients with CKD/ESRD

- Anemia:
  - Check hemoglobin preoperatively in patients with CKD/ESRD:
  - If indicated, supplement iron, supplement EPO.
  - Transfuse pRBC as per guidelines.[16]
- Potassium:
  - Typically recommended to keep <5.5.[16]
  - Ensure Low Potassium Diet, and NOT healthy heart diet if patient has CKD and high K levels, as healthy heart diet is high in potassium.
- Fluid status:
  - Ideally optimize to euvolemia.

4. Delaying surgery when appropriate

If a patient has an AKI, the decision to proceed to surgery is based on surgery urgency:

- Emergent (i.e. life threatening surgery): proceed to surgery.
- Urgent (i.e. cancer surgery or certain orthopaedic cases): delay until reversible factors corrected, unless surgery is expected to improve the AKI.
- Elective: delay until reversible risk factors corrected.[16]

5. When to involve nephrology

- Preoperative patient on dialysis
- Elective surgery and patient with AKI that is NOT recovering
- Urgent surgery and patient with AKI
- Refractory electrolyte imbalances (example: hyponatremia)

6. Preventing contrast-induced nephropathy (CIN)

Contrast agents can induce AKI by a combination of hypoxia and toxic renal parenchymal injury mediated by reactive oxygen species.[19] Mehran et al. risk score[20] for predicting CIN (Cr increased ≥25% or ≥44 µmol/L at 48 hours) post-percutaneous coronary intervention and can also be found at https://www.mdcalc.com/mehran-score-post-pci-contrast-nephropathy. The risk factors for CIN are similar as stated in the risk score by Mehran et al.

Non-pharmacologic prevention techniques[1]:

- Minimize concentration and volume of contrast media.
- Use iso-osmolar contrast agents.
- Use non-Iodine contrast imaging technique whenever possible.

Pharmacologic prevention techniques with proven evidence:

- Hydration - ideally done with isotonic crystalloid solution (NS) or isotonic sodium bicarbonate. Note that oral hydration alone is NOT recommended. Always assess volume status prior to giving IV fluids.
- Avoid other nephrotoxic meds - specifically hold metformin and consider holding RAAS inhibition depending on clinical context.[1]

7. Preventing cardiovascular mortality

Cardiovascular disease is the number one cause of mortality in patients with chronic kidney disease. These patients should therefore undergo cardiovascular risk stratification, according to the preoperative cardiovascular sections of this handbook.[16]

Postoperative acute kidney injury

The differential diagnosis of postoperative AKI should follow a standard pre-renal, renal, and post-renal approach, with specific emphasis on certain postoperative entities:

Pre-renal

- Hypotension
  - Etiologies: Sepsis, haemorrhage, volume depletion
  - Treatment: Address underlying cause (transfusions, antibiotics, inotropes/vasopressors).
  - Keep euvolemic with IV fluids (balanced crystalloid solutions preferably as normal saline is associated with worse renal outcomes in critically ill patients).

Renal

- Acute Tubular Necrosis (ATN)
  - ATN can occur with low-normal BP (SBP 90-100 mm Hg) in a patient with already impaired renal auto-regulation (i.e. old age, chronic hypertension, atherosclerosis, NSAIDs, ACE-i/ARBs, sepsis, etc.).
  - Important note: Review anaesthesia records to determine if and for how long a patient was hypotensive intraoperatively (Hint: look at the bolus phenylephrine given) as intraoperative hypotension may contribute to postoperative ATN.
  - Treatment: Hydration as per volume status, electrolyte replacement, and monitoring.

- Acute Interstitial Nephritis (AIN)
    - Can present in the postoperative period due to antibiotics including Penicillin, Cephalosporin, or Quinolones.
    - Treatment: Discontinue offending agent +/- steroids depending on context/severity.
- Contrast-Associated Nephropathy
    - Usually occurs 3-5 days post contrast exposure. Prevention: Described above.
- Cholesterol Emboli
    - Causes AKI via mechanical plugging (day 1-2) AND subsequent inflammatory response at site of plugging (up to Day 10). This is seen in patients after coronary angiography or vascular surgery.[21]

Post-renal

- Urinary retention
    - Risk factors: Benign prostatic hyperplasia (BPH), anticholinergic drugs, spinal anaesthesia, older age, male[22], female patients undergoing pelvic surgery.
    - Diagnosis: Sudden onset anuria (can happen with blocked Foley as well), bladder scan, ultrasound.
    - Treatment: Foley insertion or change, may need to relieve obstruction by nephrostomy, initiate BPH medications if indicated (e.g. alpha-1-agonists, 5-alpha reductase inhibitors).

Best practices in the setting of postoperative AKI

Once an AKI occurs postoperatively:

- Monitor electrolytes and creatinine at least once daily, and consider ultrasound to rule out post-renal etiology.
- Administer IV Fluids if low blood pressure and volume status permits.
- If patients is hypervolemic, in pulmonary edema, or has decreasing urine output, a furosemide challenge can be done.
- Medication changes:
    - Stop NSAIDs (prescribe Tylenol instead).
    - Opioids: Do not use morphine. Use hydromorphone (renally-adjust doses).
    - Dose-adjust antibiotics: Specifically vancomycin, piperacillin-tazobactam, and amphotericin B.
    - Hold blood pressure medications if hypotensive/volume-depleted/septic.

- Change to RENAL diet that is low in potassium (if patient has oliguria/anuria or high potassium).
- Consult nephrology if requires dialysis, unclear diagnosis (e.g. glomerulonephritis), or if not resolving with general medicine interventions.

Perioperative management of dialysis patients

Nephrology should always be involved in the pre- and post-op management of dialysis patients; internists should be aware of the following best practices:

Preoperative

- Dialysis Access*:* Inspect dialysis access and note the location.
- IV Access: Avoid central line insertion on the same side as fistula/graft. Avoid using the ante-cubital veins or cephalic vein.
- Fluids: Safe to use in patients with dialysis IF there are indications to do so (e.g. hypotension, volume depletion, haemorrhage). Use balanced crystalloids. Avoid maintenance fluids or TKVO as essentially the salt load has to be removed by dialysis.
- Diet: Keep on RENAL diet as this is low in potassium, NOT healthy heart diet as this contains high potassium.
- Anemia: Patients on EPO should continue their EPO perioperatively (i.e. continue on hospital admission medication reconciliation).
- Hemodialysis: Ideally *should be performed the day before surgery* to ensure K<5.5, optimal fluid status, and optimal acid-base status. Let nephrology know about proposed day of surgery so dialysis can be planned accordingly. If dialyzing on the day of surgery, nephrology will take measures (e.g. no heparin or monitoring bleeding parameters) to ensure prolonged anticoagulation does not affect operative bleeding risk.
- Peritoneal dialysis: Ideally ensure abdomen is emptied preoperatively.

Postoperative

- Pain: For non-opioid analgesia, use acetaminophen; avoid NSAIDs. For opioids, use fentanyl or hydromorphone; avoid morphine.[23,24] Doses have to renally-adjusted.

- IV Fluids: Safe to use in patients with dialysis IF there are indications to do so (e.g. hypotension, volume depletion, haemorrhage, patient in code). Use balanced crystalloids.
- Resumption of hemodialysis: Resume as per regular schedule, unless there is an acute indication for an extra session in the interim (e.g. hyperkalemia, fluid overload, or non-resolving acidosis).[25]
- Resumption of peritoneal dialysis: Defer to nephrology.
- Hypertension: If due to volume overload, adjust ultrafiltration in next dialysis session.
    - If not overloaded, can use antihypertensive (e.g. labetalol, hydralazine).

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16. THROMBOEMBOLISM

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Approach to Periprocedural Anticoagulation

With any decision to interrupt periprocedural anticoagulation, a two-step assessment must be done. The first step is a bleeding risk assessment, which determines if anticoagulation needs to be interrupted for the procedure regardless of indication. If the procedure bleeding risk is more than minimal then anticoagulation interruption is mandatory. The second step is a complex thrombotic risk assessment to determine the best interruption strategy depending on the underlying thrombotic condition, the urgency of the procedure, and therapeutic anticoagulant type (bridging or no bridging).

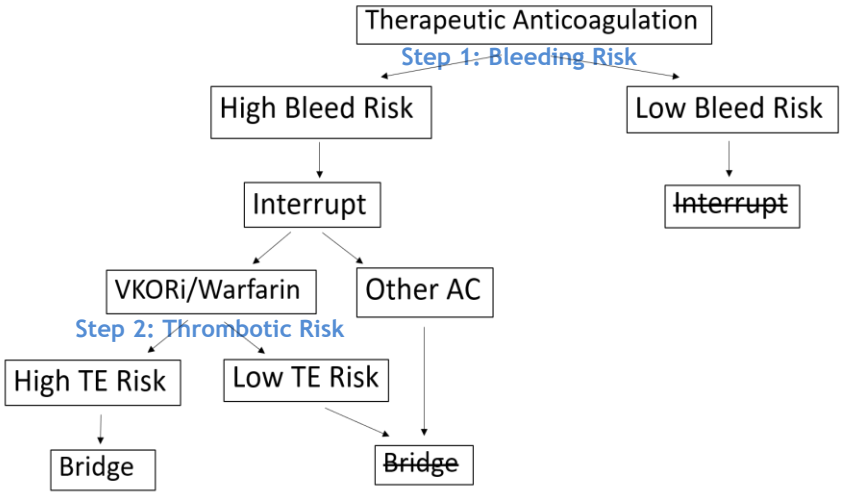

Figure 1 - Conceptualising the two-step approach (bleeding and thrombotic risk assessment) to therapeutic anticoagulation interruption and bridging. TE = Thromboembolism, VKORi = Vitamin K Epoxide Reductase Inhibitor, AC = Anticoagulant.

Assessment of Bleeding Risk

Thrombosis Canada provides a comprehensive list of common procedures and surgeries based on minimal, low-moderate, and high bleed risk (Table 1).[1] Surgeries that are minimal bleed risk, such as cataract surgery, skin biopsy, paracentesis and thoracentesis, do not require periprocedural interruption of therapeutic anticoagulation. Anticoagulation interruption is required for intrathoracic, intra-abdominal and orthopedic surgeries, and procedures such as lumbar puncture, endoscopy with biopsy, and any surgery requiring neuraxial anesthesia.

Table 1 – Bleed risk of surgeries[1]

Minimal bleed risk	Low/moderate bleed risk	High bleed risk
• Cataract surgery • Dermatologic procedure (e.g. biopsy) • Gastroscopy or colonoscopy without biopsies • Coronary angiography (using radial arterial approach) • Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used) • Selected procedures with small-bore needles (e.g. thoracentesis, paracentesis, arthrocentesis) • Dental extractions (1 or 2 teeth) • Endodontic (root canal) procedure • Subgingival scaling or other cleaning	• Abdominal surgery (e.g. cholecystectomy, hernia repair, colon resection) • Other general surgery (e.g. breast) • Other intrathoracic surgery • Other orthopedic surgery • Non-cataract ophthalmologic surgery • Gastroscopy or colonoscopy with biopsies • Coronary angiography (using femoral artery approach) • Selected procedures with large-bore needles (e.g. bone marrow biopsy, lymph node biopsy) • Complex dental procedure (e.g. multiple tooth extractions)	• Any surgery or procedure with neuraxial (spinal or epidural) anesthesia • Neurosurgery (intracranial or spinal) • Cardiac surgery (e.g. CABG, heart valve replacement) • Major vascular surgery (e.g. aortic aneurysm repair, aortofemoral bypass) • Major orthopedic surgery (e.g. hip/knee joint replacement surgery) • Lung resection surgery • Urological surgery (e.g. prostatectomy, bladder tumour resection) • Intestinal anastomosis surgery • Reconstructive plastic surgery • Selected procedures involving vascular organs (e.g. kidney biopsy, prostate biopsy), or a high bleeding risk intervention (e.g. pericardiocentesis, spinal injection, polypectomy)

It is always important to discuss the procedure with the operator and respect their comfort level and experience with therapeutic anticoagulation even for procedures considered minimal bleed risk. For example, if an electrophysiologist prefers to insert pacemakers without anticoagulation, then anticoagulation interruption should be considered. This example highlights the importance of communication between the preoperative team and the procedural operator.

Assessment of Thromboembolic Risk

Thrombosis Canada provides a comprehensive table outlining high, intermediate, and low thromboembolic risk[1] (Table 2). Of note, atrial fibrillation refers to either valvular or non-valvular chronic atrial fibrillation.

Table 1 - Thromboembolic Risk of Medical Conditions[1]

Risk	Mechanical Valve	Atrial Fibrillation	VTE
High	Any prosthetic mitral valve	$CHADS_2$ score 5-6	Recent (≤ 3 months) VTE
	Older generation (cage-ball, tilting disc) aortic valve	Recent (≤ 3 months) stroke, TIA or arterial embolism	Severe thrombophilia (Deficient protein C, protein S, or antithrombin; antiphospholipid syndrome)
	Recent (≤ 3 months) stroke, TIA or arterial embolism	Rheumatic valvular heart disease	
	Prior arterial or venous thromboembolism during appropriate interruption of warfarin		
Moderate	Newer bileaflet aortic valve prosthesis	$CHADS_2$ score 3 or 4	VTE within 3 to 12 months
Low	Bioprosthetic heart valve	$CHADS_2$ score of 0-2	Prior VTE >12 months

For patients on Warfarin, bridging is generally considered for high thromboembolic conditions and not for low-risk conditions. For most intermediate risk thromboembolic conditions, including newer generation bileaflet mechanical aortic valves and patients with chronic atrial fibrillation with $CHADS_2$ scores less than 5, bridging is not required but a discussion weighing the bleeding and thrombotic risk should be had with the patient. Practice with respect to bridging vary from physician-to-physician based on individual patient bleeding risk factors and physician/patient preference, particularly for the intermediate-high thromboembolic risk conditions. There is emerging evidence aimed at clarifying the optimal bridging strategies for the high-risk thromboembolic conditions and may change future practice guidelines.

It is important to highlight the high thromboembolic risk conditions for which patients are receiving therapeutic anticoagulation. Patients within the first three months of an arterial or venous thromboembolic event, such as VTE or stroke, have the highest thromboembolic recurrence risk and are generally advised to delay non-urgent and elective procedures for three months to avoid interruption of anticoagulation. If the procedure or surgery is urgent then consultation with a thrombosis expert is advised.

Periprocedural Warfarin Management

Warfarin should be interrupted 5 days before surgery when indicated[1] (Table 3). If bridging is required, low molecular weight heparin (LMWH) or unfractionated heparin (UFH) is started on day -3. LMWH can be prescribed either once daily (OD) or twice a day (BID). The last dose of LMWH should be administered more than 24 hours before surgery. Warfarin can be resumed on post-op day 0 (ie. day of surgery) if patient is tolerating oral intake and a bolus dose can be considered.

If a patient is bridged preoperatively, they should also be bridged postoperatively. The timing of restarting therapeutic anticoagulation for postoperative bridging depends on the surgical bleeding risk, achievement of adequate surgical hemostasis, and individual patient factors. For low/moderate bleed risk procedures, therapeutic LMWH can be started on postoperative day 1, whereas for high bleed risk surgeries it can be started on day 2 or 3 once hemostasis is achieved. Therapeutic anticoagulation with LMWH can be discontinued immediately when target INR is reached without needing overlapping anticoagulants.

Table 3 – Warfarin bridging protocol (adapted from Thrombosis Canada[1])

Day	Warfarin	INR Monitoring	LMWH
-6	Usual Warfarin dose		
-5	No Warfarin		
-4	No Warfarin		
-3	No Warfarin		Start therapeutic LMWH BID or OD in AM
-2	No Warfarin		BID or OD
-1	No Warfarin	Check INR: If INR≥1.5 give Vit K 1-2 mg po	BID AM DOSE ONLY or OD 1/2 DOSE
0 (Post-op)	No or Usual Warfarin dose		VTE Prophylaxis
1	Usual Warfarin dose		Start therapeutic LMWH for low/moderate bleed risk surgeries (or VTE Prophylaxis)
2	Usual Warfarin dose	Check INR	Start therapeutic LMWH for high bleed risk surgeries (or VTE Prophylaxis)
3	Usual Warfarin dose	Check INR	Therapeutic LMWH*

Periprocedural DOAC Management

Preoperative discontinuation of direct oral anticoagulants (DOACs) depend on two factors: renal function and surgical bleed risk[2] (Table 4). For low/moderate bleed risk surgery, 12-25% residual anticoagulant effect at time of surgery is acceptable, whereas <10% residual anticoagulant effect should be achieved for high bleed risk surgeries. DOACs do not require bridging given similar half-life to LMWH.

Resumption of DOACs postoperatively depends on several factors, including surgical bleeding risk, achievement of adequate hemostasis, and patient individual patient factors. The timing for resumption is based on data from the PAUSE trial, Thrombosis Canada and ASRA 2018 guidelines as well as well common clinical practices. DOACs should be resumed on post-op day 1 for low/moderate bleeding risk procedures, and post op day 2-3 for high bleeding risk procedures (ie. same as LMWH for Warfarin bridging). It is important to remember that VTE prophylaxis for post-op inpatients is still indicated for the duration of interruption of therapeutic anticoagulation.

Table 4 – Periprocedural Management of DOACs[2,5]

Renal Function (eGFR or CrCl, ml/min)	Half–Life (hours)	Timing of LAST Dose of Drug BEFORE Procedure			Timing of FIRST dose AFTER Procedure	
		Low/Moderate Bleed Risk Surgery	High Bleed Risk Surgery	Neuraxial anesthesia[A]	Low/Moderate Bleed Risk Surgery	High Bleed Risk Surgery
Dabigatran (Pradaxa®) 150 or 110 mg BID						
≥ 50	7 – 17	Day –2 skip 2 doses	Day –3 skip 4 doses	Day –5 skip 8 doses	Day + 1	Day +2 or +3
30 to 49	17 - 20	Day –3 skip 4 doses	Day –5 skip 8 doses	Day –6 skip 10 doses	Day + 1	Day +2 or +3
Rivaroxaban (Xarelto®) 20mg OD						
≥ 30	7 - 11	Day –2 skip 1 dose	Day –3 skip 2 doses	Day –4 skip 3 doses	Day + 1	Day +2 or +3
Apixaban (Eliquis®) 5mg BID						
≥ 30	8 - 12	Day –2 skip 2 doses	Day –3 skip 4 doses	Day –4 skip 6 doses	Day + 1	Day +2 or +3
Edoxaban (Lixiana®) 60mg or 30mg OD						
≥ 30	10 - 14	Day –2 skip 1 dose	Day –3 skip 2 doses	Day –4 skip 3 doses	Day + 1	Day +2 or +3

[A] If a neuraxial procedure (spinal or epidural) is being considered for analgesia the last dose of the pre-op DOAC MUST BE at least a day earlier compared to if not receiving neuraxial anesthesia (ASRA Guideline 2018)[5].

Periprocedural LMWH and UFH Management

The perioperative management of Heparin, LMWH and Fondaparinux is summarized in Table 5 below. These recommendations are summarized from ASRA 2018, ACCP, CCS and Thrombosis Canada. They do not replace clinical judgement and physicians must consider relative risks and benefits in each patient and refer to reference guidelines for more details and information.

Table 5 – Perioperative LMWH and UFH recommendations[6]

Drug	Timing of LAST dose BEFORE Procedure		Timing of FIRST dose AFTER Procedure	
	Low or Standard Risk of Bleeding	High or Very High Risk of Bleeding or Neuraxial Procedures[A]	Low or Standard Risk of Bleeding[D, E]	High or Very High Risk of Bleeding or Neuraxial Procedures[A, C, D, E]
Prophylactic Heparin	None within 4 – 6 hrs (usually 12 hrs*)		Day +1 (12 – 24 hrs)	
Intravenous Heparin	None within 4 – 6 hrs (usually 12 hrs*)		Day +1 or +2 (24 – 48 hrs) or per surgeon/POPS	Day +2 or +3 (48 – 72 hrs) or per surgeon/POPS
Prophylactic LMWH	None within 12 hrs		Day +1 (12 – 24 hrs)	

Therapeutic LMWH OD[B]	Last full dose on AM of day -2 (Skip 1 dose) or Last half dose on AM of day -1 (Skip 0 doses)	Day +1 or +2 (24 – 48 hrs) or per surgeon/POPS	Day +2 or +3 (48 – 72 hrs) or per surgeon/POPS
Therapeutic LMWH BID[B]	Last dose on AM of day -1 (Skip 1 dose)		
Prophylactic Fondaparinux (2.5 mg)	Low risk bleeding: Last dose on AM of day -3 (Skip 2 doses) High bleeding risk: Last dose on AM of day -5 (Skip 4 doses)	Day +1 (12 – 24 hrs)	
Therapeutic Fondaparinux (≥5mg)	Low risk bleeding: Last dose on AM of day -3 (Skip 2 doses) High bleeding risk: Last dose on AM of day -5 (Skip 4 doses)	Day +1 or +2 (24 – 48 hrs) or per surgeon/POPS	Day +2 or +3 (48 – 72 hrs) or per surgeon/POPS

Abbreviations: LMWH (low molecular weight heparin), POPS (Perioperative Pain Service)
[A] Neuraxial procedures include spinal anesthesia, epidural catheter insertion and removal.
[B] In patients at **very high risk of thrombosis** (eg. mechanical heart valve, VTE within past 30 days), a half-therapeutic dose of LMWH at 24 hr prior to procedure should be considered.
[C] Therapeutic anticoagulation is CONTRAINDICATED in patients with an indwelling **epidural catheter**. Obtain POPS approval before starting anticoagulants at any dose after an epidural catheter has been manipulated (inserted, removed, or maintained).
[D] Start **therapeutic doses** of any anticoagulant ONLY AFTER hemostasis is achieved. Full anticoagulant effect peaks at ~3-4 hr after LMWH and when PTT is therapeutic for intravenous heparin. If therapeutic dosing start is delayed, consider using prophylactic doses of LMWH (if indicated).
[E] Postoperatively, **creatinine** should be checked before restarting any NSAIDs, LMWH, Fondaparinux, or other agents that are dependent on renal clearance.

Thromboprophylaxis[3,4]

When considering thromboprophylaxis, options include pharmacologic and mechanical thromboprophylaxis. Either option is acceptable and should be individualised to each patient depending on bleeding and thrombotic risk factors.

In general, pharmacological options for thromboprophylaxis (table 6) are preferred when bleeding risk is low and there are no acute contraindications (ie. no active bleeding, platelets >40, no heparin-induced thrombotic thrombocytopaenia, etc). If mechanical thromboprophylaxis is chosen in high bleeding risk scenarios, options include sequential/pneumatic compression devices, which are preferred over elastic compression stockings. Caution should be used when considering mechanical thromboprophylaxis in severe thrombocytopenia (platelets < 30) as blunt forces from mechanical compression can cause bleeding and create a consumptive coagulopathy.

The principles of thromboprophylaxis for surgical patients are similar to medical patients, although surgical patients tend to have higher rates of venous thromboembolism[3,4] (Table 7). Orthopedic surgeries have particularly high thromboembolic risk, therefore hip and knee arthroplasty and hip fracture patients need routine postoperative

thromboprophylaxis up to 35 days. Of note, DOACs are only recommended for thromboprophylaxis for elective hip and knee arthroplasties, and not for hip fractures. In some cases, the duration of thromboprophylaxis may be longer and extend beyond hospitalization (e.g. until discharge from rehab).

Low risk procedures or procedures not requiring overnight stay or uncomplicated spine surgery with early post-op mobilization generally do not require thromboprophylaxis[3,4].

Table 6 – Thromboprophylaxis dosing[3,4]

CrCl > 30	<40 Kg	40 to 100 Kg	>100 Kg	CrCl<30 (40-100kg*)
Heparin	5000 units BID	5000 units BID	5000 units TID	5000 units BID
Dalteparin	2500 units daily	5000 units daily	5000 units BID	5000 units daily
Enoxaparin	30 mg daily	40 mg daily	40mg BID	30mg daily
Tinzaparin	2500 units daily	4500 units daily	4500 units BID	4500 units daily
Rivaroxaban	10 mg daily			-
Apixaban	2.5 mg BID			
Dabigatran	220 mg daily			-
Fondaparinux	2.5 mg daily			-

*In patients with CrCl <30 and weights out of 40-100 Kg range, thromboprophylaxis dosing may require adjustment based on weight

Table 7 – Thromboprophylaxis for different patient groups[3,4]

Patient Group	Thromboprophylaxis Options	Duration
Medical inpatients	LMWH	Length of hospitalization
Non-orthopedic surgery (eg. General surgery, gynecologic surgery, urologic surgery)	LMWH Mechanical if bleeding	Length of hospitalization
Hip/Knee Arthroplasty	LMWH or Fondaparinux or DOACs*	14-35 days
Hip fracture	LMWH or Fondaparinux	14-35 days
Major orthopedic trauma Lower extremity amputation	LMWH Mechanical if bleeding	Until discharge (including rehabilitation)

*For patients undergoing total hip or knee arthroplasty, Aspirin can be used for thromboprophylaxis per ASH 2019 Guidelines (conditional recommendation, very low certainty of evidence).

Venous Thromboembolism[7-15]

Diagnosis

Diagnosing venous thromboembolism (VTE) can be challenging as there are various diagnostic approaches and validated clinical decision-making tools. The essence of any approach is to risk stratify patients into likeliness of having venous thromboembolism. Those at very low risk can be ruled out of having a VTE, whereas everyone else would need further diagnostic testing.

"Who is at very low risk?"

1) No presence of major or minor or oestrogen-related VTE risk factors
AND
2) Clinical suspicion for VTE is low
AND
3) Clinical decision-making rule is NEGATIVE (low clinical probability)
AND
4) Negative d-dimer test
(OPTIONAL)
5) Negative PERC Rule for Pulmonary Embolism

"Which clinical decision-making rule should I use?"

There are many validated clinical decision-making rules (mainly validated for outpatients* NOT inpatients). Some but not all clinical-decision making rules include d-dimer which simplifies the risk-stratification process. The following are commonly used:
1) Deep Vein Thrombosis (DVT)[7-10]:
   - Wells' criteria for DVT
2) Pulmonary Embolism (PE)[7-13]:
   - Wells' criteria for PE
   - PERC rule
   - YEARS algorithm – includes d-dimer, requires further validation in non-pregnant patients

"Which diagnostic test should I choose?"

The choice of diagnostic test will depend on availability and feasibility of test, and patient factors (e.g. pregnancy, contrast allergy, certain underlying lung diseases).

1) DVT[7-8]
- Compression ultrasound (CUS)

2) PE[9-10]
- CTPA
- V/Q Scan – Ideally best suited when baseline chest-X-ray is grossly normal, CT contrast allergies, or chronic thromboembolic pulmonary hypertension (CTEPH) is suspected. It is preferred in pregnancy due to lower risk of breast exposure to ionizing radiation (see Chapter 27).

"How do I diagnosis DVT and PE using clinical decision-making rules and diagnostic tests?"

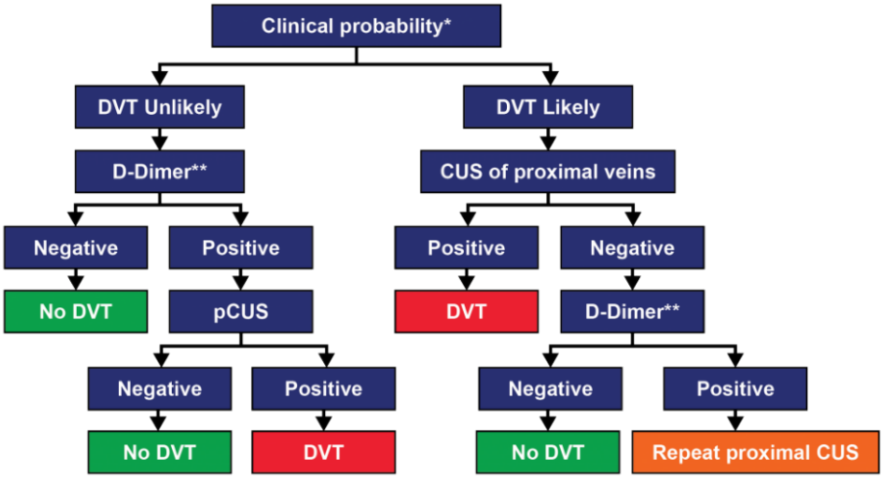

Figure 2 – Diagnostic algorithm for suspected DVT (Thrombosis Canada)[7-8]

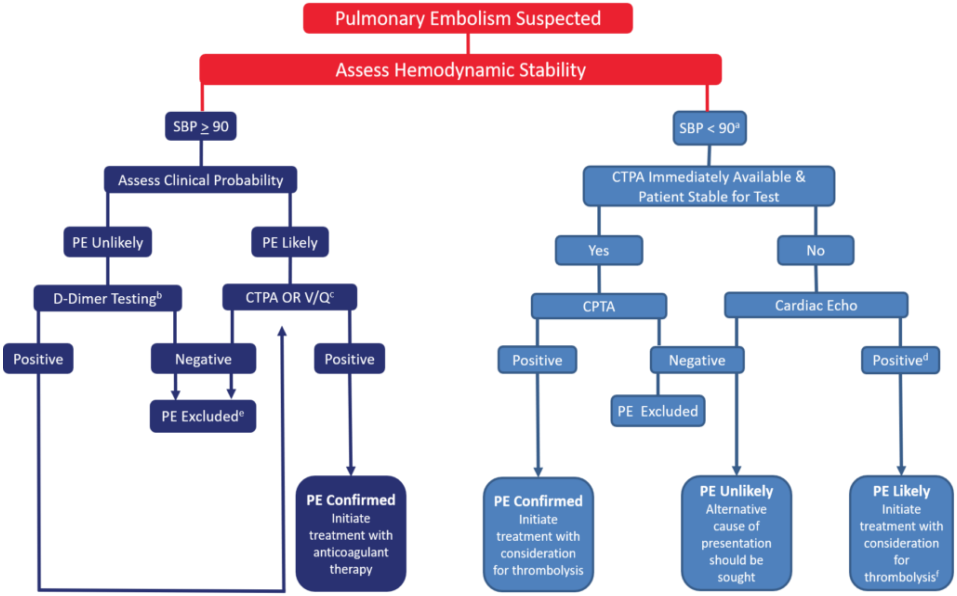

Figure 3 – Diagnostic algorithm for suspected pulmonary embolism (Thrombosis Canada) [9-10]

Treatment[8,10, 11-15]

Treatment for VTE include oral, injectable, and intravenous options and will depend on individualised patient factors.

1) Oral

- DOACs (apixaban, rivaroxaban, edoxaban, and dabigatran)
- VKORi (warfarin)

Oral is generally the preferred option. However, oral agents may not be appropriate if GI absorption is unreliable (e.g. unable to tolerate oral intake, GI losses, or short bowel syndrome). DOACs are the preferred agents in most cases, including cancer-associated thrombosis, but not for certain conditions such as antiphospholipid syndrome. DOAC use is limited by renal function and generally caution is advised when creatinine clearance is below 25-30. Limited data is available on use of DOACs in chronic kidney disease when creatinine clearance is less than 15. Warfarin is mainly used in antiphospholipid syndrome and when

creatinine clearance is less than 15. Warfarin initiation is prothrombotic in acute thrombosis and must be OVERLAPPED/COMBINED with another anticoagulant for at least 5 days AND until INR is within therapeutic range (generally 2-3).

2) Injectable

- LMWH (enoxaparin, dalteparin, tinzaparin)

LMWH can be use in the acute treatment of VTE. It can also be used for the entire duration of anticoagulation such as in cancer-associated thrombosis. Practically, LMWH are typically used when OVERLAPPING therapy with Warfarin is required. LMWH is easy to self-administer, have good bioavailability, is weight-based dosing (no maximum dose), can be renally adjusted (tinzaparin is preferred for patients with creatinine clearance ~20), and does not require therapeutic monitoring. The risk of heparin-induced thrombotic thrombocytopaenia is lower with LMWH compared to UFH.

3) Intravenous

- UFH infusion

UFH use is limited by a narrow therapeutic window and need for frequent PTT monitoring. UFH use is considered when bleeding risk is high in whom rapid reversal may be required, or in patients with acute thrombosis and an anticipated need for thrombolysis.

Table 8 – Duration of anticoagulation (Thrombosis Canada)[8,10, 11-15]

VTE Type	Duration of Anticoagulation
Provoked VTE with reversible and modifiable risk factor	Minimum 3 months then stop
Provoked VTE with non-reversible and non-modifiable risk factor	Minimum 3 months then continue for extended duration
Unprovoked VTE	Minimum 3 months then continue for extended duration
Recurrent VTE	Minimum 3 months then continue for extended duration
Cancer-associated thrombosis	Minimum 6 months then continue until disease is in remission AND NOT on active cancer treatment
Estrogen-related thrombosis (OCP/HRT)	Minimum 3 months

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17. DIABETES

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History:

- Assess the patient's baseline glycemic control, including frequency and awareness of hypoglycemia
- Check for microvascular and macrovascular diabetic complications, e.g. retinopathy, nephropathy, neuropathy, coronary artery disease, ischemic stroke, peripheral arterial disease; (you may be the first to identify these abnormalities)

Treatment goals:

- Try to optimize Blood Glucose (BG) before the OR.
- Perioperative BG target should be individualized to patient's characteristics:
    - E.g. 5-10 mmol/L for most individuals, higher if frail elderly or history of severe hypoglycemia/hypoglycemia unawareness
- Goals of management:
    - Avoid hypoglycemia (BG <4 mmol/L)
    - Avoid gross hyperglycemia (BG >14 mmol/L) resulting in volume depletion or ketoacidosis

Three example scenarios:

1. Patient on insulin preoperatively, undergoing a procedure where the procedure plus NPO/recovery time is <2-4hr
2. Patient on insulin preoperatively, undergoing a procedure where the procedure plus NPO/recovery time is >2-4hr
3. Patient on non-insulin antihyperglycemic agents only

Scenario #1: Patient on insulin booked for procedure <2-4hr

Table 1 – Instruction for basal insulin perioperatively[1-2]

Medication	Preop	Day of OR	Postop
Ultra-long acting (degludec)	80% of usual dose for 3 days preop	80% of usual dose	Titrate back to usual dose
Long-acting (glargine, detemir)	If AM - usual dose; if HS – 75% of usual	75% of usual dose night before OR	Titrate back to usual dose
Intermediate-acting (NPH)	HS dose – 75% of usual	AM dose – 50% of usual	Titrate back to usual dose
Premixed Insulin	Consider converting to long acting evening prior or give 50% AM dose	AM dose – 50% of usual or convert to a long acting basal night before	Titrate back to usual dose if eating. If not eating consider converting to long acting basal.

- Hold mealtime insulin while NPO
- **Patients on high basal insulin (>60% of TDD) or >80 units or at high risk of hypoglycemia (elderly, CKD/Hepatic insufficiency, prior hypoglycemic episodes) basal insulin dose should be reduced by 50% to minimize hypoglycemia.**

If on pump therapy, recommend endocrinology consult to assess candidacy for continuing insulin pump perioperatively

- If the device is compatible with the type of procedure & procedure does not require general anesthesia:
  - Recommend using pump for basal rates only
  - If on open loop therapy, can set a 50% temporary basal rate as safety margin during the operation
  - If on hybrid closed loop therapy (i.e. Tandem Control IQ, Medtronic auto mode), can temporarily change BG target to 7-10 for safety
  - Return to usual pump settings postoperatively once eating
- If pump therapy is not compatible with type of procedure:
  - If procedure is short <2hr, may consider giving a bolus dose equivalent to basal rate over 1 hr via pump then discontinue pump
  - Postoperatively, once regains consciousness reconnect and restart pump

Scenario #2: Patient on insulin booked for a procedure >2-4hr

If on insulin injections:

- See Scenario #1 for instruction for basal insulin
- Hold mealtime insulin while NPO
- Consider perioperative insulin infusion if procedure duration >4 hr, poor baseline glycemic control, or medically unstable

If on pump therapy, recommend endocrinology consult for perioperative glycemic management:

- Determine patient's total daily dose (TDD) based on pump settings
- Discontinue pump prior to OR and start IV insulin infusion (see sample nomograms, selected based on TDD)
- Start IV dextrose (D5W or 2/3 1/3) unless BG >14
- Check POCT Q1H while on infusion

Table 2 - IV Insulin infusion - Insulin sensitive patient

Patient's total daily dose: <40 units	
Blood Glucose	**IV Insulin**
0.0 - 3.9	Call MD
4.0 - 8.0	0.3 units/hour
8.1 - 10	0.5 units/hour
10.1 - 12	1.0 units/hour
12.1 - 14	1.5 units/hour
14.1 - 16	2.0 units/hour
16.1 - 18	2.5 units/hour
> 18.1	Call MD

Table 3 - IV Insulin infusion - moderately insulin resistant patient

Patient's total daily dose: 40.1 - 80 units	
Blood Glucose	**IV Insulin**
0.0 - 3.9	Call MD
4.0 - 8.0	0.5 units/hour
8.1 - 10	1.0 units/hour
10.1 - 12	1.5 units/hour

12.1 - 14	2.0 units/hour
14.1 - 16	2.5 units/hour
16.1 - 18	3.0 units/hour
> 18.1	Call MD

Table 4 - IV Insulin infusion – severely insulin resistant patient

Patient's total daily dose: >80 units	
Blood Glucose	**IV Insulin**
0.0 - 3.9	Call MD
4.0 - 8.0	1.0 units/hour
8.1 - 10	1.5 units/hour
10.1 - 12	2.0 units/hour
12.1 - 14	2.5 units/hour
14.1 - 16	3.0 units/hour
16.1 - 18	4.0 units/hour
> 18.1	Call MD

N.B.

- Patients with Type 1 Diabetes should **NOT** have their insulin infusion stopped for >1hr due to the risk of ketoacidosis
- Infusion should be used for patients who are medically unstable, going for a procedure or have a prolonged NPO order
- Capillary glucose should be checked q1 hour x3 then q2 hours x3 then q3 hours.

Blood glucose < 4.0 mmol/L (call MD)

- If patient can take PO, give 250 mL juice/pop or 5 glucose tablets.
- If patient cannot take PO, give 25 mL (1/2 amp) of D50 as IV push.
- If patient does not have PO or IV access, give glucagon 1mg SC/IM.
- Check finger capillary glucose q15 minutes and repeat above if blood glucose < 4.4 mmol/L.

Scenario #3: Patient on non-insulin antihyperglycemics

Table 5 - Recommendations on perioperative management of non-insulin antihyperglycemic medications[1-3]

Medication	Day before OR	Day of OR	Restart
Biguanides (metformin)	Continue at usual dose	Hold	Restart unless eGFR <30
SGLT-2 inhibitors (-gliflozins)	Hold 3 days before surgery	Hold	Restart when eating/drinking well
DPP4 inhibitors (-gliptins)	Continue at usual dose	Hold	Restart when eating well
GLP-1 analogue (-glutides)	Continue at usual dose	Hold	Restart when eating well
Sulfonylureas or Meglitinides	Continue at usual dose	Hold	Restart when eating well

- Check patient's BG the morning of OR
- If BG >14 mmol/L or if OR duration >4hr, recommend starting insulin infusion as per insulin sensitive nomogram shown in Scenario #2

Some Useful Terminology and Calculations:

- **Total daily dose** (TDD): a person's total insulin requirement in an average day
    - If on multiple daily injection regimen, calculate TDD by adding up the sum of basal insulin and mealtime insulin doses
    - If on pump therapy, pump settings can reveal the 7-day average TDD based on the patient's basal program and mealtime boluses administered
- **Insulin sensitivity factor** (ISF): the degree of glucose lowering (by mmol/L) 1 unit of insulin achieves
    - Estimate based on the "rule of 100" (ISF = 100 / TDD)
    - Ie. if TDD is 50, then ISF is 2. One unit of insulin lowers blood glucose by 2 mmol/L.
    - If on pump therapy, ISF can be found in pump settings
- **Insulin to carbohydrate ratio** (ICR): the amount of carbohydrate intake (in grams) 1 unit of insulin accounts for
    - Estimate based on the "rule of 500" (ICR = 500 / TDD)

- Ie. If TDD is 50, then ICR is 10. One unit of insulin is required for every 10 grams of carbohydrates.
- If on pump therapy, ICR can be found in pump settings

A Note on Technology: [4-5]

Continuous glucose monitoring (CGM): a small sensor inserted in the abdomen or upper arm measures interstitial glucose level every few minutes

Real-time CGM **(rtCGM): sensing device continuously transmits the data to a device with real-time display for viewing at any time, usually has built-in alarm for hypoglycemia; e.g. Dexcom G6, Freestyle Libre 2**. Covered by most private insurance plans for patients with type 1 diabetes, but some patients with type 2 diabetes may have them too.

- **Intermittent-scanned CGM** (isCGM): sensor device does not transmit data automatically, a reader device or phone must be used to intermittently scan the sensor to obtain glucose trends; e.g. the original Freestyle Libre. Covered by most private insurance plans and the Ontario Drug Benefit program (i.e. anyone age >=65, enrolled in the Trillium Drug Program, or receiving Ontario Works or Ontario Disability Support Program benefits) for patients with diabetes on insulin therapy.

Ambulatory glucose profile (AGP) reports: visual representation of glucose levels of a typical standard day of the most recent 14 days for a person with diabetes

- Can be shared by patients with their provider through online platforms (e.g. Libreview for Freestyle Libre, Clarity for Dexcom G6)
- **Glucose management indicator** (GMI): estimated A1c based on average glucose levels for 14 or 30 days; targets are individualized <7%-<8.5%
- **Time in range** (TIR): % of values at target (targets are individualized, most are 3.9-10 mmol/l but may be higher if elderly/frail); target most patients >70%
- **Time below range** (TBR): % of values <3.9 mmol/L; target <4%
    - % of values <3.0 mmol/L; target <1%
- **Time above range** (TAR): % of values >10.1 mmol/L; target <25%
- **Glycemic variability**: coefficient of variation; target <=36%

- These targets were derived from Diabetes Canada 2021 Updated Chapter on glucose monitoring, applies to most individuals excluding children, older frail adults, and pregnant women.[4]

Insulin pumps: commonly encountered models include Medtronic MiniMed 670G or 770G, Tandem T-Slim X2, Omnipod DASH system

- All models can run in open loop (i.e. the pump has a preset basal rate program, and the user must administer food and correction boluses by entering their glucose values after checking with a traditional glucometer or CGM).
- Some models allow for hybrid closed loop (i.e. the pump can adjust basal insulin program based on glucose readings of a paired CGM, however the user must still administer bolus insulin for food).[5]
- Current hybrid-closed loop programs include the Medtronic Auto-Mode (users must have the 770G pump and Medtronic Guardian CGM sensor) and Tandem Control IQ (users must have the T-Slim X2 pump and Dexcom G6 sensor).

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18. STROKE

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Table 1 - Perioperative Stroke Incidence and Pathophysiology

Procedure		Risk of Stroke (%)
Cardiac and Vascular Procedures	CABG	1.1-4.1
	Combined CABG and valve	7.4-7.9
	Isolated AVR	1.5-1.8
	Isolated MVR	1.4-8.8
	Multiple valves	9.7
	Aortic repair	4.7-7.2
	PCI	0.1-0.5
	TAVI	2.7
	Carotid endarterectomy	5.5-6.1
	Peripheral vascular surgery	0.8-3.0
Other Surgeries	Head and neck surgery	0.2-4.8
	Pulmonary surgery	0.6-0.9
	Orthopedic surgery	0.2-0.9
	General surgery	0.08-0.7

Intraoperative strokes: 70-80% due to thromboembolism (especially in cardiac and vascular procedures). 20-30% due to hypoperfusion (watershed distribution)

Postoperative strokes: early postoperative strokes (<7 days, due to arrhythmia or hemodynamic factors) and late postoperative strokes (7-30 days, reflective of patient atherosclerotic risk factors)

Table 2 - Risk Factors for Perioperative Strokes

Risk Factors for Perioperative Stroke
Patient-related risk factors
Older age (>70)
History of stroke or TIA
Renal disease and dialysis
Cardiac disease (AF, CHF, valvular disease, ischemic heart disease)
Carotid stenosis (especially if symptomatic)
COPD, PVD, HTN, smoking
Atherosclerosis of the ascending aorta
Abrupt discontinuation of antithrombotic therapy before surgery

Procedure-related risk factors
Timing of surgery (urgent vs elective)
Type and duration of the surgical procedure
Type of anesthesia (general or local)
Duration of surgery and, in cardiac procedures, duration of cardiopulmonary bypass and aortic cross-clamp time
Manipulations of proximal aortic atherosclerotic lesions
Intraoperative or postoperative arrhythmias
Hyperglycemia
Dehydration
Blood loss

Risk Scores/Models

- Society of Thoracic Surgeon (STS) Risk Score: stroke risk stratification in cardiac surgeries
- American College of Surgeon (ACS)/NSQIP Risk Calculator: not specific to stroke.
- Revised Cardiac Risk Index (RCRI): major cardiac complications in non-cardiac surgeries
- Halm Risk Score: for carotid endarterectomy

Preoperative Screening and Stroke Prevention in Cardiac and Vascular Surgeries

- Carotid duplex: patients with recent history of stroke or TIA (<6 months) or at high neurological risk (STS stroke risk >5) (AHA 2020 Statement)
- Consider CT chest to screen for aortic atherosclerosis in patients underlying myocardial revascularization if age >70, or with signs of extensive generalized atherosclerosis (AHA 2020 Statement)
- Consider echo to screen for LV thrombus in patients with HF, severe LV dysfunction or recent MI (AHA 2020 Statement)
- Medical optimization: continue beta blocker in patients previously on therapy and consider initiating beta blocker 2-3 days before surgery (do not start on the day of surgery), appropriate perioperative antithrombotic management with bridging in high-risk patients.

Postoperative Atrial Fibrillation (POAF)

- Occurs in 27-40% of patients after cardiac surgery and associated with increased risk of postoperative strokes
- Consider anticoagulation if persistent > 48 hours. AHA Statement suggests considering using LMWH or UFH 12-48 hours after the operation once hemostasis achieved and then transition to oral anticoagulant for 4 weeks.
- Other strategies: beta blocker (continue if patient on it at home), electrolyte supplementation (Mg, K).

Carotid Artery Disease and Stroke

- Accounts for 10-20% of all strokes.
- Prevalence 2-3% in general population but increases with age and in men.
- >50% stenosis occurs in 7% of women and 9% of men aged > 65
- Stroke mechanisms: 1) artery to artery embolization (cholesterol emboli or plaque rupture/thrombosis) and 2) flow reduction in high-grade stenosis causing watershed infarcts or limb-shaking TIAs
- **Symptomatic** carotid stenosis: ipsilateral carotid-territory cerebral or retinal stroke within 6 months. Symptomatic carotid stenosis is associated with very high risk of recurrent strokes, estimated to be 12-18.8% by 90 days and warrants urgent assessment for revascularization.
- **Asymptomatic** carotid stenosis has a low annual stroke risk of <1%/year with modern therapy and therefore is usually managed medically.

Carotid Revascularization

- Indicated in symptomatic carotid stenosis >50% in men and >70% in women. It may be considered in women with 50-69% stenosis at high stroke recurrence risk.
- Carotid endarterectomy (CEA) generally more appropriate for patients >70 otherwise fit for surgery. Current evidence suggests stenting carries a higher periprocedural risk of stroke and death in older patients.
- Revascularization should be performed as early as possible in medically stable patients, ideally within 14 days.

Table 3 - Halm Risk Score for complications following endarterectomy

Risk Factors (1 point)
active coronary artery disease (unstable angina or CCS III or IV angina)
stroke as indication for surgery
contralateral stenosis > 50%
Protective Factor (-1 point)
use of local anesthesia

Risk Model	Class	Death or Stroke (%)
Halm Score	-1	0.7
	0	1.7
	1	5.8
	≥2	13

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19. DELIRIUM

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Detecting Delirium

The gold standard for the diagnosis of delirium is based on the DSM-IV-R criteria. However, this can be cumbersome and time consuming. Rather, the following instrument, the Confusion Assessment Method (CAM),[1] takes only five minutes to administer (Sensitivity: 94-100%, Specificity: 90-95% Reliability K 0.81-1.00):

1. Acute onset and fluctuating course
2. Inattention (ex. serial sevens, spelling WORLD backwards)
3. Disorganized thinking
4. Altered level of consciousness

Delirium: Presence of 1 and 2; and either 3 or 4.

Note: CAM-ICU has been developed to operationalize CAM in the context of mechanically ventilated patients.[2]

Predicting Delirium

A recent systematic review found the following risk factors were associated with development of postoperative delirium[3]:

- Cognitive impairment
- Age
- Functional dependence
- Alcohol abuse
- Electrolyte disturbance
- Sensory impairment
- Depression
- Psychotropic drug use
- Presence of psychopathological symptoms
- Institutional residence was associated with delirium in the orthopedic surgery setting

Delirium after <u>Elective Noncardiac Surgery:</u> derived and independently validated clinical predication rule.[4] Patients were over age 50 years undergoing major, elective noncardiac surgery (defined as expected length of stay ≥ 2 days).

Table 1 - Risk factors for development of delirium after non-cardiac surgery

Risk Factor	Points
Age ≥ 70	1
Alcohol abuse	1
Cognitive impairment[a] Severe physical impairment[b]	1 1
Marked abnormal perioperative labs[c]	1
AAA surgery	2

Table 2 - Risk of postoperative delirium after non-cardiac surgery

	Risk (Derivation Cohort)	Risk (Validation Cohort)
0 points (low risk)	< 1%	2%
1-2 points (medium risk)	8-19%	8-13%
3 points (high risk)	45%	50%
ROC	0.81 ± 0.04	0.78 ± 0.04

[a] Telephone Interview for Cognitive Status score < 30; equivalent to MMSE < 24
[b] Specific Activity Scale class IV (unable to walk 4 km/h for one block, cannot dress self or make their bed without stopping)
[c] Na < 130 or > 150 mmol/L; K < 3.0 or > 6.0 mmol/L; or glucose < 3.3 or > 16.7 mmol/L

Delirium After Cardiac Surgery: The following is a prospectively derived and independently validated clinical predication rule.[5] Patients were 60 years or older planning to undergo cardiac surgery (CABG, mitral or aortic valve replacement or repair, or combined CABG-valve).

Table 3 - Risk factors for development of delirium after cardiac surgery

Risk Factor	Points
MMSE ≤ 23	2
MMSE 24-27	1
History of TIA/stroke	1
Geriatric Depression Scale (15-item) score > 4	1
Abnormal albumin[a]	1

[a] ≤ 35g/L or ≥ 45 g/L

Table 4 - Risk of postoperative delirium after cardiac surgery

Score	Delirium Risk (Derivation Cohort)	Delirium Risk (Validation Cohort)
0 points (low risk)	19%	18%
1-2 points (medium risk)	47-63%	43-60%
≥ 3 points (high risk)	86%	87%
C-statistic	0.74	0.75

Assessment of Delirium

There are no evidence-based trials on which the assessment and investigations for a patient with delirium are based. The following is based on expert opinion and available guidelines.[6-9]

HISTORY including collateral information whenever possible and with special attention to **medications**, **pain management**, and **past medical illnesses** which may be contributing to presentation of delirium.

PHYSICAL EXAMINATION with special attention to neurological examination including mental status, nutritional status, evidence of infection and possible source, evidence of alcohol use/withdrawal.

ASSESSMENT OF CONTRIBUTING ENVIRONMENTAL FACTORS such as sensory deprivation (windowless room), sensory overload (too much noise), isolation from familiar surroundings, absence of orientation (clock, watch, calendar), missing vision/hearing aids, use of restraints

INVESTIGATIONS must be guided by the individual patient's medical history, findings on physical and neurologic examination, and clinical setting.

- CBC, BUN, creatinine, electrolytes, Ca, Mg, PO4, glucose, albumin, AST, ALT, bilirubin, ALP, TSH, B12, POCT Glucose, ABG or SpO2
- ECG, CXR
- PVR, Urinalysis

Additional considerations:

- Cortisol level
- Cultures (blood, urine, joint, CSF)
- Drug levels, Toxicology screen
- Neuroimaging
- CTPA
- AXR (for fecal impaction)
- LP, EEG

Indications for neuroimaging in the patient with delirium:

1. New focal neurologic signs
2. History or signs of head trauma
3. Fever and acute change in mental status, in whom encephalitis is suspected
4. No other identifiable cause of delirium
5. Neurologic examination cannot be completed

Delirium Prevention in the Surgical Population[7,10]

1. Identify and target individual risk factors

2. Multidisciplinary intervention for **moderate to high-risk individuals**

- **Orientation** protocol for those with cognitive impairment
- Non-pharmacological **sleep** strategies (avoid sedatives)
- Early **mobilization**
- Optimize vision and hearing with **glasses**, **hearing aids or pocket talker** (consider other reversible causes)
- Avoid dehydration, encourage oral fluid intake first
- Optimize contributing environmental factors (see above)

3. Early identification and treatment of post-op complications

4. Intraoperative considerations:

- There is evidence that intraoperative monitoring (ex. Bispectral index monitor) of depth of sedation is associated with reduced postoperative delirium[11]
- Perioperative dexmedetomidine is associated with reduced postoperative delirium, and may be considered for patients at high risk for developing delirium[12]

5. No psychopharmacological interventions routinely recommended*
*Exception: There is evidence for use of dexmedetomidine for delirium prevention in select critically ill patients[13]

Sample Multidisciplinary Intervention

A randomized, blinded trial showed decrease in cumulative delirium incidence using a multi-disciplinary intervention as outlined below (OR 0.48 [95% CI 0.23, 0.98]; RR 0.64 [95% CI 0.37, 0.98]), suggesting an **NNT of 5.6** patients to prevent one case.[14]

The intervention consisted of daily visits, starting preoperatively or within 24 hours postoperatively. Recommendations were prioritized and limited to five after initial visit; and three after follow-up visits.

Table 5 – Interventions to treat postoperative delirium

Adequate CNS oxygen delivery	a. Supplemental oxygen to keep saturation > 90% b. Treatment to raise SBP to > 2/3 baseline or > 90 mmHg c. Transfusion to keep hct > 30%
Fluid/ electrolyte balance	a. Treatment to restore Na, K, glucose to normal limits b. Treat fluid overload or dehydration by examination and/or blood tests
Treatment of severe pain	a. Around-the-clock acetaminophen (1 gram qid) b. Early-stage break-through pain: low dose sc morphine, avoid meperidine c. Late-stage break-through pain: oxycodone prn
Eliminate unnecessary medications	a. Discontinue/minimize benzodiazepines, anticholinergics, antihistamines b. Eliminate drug interactions, adverse effects, modify drugs accordingly c. Eliminate medication redundancies
Regulate bowel/bladder function	a. Bowel movement by POD#2 and q48h b. D/c urinary catheter by POD#2, screen for retention or incontinence c. Skin care program for patients with established incontinence
Adequate nutrition	a. Dentures, proper positioning for meals, assist as needed b. Supplements: 1 can Ensure; 3 cans Ensure for poor oral intake c. If unable to take food orally, feed via temporary NGT
Early mobilization and rehabilitation:	a. Out of bed on POD#1 and several hours daily b. Mobilize/ambulate by nursing staff as tolerated, such as to bathroom c. Daily physiotherapy, occupational therapy if needed
Prevention, early detection, and treatment of postoperative complications	a. MI: ECG, cardiac enzymes b. Supraventricular arrhythmias / a.fib.: appropriate rate control, electrolyte adjustments, anticoagulation c. Pneumonia/COPD: screening, treatment, including chest therapy d. PE: appropriate anticoagulation e. Screening for and treatment of UTI
Environment	a. Appropriate use of glasses and hearing aids b. Provision of clock and calendar c. If available, use of radio, soft lighting
Treatment of agitated delirium	a. Appropriate diagnostic workup/management b. Calm reassurance, family presence, and/or sitter c. If necessary, low dose haloperidol 0.25-0.5 mg q4h prn; if contraindicated, lorazepam at same dose

Delirium Management in the Surgical Population[7,10]

1. Identify and treat the precipitant and/or predisposing factors
2. Non-pharmacological interventions as outlined under prevention
3. Pharmacological:
    a. Antipsychotics should not be used for hypoactive delirium.
    b. Use of haloperidol or an atypical antipsychotic at the lowest effective dose for the shortest possible duration can be considered to treat patients who are severely agitated or distressed or at risk of harm to self or others.
    c. Quetiapine is preferred for patients with known or suspected parkinsonism.[15]
    d. Benzodiazepines should not be used to manage agitation in postoperative delirium except when specifically indicated (e.g. alcohol or benzodiazepine withdrawal).
    e. Clonidine is associated with increased risk of developing delirium and reduced likelihood of delirium resolution.

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20. OSTEOPOROSIS

Author: Lianne Tile MD MEd FRCPC

Background

- The presence of a low trauma fracture (from a fall from standing height or less, and walking pace or less) in older adults strongly suggests the diagnosis of osteoporosis, once malignancy and metabolic abnormalities have been ruled out.
- Low trauma fracture of the hip or spine implies a high (>20%) 10 year fracture risk, irrespective of the bone mineral density.
- There are effective medications for secondary prevention of fractures.

Risk factors for low bone mineral density, fractures, and falls

- Fragility fracture
- Glucocorticoid use: Prednisone 7.5 mg or more for >3 months
- Medical disorders associated with osteoporosis/decline in BMD
- Other medications: glucocorticoids at lower dose/frequency, androgen and estrogen deprivation therapies, other (heparin, seizure medication, PPIs, SSRIs)
- Parental history of hip fracture, low BMI, smoking, ETOH > 3 units/day
- Falls in previous 12 months

Investigation

- Physical examination:
    - General exam
    - Vertebral fractures: height loss, kyphosis, occiput-wall and rib-pelvis distance
    - Falls risk: proximal muscle strength, gait and balance
- Screening labs for secondary causes of bone loss:
    - Calcium, Albumin, Phosphate
    - CBC
    - Creatinine
    - ALP (often high after acute fracture)
    - TSH
    - Serum protein electrophoresis (if vertebral fractures)
    - 25 OH vitamin D level
    - PTH and 24 hour urine collection if hypercalcemic
- Imaging as needed to evaluate for atypical femur fracture/pathologic fracture/underlying malignancy

Management

- Elemental calcium: 1200 mg per day through diet and supplements combined; supplement as needed up to 600 mg
- Vitamin D3: 800-2000 IU per day
- Exercise: strength, balance, posture exercises
- Consider osteoporosis medication:
    - Bisphosphonate therapy for up to 5 years reduces fracture risk by up to 50%.
        - Alendronate 70 mg or Risedronate 35 mg per week
        - Cautions – Avoid in CKD with CrCL< 30, risk of esophagitis and GI intolerance
        - IV Zoledronic Acid (Aclasta) 5mg once a year decreased fractures *and* mortality (limited use).
    - Denosumab 60 mg sc q6months is an alternative (limited use).
        - Can be used first line or if there are fractures while on bisphosphonate
        - Risk of decline in BMD and rebound vertebral fractures if dose is delayed
    - Bone formation medications teriparatide (1-34 PTH, daily injection) or romosozumab (sclerostin inhibitor, monthly injection) can be considered in severe osteoporosis or in those who fracture while on bisphosphonates.
- Patients with atypical femur fractures should not receive bisphosphonates or denosumab.
- For vertebral fractures:
    - Pain management
    - Physiotherapy for mobilization and spine decompression
- If possible, a bone mineral density study should be done as a baseline, and can be followed up in 2-3 years to monitor response to therapy.

Complex osteoporosis patients can be referred to the UHN osteoporosis program: FAX 416-340-3750.

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21. HYPERTENSION

Authors: Victoria Walter MbChB, Tarek Abdelhalim MD FRCPC

General Principles

- Cancelling an elective surgery for the sole purpose of uncontrolled hypertension should be a rare occurrence (<1%).[1]
- There is unlikely to be excess mortality or risk with preoperative systolic blood pressures that are <180.[1,2]
- Blood pressure may become transiently elevated during anaesthesia induction due to anxiety, acute stress response and instrumentation to secure the airway.[3]
- Intraoperative hypotension is the more frequent hemodynamic concern due to the vasoactive properties of anesthetic drugs inducing peripheral vasodilatation.[3]
- Intraoperative hypotension is associated with excess 30 day mortality, but NOT intraoperative hypertension.[2]

It is generally safer for patients to undergo non cardiac surgery with a higher BP and more lenient perioperative BP control than to proceed with a tightly controlled BP due to the risks of intraoperative hypotension.

Approach to Consult for Perioperative Hypertension

1. Is the hypertension new or pre-existing?
    - If new, what is driving it?
        - Pain? Anxiety? Retention?
        - Any evidence of end organ dysfunction worrisome for HTN Emergency?
            - aLOC, severe headache, visual disturbance, chest pain
    - If pre-existing, what is their baseline blood pressure?
2. Comorbidities
    - CAD, DM, Renal disease
3. Home antihypertensive medications
4. What surgery are they going for?
    - Duration of surgery changes risks of intraoperative hypotension

Hypertension Medication Management Perioperatively[4]

- Beta blocker - continue in perioperative setting due to risks of reflex hypertension and tachycardia

- ACEI/ARB – hold 24 hrs before surgery and restart postoperatively once systolic BP >140 and electrolytes and creatinine are stable
- CCB – can be continued or held on the day of surgery depending on the patient's baseline BP control and duration of surgery
- Diuretics – hold on the day of surgery, restart once the patient is stable postoperatively, has BP >140, and is eating and drinking

There is high risk of intraoperative hypotension with induction agents and anaesthetics so in the immediate preoperative period, do not aim for tight BP control.

When to Postpone Surgery[1]

- If any evidence of end-organ damage (as discussed above)
- If BP >180/110 consider delaying until BP falls <180/110

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22. STEROID MANAGEMENT

Authors: Mustafa Turabi MD, James Rassos MD MHPE FRCPC

Hypothalamic-Pituitary-Adrenal Axis

- Physiologic and mental stress stimulate the hypothalamus to release CRH which acts on the anterior pituitary to secrete ACTH.
- ACTH then acts on the adrenal cortex to produce cortisol.
- Cortisol mediates vascular tone and contributes to synthesis and release of catecholamines.
- Cortisol secretion exerts negative feedback and inhibits secretion of CRH and ACTH.
- Exogenous corticosteroids exert negative feedback control on the HPA axis by suppressing CRH secretion and subsequently ACTH secretion.
- These patients may have atrophy of the adrenal zona fasciculata and decreased cortisol production as a result.
- Patients with long-term steroid use may have reduced cortisol secretion in response to severe illness or stress (like surgery).

Table 1 – Synthetic glucocorticoids and their properties

Synthetic Glucocorticoid	Equivalent dose (mg)	Anti-inflammatory activity[1]	Duration of action (hours)
Short Acting			
Hydrocortisone	20	1	8-12
Cortisone	25	0.8	8-12
Intermediate Acting			
Prednisone	5	4	12-36
Prednisolone	5	4	12-36
Methylprednisolone	4	5	12-36
Triamcinolone	4	5	12-36
Long acting			
Dexamethasone	0.75	30	36-72
Betamethasone	0.6	30	36-72

[1]Relative to hydrocortisone

Perioperative steroids

Perioperative adrenal insufficiency is an uncommon complication of surgery. If perioperative glucocorticoid coverage is provided, it should be dependent on:

1. Degree of HPA suppression (duration and dose of previous glucocorticoid therapy)
2. Surgical stress
3. Conversion of current corticosteroid dosage to equipotent parenteral corticosteroid

Table 2 – Perioperative steroid management of non-suppressed HPA axis or uncertain suppression (UpToDate)

Definition	Supplementation
Non-suppressed HPA Axis	
• Prednisone at doses of **less than** 5 mg per day (for any length of time) • Any dose of glucocorticoid for less than 3 weeks • Patients being treated with less than 10 mg of prednisone or its equivalent every other day	• Maintain on normal daily dose of glucocorticoid during perioperative period • Does not require testing for HPA axis suppression • Monitor for hemodynamic instability perioperatively
Uncertain if HPA axis is suppressed	
• Patients taking prednisone 5-20 mg for more than 3 weeks • Patients who have used prednisone of at least 5 mg per day for more than three weeks in the **6-12 months prior** to surgery • These patients should undergo preoperative evaluation of HPA axis* ○ **Exception**: *urgent* or *emergency* surgery – patients should receive empiric perioperative glucocorticoid therapy and go to OR	Minor Procedure: • Give usual glucocorticoids if taking OR • No supplementation Moderate or Major Surgical Stress • Evaluate HPA axis suppression • Give supplemental glucocorticoids if suppressed

*Evaluation with AM cortisol and ACTH Stimulation Test:

- If AM cortisol level < 138 nmol/L 24 hours off steroids: highly suggestive of impaired HPA axis → **supplementation suggested**
- If AM cortisol is > 275 nmol/L, the patient does not have suppression of the HPA axis → continue current steroid replacement
- If AM cortisol is 138-275 nmol/L, further evaluation with ACTH stimulation test is suggested (or empiric additional perioperative therapy)
- ACTH Stimulation Test:
    - Give corticotropin 250 mcg
    - Measure serum cortisol 0, 30 and 60 minutes – HPA axis NOT suppressed if peak serum cortisol > 500 nmol/L

Table 3 – Perioperative steroid management of suppressed HPA axis (UpToDate)

Suppressed HPA Axis	

• Taking prednisone 20 mg per day or more for more than 3 weeks
 	
• Any patient on glucocorticoid who has clinical Cushing's syndrome
 	
• Biochemical adrenal insufficiency on AM cortisol or ACTH stimulation test
	Minor Procedures
	• Example: minor procedure or surgery under local anesthesia
	• Take usual morning steroid
	• No extra supplementation necessary
	
	Moderate Surgical Stress
	• Example: lower extremity revascularization, total joint replacement
	• Plan:
	  ○ Give usual morning steroid dose
	  ○ Give Hydrocortisone 50 mg IV just before procedure
	  ○ Give Hydrocortisone 25 mg IV Q8H x 24 hours postoperatively, then resume usual dose
	
	Major Surgical Stress
	• Example: open heart surgery, total proctocolectomy, esophagogastrostomy
	• Plan:
	  ○ Give usual morning steroid
	  ○ Give Hydrocortisone 100 mg IV just before surgery
	  ○ Give Hydrocortisone 50 mg IV Q8H x 24 hours postoperatively then taper dose by half daily to maintenance level (i.e., then hydrocortisone 25 mg IV Q8H x 24 hours, and so on)

23. ENDOCARDITIS PROPHYLAXIS

Authors: Nicole Gibbings MD, Abdu Sharkawy MD FRCPC

Recommendations for antibiotic prophylaxis for the prevention of infective endocarditis [IE] are based on limited evidence and pathophysiologic considerations of who is at highest risk. A 2013 Cochrane review found no evidence to determine if antibiotic prophylaxis is effective in preventing IE in those undergoing dental procedures[1]. In particular, Viridans group streptococcus IE is much more likely to develop from transient bacteremia from routine activities [i.e. chewing food, brushing teeth] than after a dental procedure.

This summary is primarily adapted from the 2020 ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease[2]. It is the consensus of the writing committee that antibiotic prophylaxis is ***reasonable*** for those at highest risk of developing IE and adverse outcomes from IE. Antibiotic prophylaxis must be balanced against the risk of the development of resistant organisms, C. difficile infection, drug toxicities, and drug-drug interactions. Shared decision-making between patients and physicians regarding the benefits and risks of IE prophylaxis is recommended. Patients should be educated about the signs and symptoms of IE to facilitate early diagnosis.

Table 1 - Conditions for which antibiotic prophylaxis is reasonable*

Prosthetic cardiac valve [including TAVI/transcatheter-implanted valves]
Prosthetic material for cardiac valve repair [including annuloplasty rings, chords, clips]
LVAD or implantable heart
Previous IE
Congenital heart disease • Unrepaired cyanotic congenital heart disease • Congenital heart defect post-repair within 6 months • Congenital heart defect post-repair with residual defect [shunt or valvular regurgitation at/adjacent to the site of a prosthetic patch/device] • Surgical or transcatheter pulmonary artery valve or conduit [Melody valve, Contegra conduit]
Cardiac transplant recipients with valve regurgitation attributable to structurally abnormal valve

Table 2 - Procedures for which antibiotic prophylaxis is reasonable*

PROCEDURES	NOTES
All dental procedures that involve manipulation of gingival tissue, manipulation of periapical tissue, and/or perforation or oral mucosa	
Respiratory tract procedures that involve incision or biopsy of the respiratory mucosa [includes tonsillectomy, adenoidectomy]	If undergoing an invasive respiratory tract procedure to treat an established infection [example: drainage of an abscess or empyema], regimen should contain an agent active against viridans group streptococci. If there is concern for MRSA, add vancomycin or another agent with activity against MRSA.
Procedures through infected tissues [skin, skin structure, MSK]	Most patients with these infections are already on agents with activity against S. aureus and ß-hemolytic streptococci. If there is concern for MRSA, add vancomycin or another agent with activity against MRSA.

*Based on Class 2a [moderate] recommendations, based on Level C [limited] evidence

Procedures that DO NOT require antibiotic prophylaxis

- Gastrointestinal, genitourinary, obstetrics/gynecological procedures
- Examples: TEE, cystoscopy, OGD, colonoscopy – including with biopsy/polypectomy], in the absence of known infection.†

†In patients with known bacteriuria, antimicrobial therapy before elective procedures, including lithotripsy, is typically provided.

Table 3 - Antibiotic regimens for infective endocarditis prophylaxis
Note: Give 30-60 mins prior to procedure

CLINICAL SITUATION	AGENT	DOSE
Able to take PO	Amoxicillin	2g PO x1
NPO	Ampicillin OR Cefazolin/Ceftriaxone	2g IV/IM x1 1g IV/IM x1
Able to take PO with Penicillin allergy	Cephalexin OR Azithromycin/Clarithromycin OR Doxycycline	2g PO x1 500mg PO x1 100mg PO x1
NPO with Penicillin allergy	Cefazolin/Ceftriaxone	1g IV/IM x1
Patient already on antibiotics pre-procedure	Preferable to choose an agent from an alternate class from the table	

Note: Cephalosporins should NOT be used in individuals with a history of anaphylaxis, angioedema, or urticaria to penicillins or ampicillin. The exception is Cefazolin, which can be safely used in patients with penicillin allergy unless the reactions are Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), or DRESS.

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24. OPIOIDS

Authors: Ashley Jensen MD MPA, Laura Rodger MD FRCPC

Introduction

I. Opioid pharmacology

Most opioids exert their major actions at the mu opioid receptors.[1] They can be full agonists, such as morphine, hydromorphone, oxycodone, and methadone, or partial agonists such as buprenorphine. Opioids can also be divided by duration of action into short and long-acting opioids.

Opioid tolerance develops within days to weeks. The FDA defines opioid tolerance as an individual who has received an equivalent to oral morphine 60 mg/day, transdermal fentanyl 25 mcg/hour, oral oxycodone 30 mg/day, oral hydromorphone 8 mg/day, or oral oxymorphone 25 mg/day for 1 week.[2]

Cross tolerance means the effects of pharmacologically related drugs, particularly those that act on the same receptor site. However, when switching to another opioid, clinicians need to assume that cross-tolerance is incomplete, which means that the starting dose of the new opioid must be reduced by at least 50% of the calculated equianalgesic dose to prevent overdosing.[3]

II. Opioid equivalency[4]

The dose of an opioid can be represented in morphine equivalents. Morphine is the gold standard for all calculations. Please refer to Appendix Tables 1 & 2 for conversion and equianalgesic guides.

This is relevant in the perioperative setting if a patient requires interruption of chronic opioid therapy or opioid rotation, related to surgical issues such as NPO status, administration limitations with nasogastric (NG) tubes, renal or hepatic dysfunction, or to consolidate short acting opioids.

Steps to calculate morphine equivalents (MEQs)

1. Calculate the 24-hour dose of opioids (all scheduled and PRN doses)
    a. If administered IV, convert to oral
2. Use the conversion table (Table 1 and Table 2)
    a. There are many online calculators which can help with calculations

b. See Toronto Academic Pain Medicine Institute Manual (Appendix)

3. Reduce the new opioid dose by 50%

Multimodal Pain Management

Postoperative pain is common. Negative outcomes are associated with unmanaged postoperative pain, including development of chronic post-surgical pain, and increased healthcare utilization.[5] It is also a common concern of patients undergoing surgery.[6] However, harms of opioid prescribing around the time of surgery include opioid-related side effects such as constipation and sedation, as well as prolonged use leading to dependency.[7]

Multimodal analgesia is the standard of care. Multimodal analgesia is defined as "the use of a variety of analgesic medication and techniques that target different mechanisms of action in the peripheral and/or central nervous system (which might also be combined with non-pharmacological interventions) might have additive or synergistic effects and more effective pain relief compared with single-modality interventions".[8] Patients often experience nociceptive pain and neuropathic pain from a surgical procedure.

In addition to local anesthetic at the surgical site, peripheral regional anesthesia and neuraxial therapies can be used at the discretion of anesthesia to improve postoperative pain.

Table 1: Multimodal analgesia for acute pain management[9]

Table 1. Multimodal Analgesia for Acute Pain Management

Drug Class	Drugs	Clinical Considerations
NSAIDs	Ibuprofen, naproxen, diclofenac, meloxicam, sulindac	Antiplatelet effects. GI bleeding risk; consider PPI use. CV risk; renal and hepatic considerations. Interactions with lithium. Available in topical, oral, and parenteral formulations
Acetaminophen		Maximum-dose considerations. Analgesic ceiling effects. Hepatic considerations. Available in oral and parenteral formulations
Opioids	Morphine, hydromorphone, oxycodone, hydrocodone, fentanyl, methadone	May be given as long-acting or short-acting formulation. Side effects and withdrawal symptoms. Assess renal and hepatic function. Available in topical, oral, and parenteral formulations
Mixed-acting analgesics	Tramadol, tapentadol	Low affinity for opioid receptors. Analgesic ceiling effect. Risk of lowering seizure threshold. May be considered adjuvant for neuropathic pain
NMDA receptor antagonists	Ketamine, methadone	May inhibit opioid tolerance. May be considered as adjuvant in opioid-tolerant patients. Ketamine shown to enhance morphine analgesic effects. Methadone administered as adjuvant to prevent opioid withdrawal
Anticonvulsants	Carbamazepine, gabapentin, pregabalin	Slow onset of pain relief. Gabapentin and pregabalin useful for neuropathic symptoms. Utility in opioid-tolerant patients not well established
Antidepressants	Venlafaxine, duloxetine, milnacipran, nortriptyline, amitriptyline	Greater evidence with neuropathic pain. Risk of serotonin syndrome with SNRIs. Risk of unpleasant side effects. Renal and hepatic considerations
Alpha$_2$ agonists	Dexmedetomidine, clonidine	Helps suppress opioid-withdrawal symptoms. Considered opioid-sparing and antihyperalgesic. Potentiates systemic analgesics
Corticosteroids	Dexamethasone	Possible analgesic adjuvant in opioid tolerance. Place in therapy unclear

CV: cardiovascular; GI: gastrointestinal; NMDA: N-methyl-D-aspartate; NSAID: nonsteroidal anti-inflammatory drug; PPI: proton pump inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor. Source: References 4, 5, 7, 8, 28-30, 32.

Table 2: Multimodal postoperative analgesia orders[5]

Postoperative
Comprehensive daily pain assessments
Mild pain/Minor surgical procedure
Acetaminophen 500–1000 mg PO every 6 h for 3–5 days
and one of the following
Celecoxib 100–200 PO BID for 3–5 days
Ibuprofen 200–800 mg PO BID every 4 h for 3–5 days
Naproxen 250–500 mg PO BID for 3–5 days
(If cannot take oral medications)
Acetaminophen 1000 mg IV every 6 h (if available) for 3–5 days
Ketorolac 15 mg IV every 8 h for 3 days
In addition to one of the following:
Oxycodone 5–10 mg PO every 4 h as needed
Hydromorphone 1–2 mg PO every 4 h as needed
Morphine 5–15 mg PO every 4 h as needed
Moderate pain/Invasive surgical procedure
Options in order of increasing difficulty in managing pain
1. Standing Acetaminophen and NSAIDs (if possible)
2. Consider Patient Controlled Analgesia
3. Consider postoperative regional anesthetic technique
4. Consider Ketamine infusion
5. Consider Lidocaine infusion
6. Consider Cannabinoids
7. Consider Gabapentinoids

Patients with Opioid Use Disorder

Opioid use disorder (OUD) is increasingly common in Canada and can complicate pain management and recovery from surgery. For patients with OUD the perioperative period can be one of vulnerability as they may worry about facing stigma, experiencing withdrawal symptoms, having inadequate pain relief, and relapsing (Ward 2018). Patients with OUD should be identified preoperatively and anesthesia notified about their history. Consultation from an inpatient Addiction Medicine service should be sought where available for assistance in management of patients with OUD in the perioperative setting.

I. Patients on Opioid Agonist Therapy (OAT)

Medications including methadone and buprenorphine are effective treatments that reduce illicit opioid use. Unfortunately, there is a paucity of standardized clinical guidelines to direct the management of these patients in the perioperative period.

Methadone and Buprenorphine

Methadone is a long-acting synthetic opioid and is a full mu-receptor agonist. It has a long and variable half-life (15-55 hours)[10](Wolff, K 2002). Buprenorphine is a partial opioid agonist with a strong binding affinity for the mu-receptor although it has low receptor-stimulating activity leading to less euphoria, respiratory depression and sedation even at higher doses; this makes it an effective option for OAT[11] (Sritapan, 2020).

For patients on methadone or buprenorphine prior to surgery:

1. Continue methadone and buprenorphine at their usual dose on the day of surgery.
    a. Depending on timing of surgery the patient may require a carry dose from their usual prescriber.
    b. Ensure anesthesia is aware of their diagnosis and methadone use.

2. Patients should continue their usual maintenance dose throughout the perioperative period.
    a. For both methadone and buprenorphine, analgesia lasts about 8 hours, and it may be helpful to divide the daily dose and provide it Q8H for extra analgesia.
    b. The total daily dose of either buprenorphine or methadone can be increased in this setting to increase the analgesic effect.

c. There is concern that for patients continued on buprenorphine pain management will be inadequate due to the difficulty of overcoming the high mu-receptor affinity, however evidence has **not** shown that continuation of buprenorphine prevents adequate analgesia from opioids and other multi-modal pain management[12-15] (Van Neil, 2016; Hansen 2016; Martin 2019).
d. Due to opioid tolerance additional opioids for pain at higher doses and multi-modal pain management will be needed. This is particularly true for buprenorphine which is a partial opioid agonist.

3. For patients strictly NPO or unable to take their usual dose refer to Table 3

Table 3 - Methadone and Buprenorphine for patients who are strictly NPO or unable to tolerate usual dose

Methadone	Buprenorphine
• Consider NG tube placement for methadone continuation where possible as IV formulations are not available; therefore, if strict NPO >3 days, will need to convert to another agent to avoid withdrawal symptoms. (Appendix Table 1)* • If strictly NPO from GI surgery, switch to IV methadone although noting that conversion is challenging. In general, the dose should be reduced by 50% and given q6-8 hours. This should be co-managed with Anesthesia and Addiction medicine.	• Can be administered transdermally or sublingually. It has poor GI absorption and is not administered orally.

*dose conversions with methadone are approximate, and should only be used in select situations

4. At time of discharge:
    a. Continue usual dose of methadone or buprenorphine as well as multi-modal pain management
    b. Ensure that there are clear written instructions for any tapering or use of additional opioid therapy in addition to OAT. To reduce risk of overdose and misuse, prescribe in short supplies with more frequent refills.
    c. Ensure outpatient methadone or buprenorphine prescriber aware of discharge and follow-up established to ensure not missed doses. Make sure this prescriber is aware of any changes in dose or frequency.

II. Other OAT

There may be circumstances in which patients are on alternative forms of OAT for OUD. For those on slow release oral morphine or injectable OAT, they can be managed similarly to patients on chronic opioid therapy. Although not commonly used in Canada for OUD, naltrexone can be used for both OUD and alcohol use disorder. Oral naltrexone should be discontinued at least 72 hours prior to elective surgery in which treatment with opioids is expected[17] (ASAM Guidelines 2020). Patients should be off any postoperative opioids for 3-7 days prior to resuming naltrexone[17] (ASAM guidelines, 2020). In situations where these alternative forms of OAT are used, be sure to involve the surgical, anesthesia and addiction medicine teams for management in the perioperative period.

III. Patients with OUD and ongoing use

For patients with ongoing opioid misuse undergoing surgery, careful monitoring for opioid withdrawal will be required. Active opioid withdrawal can complicate the postoperative course and increase pain sensation[18] (Ward, 2018). For these patients consultation with Addiction medicine and anesthesia are important. Patients may require high doses of opioids to manage both pain and withdrawal symptoms and benefit from multi-modal pain management. Hospitalization may represent an opportunity to engage patients in treatment for opioid use disorder and start OAT in conjunction with social supports.

Chronic Opioid Management

If a patient is identified as opioid-tolerant based on the preoperative medication history, they should be counselled on the following:

1. Continue taking any prescribed opioid medications up to and including the day of surgery, as abrupt discontinuation can lead to withdrawal.
    a. Ensure Anesthesia is aware of chronic opioid use.

2. Continue chronic opioid therapy during admission.
    a. Patients may require higher doses of breakthrough medication.
    b. Multimodal analgesia is particularly important.
    c. If pain management is challenging, consider an opioid rotation.

3. Cases where chronic therapy may not be feasible to continue
    a. Extended-release medications cannot be administered through NG tubes → convert to short acting and schedule doses at regular intervals.
    b. Strict NPO → convert to parenteral or transdermal therapy.

4. Provide clear instructions and handover at the time of discharge.
    a. If a patient has a history of substance use disorder, consider frequent dispensations of any PRN medication at discharge.
    b. Ensure the patient's regular opioid prescriber is aware of the duration in hospital - do not provide a new prescription for chronic opioid therapy without discussion with their primary prescriber.
    c. Patients and providers should receive clear instructions that PRN opioids at discharge will continue to be tapered.

Opioid Toxicity and Overdose

Signs of opioid toxicity include decreased level of consciousness, depressed respiratory rate, constricted pupils, and decreased bowel sounds to full respiratory arrest. Note that the absence of constricted pupils does not exclude the diagnosis of opioid toxicity; patients on meperidine or taking other medications or drugs (such as anticholinergics or sympathomimetics) may have normal pupils.

The treatment of suspected overdose is naloxone. Note that the goal of therapy is not a normal LOC but adequate ventilation. For spontaneously breathing patients start with 0.04mg IV naloxone and titrate up. For

apneic patients start at 0.2-1mg IV and for those in respiratory arrest, start with a higher dose of 2mg IV.

For non-apneic patients with evidence of toxicity in the perioperative period, reduce the dose of opioids.

Appendix Table 1 - Opioid conversions

Opioid (mg/day unless specified)	Conversion Factor
Codeine	0.15
Fentanyl transdermal (mcg/hr)*	2.4
Hydrocodone	1
Hydromorphone	4-5
Methadone* 1-20mg/day 21-40mg/day 41-60mg/day >61-80mg/day	 4 8 10 12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

*inexact calculation - many variables impact pharmacology

Appendix Table 2- Equianalgesic table

Opioid Agonist	*Oral (mg)*	*Parenteral (mg)*
Morphine	30	10
Hydrocodone	25-30	
Oxycodone	20-30	
Hydromorphone	7.5	1.5
Oxymorphone	10	
Fentanyl (IV only one time dose)*		0.1 (100mcg)
Tramadol	120	

Appendix Table 3: Switching between opioids

OPIOID MANAGER SWITCHING OPIOIDS

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- Opioid withdrawal symptoms are unpleasant, but not life-threatening. What is life-threatening with opioids is overdose. So remember, it is safer to underdose. Be careful during pregnancy, because severe acute withdrawal has been associated with premature labour and spontaneous abortion.
- After switching, it is important to warn the patient (and relative or friends) about signs of overdose: slurred or drawling speech, emotional lability, ataxia, "nodding off" during conversation or activity.
- Consider a 3-day "tolerance check:" contact the patient 3 days after starting the new opioid to check for signs of over-sedation and to ensure that pain relief is at least comparable to the pre-switch treatment.
- Patients at higher risk of overdose include: elderly, on benzodiazepines, renal or hepatic impairment, COPD, sleep apnea, sleep disorders and cognitive impaired.
- These doses are approximations due to inter-individual variation.

The form below is designed to guide the provider in switching from one opioid to another using the table of morphine equivalent suggested by the guideline. A copy of the completed form may be given to the patient and should be sent to the pharmacist.

Morphine Equivalence Table

Opioid (Oral Dose)	Equivalent Doses (mg)	Conversion to MEQ
Morphine	30	1
Codeine	200	0.15
Oxycodone	20	1.5
Hydromorphone	6	5
Meperidine	300	0.1
Methadone & Tramadol	Dose Equivalents unreliable	
Transdermal fentanyl	60 – 134 mg morphine = 25 mcg/h 135 – 179 mg = 37 mcg/h 180 – 224 mg = 50 mcg/h 225 – 269 mg = 62 mcg/h 270 – 314 mg = 75 mcg/h 315 – 359 mg = 87 mcg/h 360 – 404 mg = 100 mcg/h	

Switching Opioids:	
If previous opioid dose was:	Then, SUGGESTED new opioid dose is:
High	50% or less of previous opioid (converted to morphine equivalent)
Moderate or low	60-75% of the previous opioid (converted to morphine equivalent)

Switching Opioid Form

Patient name:..... Today's date: ...../...../.....

Switching from ..... to .....

Start switching on Monday: ...../...../..... (mm/dd/yy)

Current opioid(s) regimen:

- Opioid name, dose and frequency: .....
- Opioid name, dose and frequency: .....
- Opioid name, dose and frequency: .....

Current total daily dose of opioid: ..... / day

Switching from current opioid to morphine equivalent:

Morphine to morphine:	multiply by 1
Oxycodone to morphine:	multiply by 1.5
Hydromorphone to morphine:	multiply by 5

Current **morphine** equivalence dose: ..... / day

Proportion of the initial daily dose that will be switched to the new opioid: ( ) 50% ( ) 60% ( ) 75% ( ) other: .....

Total morphine equivalents that will be switched to the new regimen: ...../day

Switching from morphine equivalent to the new opioid:

Morphine equivalent to morphine:	multiply by 1
Morphine equivalent to oxycodone:	multiply by 0.667
Morphine equivalent to hydromorphone:	multiply by 0.2

From morphine equivalent to the new opioid: The total daily dose of the new opioid is: ..... /day

New opioid regimen:

- Opioid name, dose and frequency: .....
- Opioid name, dose and frequency: .....
- Opioid name, dose and frequency: .....

Comments:

.....

.....

For questions, please call Dr. ..... Phone number: (.....) .....

To access the Canadian Guideline for Safe and Effective Use of Opioids for Non Chronic Cancer Pain and to download the Opioid Manager visit **http://nationalpaincentre.mcmaster.ca/opioid/**

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25. Common Postoperative Complications

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1. Postoperative Fever (POF)[1,2]

Table 1 - 5 "Ws" of postoperative fever

Table 1
Classic "Ws" of postoperative fever

W	Cause	Timing
Wind	Atelectasis	POD 1–2
Water	Urinary tract infection	POD 2–3
Wound	Wound infection	POD 3–7
Walking	Deep vein thrombosis/thrombophlebitis	POD 5–7
Wonder drug	Drug fever	POD >7

Abbreviation: POD, postoperative day.
Data from Cline D, Stead LG. Abdominal emergencies. New York: McGraw Hill; 2007.

Note: a cause can be identified in 50-90% of POFs that persist beyond 5 days. Orders of frequency for infectious source: wound > urine > lung (pneumonia).

Table 2 - Management pearls and clinical rationale

Clinical Recommendation	Rationale
Only treat with antibiotics if: • Vitally unstable • Immunocompromised • Known/obvious source (e.g. wound)	Postoperative fever < 72 hours is secondary to inflammatory changes from release of cytokine in 80% of cases.
Do not routinely order investigations for early-onset POF including chest radiography, urine or blood cultures.	As above
Do not routinely use antipyretics including acetaminophen.	3 RCTs conducted with a total sample of 320 patients found no benefit in mortality or length of stay between treatment and control arms; can be used for symptomatic management.
Isolated fever alone is not sufficient ground for ongoing inpatient care.	Isolated fever alone at time of discharge has no impact on the rate of subsequent readmission.

2. Postoperative Anemia[3]

- Perioperative blood loss – dependent on type of procedure
    - <500mL: hip fracture repair, appendectomy, cholecystectomy, most urologic/gynecologic procedures
    - 500-1000mL: total knee/hip arthroplasty, CABG
    - >1000mL: organ transplant, radical hysterectomy

Table 3 - Pillars of Patient Blood Management (PBM)

Detect Postoperative Anemia	Reduce Perioperative Blood Loss	Harness + Optimize Patient-Specific Physiologic Reserve
All major surgeries (EBL > 500mL or last >2 hours) need screening.	Some modifiable elements: • Anticoagulation • Type of anesthesia (beyond scope of this handbook) • Selective use of pharmacotherapy (e.g. TXA)	Replenish iron and blood stores, but with some important clinical considerations (see below).

Table 4 - Management pearls and clinical rationale

All major surgeries need postoperative anemia screening.	There have been studies demonstrating clear association of postoperative anemia with prolonged recovery, increased mortality and likelihood of readmission.
CBC monitoring should continue at least until POD #3.	The nadir for blood loss is most observed on POD #3, as the end of surgical procedure does not signify the end of blood loss.
IV iron is preferred over oral iron in the postoperative period.	Oral iron is often not tolerated or well absorbed immediately postoperatively due to a pro-inflammatory state and poor motility. Note: there are currently no studies to identify the best time to start postoperative iron supplementation.
Adopt a restrictive transfusion threshold.	Most guidelines recommend <70g/L in most cases and <80g/L for orthopedic/cardiac surgeries or if there is concomitant chest pain or hemodynamic instability not responsive to fluids. Allogenic transfusions are associated with an increase in perioperative morbidity/mortality, and there is also a worldwide shortage in blood.

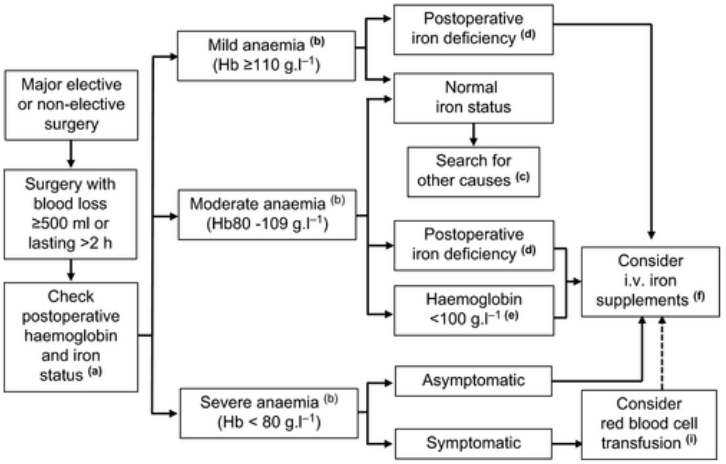

Figure 1 - Suggested algorithm for management of postoperative anemia. (Source: Association of Anesthesiologist)

3. Postoperative Urinary Retention (POUR)[4,5]

Diagnosis of POUR

- Clinical criteria: patient discomfort (full sensation), palpable/distended bladder, inability to empty bladder 10 hours postoperatively
- Ultrasound criteria: residual volume > 500mL

Table 5 - Management pearls and clinical rationale

Once POUR is confirmed, decompression should be the management priority.	If untreated, POUR can lead to bladder over-distension and detrusor muscle damage. The degree of detrusor dysfunction is directly proportional to the duration of urinary retention.
Decision about which patient to catheterize, when, and by which approach, should remain mostly at the discretion of the attending physician and hospital protocols.	There is no conclusive evidence regarding which individuals with POUR would benefit the most from catheterization. The optimal duration of bladder catheter also remains controversial. Prior studies demonstrated no significant difference between in/out and indwelling catheter x24h with regards to need to re-catheterize and incidence of urinary tract

	infection, but indwelling catheter insertion does increase hospital stay by an average of 1 day.
Catheterization aside, the evidence for other management modalities is still actively evolving.	Interventions with good evidence: • Alpha blockers (for known BPH) • Early postoperative mobilization Interventions with some evidence: • Oral fluid restriction • NSAID suppositories (for hemorrhoidectomies) • Postvoid residual monitoring Interventions with no evidence: • Electroacupuncture • External bladder stimulator • Straight catheterization in the recovery room

4. Postoperative Pulmonary Complications (PPCs)[6,7]

Table 6 - Common types of pulmonary complications

Atelectasis	• Risk factors: general anesthetic effect, neuromuscular blockade, recumbent position, increased intra-abdominal pressure • CNS depression → loss of hypoxic drive → formation of atelectasis • Most affected area = basal segments
Postoperative Pneumonia	• Highest risk in first five postoperative days, directly associated with degree of atelectasis • Aspiration of subglottic secretions coinciding with depression of protective reflexes 2 hours immediately post-op (i.e. highest risk of aspiration)
Postoperative Acute Lung Injury (ALI)	• Hypoxemic respiratory failure with decreased lung compliance and noncardiogenic pulmonary edema • Primary ALI: immediately post-op, due to systemic inflammatory response secondary to surgical insult • Secondary ALI: 3-12 days after surgery, due to postoperative complications/events such as sepsis, pulmonary embolism, aspiration of gastric contents, pneumonia or transfusion
Pulmonary Embolism	Discussed in Chapter 16, Thrombosis.

Management of postoperative pulmonary complications is mostly preventative (early mobilization, improve nutrition, avoid liberal transfusion, remove airway secretions), supportive (oxygen, CPAP) and correction of underlying etiology. There remain no clear recommendations for pulmonary complications that are specifically dedicated to the postoperative setting.

Of note, prevention of postoperative complications heavily relies on optimizing modifiable risk factors during the preoperative period, which would include:

- Optimizing underlying comorbidities: COPD, CHF, OSA, or chronic liver disease
- Cessation of smoking (cessation for >4 weeks before surgery decreases PPCs by 23%, >8 weeks by 47%)
- Anemia with hemoglobin <100 has a 3-fold increased risk of PPC. Management would involve supplementation and guidelines do not recommend transfusion, which on its own has been independently associated with increased PPC risk.

5. Postoperative Cardiovascular Complications[8-10]

Most common postoperative complications:

- Postoperative sinus tachycardia[11]
    - Defined as sinus rhythm at a rate greater than 100bpm
    - This differs from "inappropriate sinus tachycardia", which is a condition a) not due to an identifiable cause, b) classically associated with a drop during sleep, c) often symptomatic with palpitations or presyncope.
    - Inappropriate sinus tachycardia only very rarely (case reports) leads to cardiomyopathy.
- Other postoperative arrhythmias (see Chapter 8)
    - Peak incidence 1-3 days postoperatively, positively correlated with age, male sex and preoperative heart rate
    - Atrial fibrillation and atrial flutter are the most common sustained arrhythmias in the postoperative setting.
- MINS – Myocardial Injury After Noncardiac Surgery (see Chapter 3)
    - Defined as elevation in cardiac biomarkers without symptoms or electrocardiographic evidence of myocardial injury

Table 7 - Management pearls and clinical rationale

An ECG should be performed in the PACU if clinically indicated.[1]	New ischemic findings on ECG were found to be an independent predictor of subsequent major cardiac events, with an adjusted OR of 2.2.
Daily troponins should be done for 48-72 hours as clinically indicated.[1]	Most myocardial infarcts occur within 48 hours of noncardiac surgery. This is also when patients are receiving analgesia that may mask ischemic symptoms As per the VISION trial, high postoperative troponins are the strongest predictor of 30-day mortality.
Individuals with identified MINS should be initiated on cardiac medication intensification.	Canadian Cardiology Society 2017 Perioperative guidelines recommend the initiation of long-term ASA and statin in patients who suffer a myocardial injury or myocardial infarction after noncardiac surgery (see Chapter 3).
When treating arrhythmias, it is important to identify the type of arrhythmia and presence of underlying systolic heart failure (HF).	It is important to distinguish between atrial flutter and other supraventricular tachycardias that may respond to vagal maneuvers or nodal agents (e.g. adenosine). Beta blockers and non-DHP CCB (diltiazem or verapamil) remain first line agents for treatment for stable cases, except for those with systolic heart failure, as substantial negative inotropy may precipitate or worsen HF. Digoxin may be preferred in these cases instead.
In postoperative sinus tachycardia, precipitating factors should be ruled out.	Identify and correct factors such as pain (including at the surgical site, bladder distension, constipation), blood loss, volume depletion, sepsis/infection, hypoxia, ischemia, electrolyte abnormalities, fluid overload, pulmonary embolism, and drug use or withdrawal (including stimulant use or alcohol withdrawal). A common initial approach will include drug and substance review, CBC, electrolytes, creatinine, lactate, troponin, TSH (if relevant), doppler US or CTPA (if clinically indicated). Trial of fluid bolus could be considered. If normal workup, reassurance can be provided to the surgical team. A beta-blocker is essentially never indicated. Rather, appropriate follow-up is needed by outpatient providers after the postoperative period to reassess heart rate.

[1]Clinically indicated (baseline risk >5%) = 1 of: increased BNP, RCRI score of 1 or more, >65 years, or 45-64 with significant cardiovascular disease

6. Perioperative electrolyte abnormalities[12,13]

Table 8 - Management pearls and clinical rationale

Electrolyte Derangement	Etiology	Investigation and Treatment
Hyponatremia	Appropriate ADH secretion = hypovolemia (NPO pre-surgery, fluid loss during surgery) OR decreased effective circulating volume (CHF, cirrhosis, hypo-albuminemic state) Inappropriate ADH secretion (i.e. SIADH) = post-operative pain, nausea, stress, pneumonia/aspiration, neurosurgery, hypothyroidism, adrenal insufficiency, drugs (thiazide, TCA, SSRI) No ADH secretion = excess water from polydipsia, or iatrogenic e.g. over resuscitation with hypotonic fluid (D5 or 2/3 and 1/3) and intravasation of irrigation fluid in OR	Initial workup includes serum electrolytes/osmolality and urine electrolytes/osmolality (ideally before any management instituted), as well as medication review. Serum Na < 120 requires close monitoring Urine Na < 20 suggests hypovolemia Urine Osm < 100 suggests polydipsia or increased free water administration. Treatment for hypovolemia includes fluid resuscitation, whereas treatment for SIADH includes fluid restriction, management of underlying cause (pain, nausea, review of medications), salt tablets and avoidance of IV fluids. Hypertonic saline is used for severe hyponatremia with neurological symptoms (seizures, coma). Serum sodium should be increased by 6-8 in a 24 hour period, and urine output >100-200 mL/hr suggests possible rapid overcorrection.
Hypernatremia	Decreased free water intake (particularly in dementia or delirium) or free water loss, e.g. diabetes insipidus (central vs. nephrogenic)	Administer free water enterally if possible (oral or via NG flushes) or with D5W infusion. Consider central DI in neurosurgical patients.

Electrolyte Derangement	Etiology	Investigation and Treatment
Hypokalemia	Decreased intake Hypomagnesemia Potassium Losses • Vomiting, diarrhea, high ostomy output • Excessive diuresis (diuretics, post-obstructive from urinary retention, renal transplant patients or post-operative autodiuresis) • Aldosterone (from perioperative stress resulting in potassium and magnesium excretion) Shifting of potassium • Refeeding syndrome • Third spacing and the subsequent auto-diuresis from third-spaced fluid returning to the vascular space	Hypomagnesemia should be corrected simultaneously (see below). Hypokalemia can be replaced orally (K-dur) or IV (added to IV fluids). Every 40 mEq of potassium raises the serum potassium by about 0.4 mmol/L. IV potassium can only be run at 10 mEq per hour in a low concentration via peripheral IV as it is caustic and to prevent transient hyperkalemia.
Hyperkalemia	Decreased excretion • Renal failure • Hypoaldosteronism – adrenal insufficiency • Medications (heparin, ACE/ARB, etc) Shifting and cell lysis • Mechanical tissue injury (surgical procedure itself) and rhabdomyolysis • Blood transfusions (lysed RBCs) • Hemolysis	Ensure it is not a hemolyzed sample. Review medications (e.g. ACEi, ARB, spironolactone). Other management will depend on cause. If severe hyperkalemia (K > 6), ECG should be obtained to assess for changes (PR flattening, widened QRS, peaked T-waves or arrhythmia). Severe hyperkalemia (K > 6.5 or any ECG changes): • Temporize: Calcium gluconate 1g IV • Shift: 1 amp D50 followed by 10U IV Regular Insulin and D50, Sodium bicarbonate • Removal: Lasix, laxatives, Lokelma

Electrolyte Derangement	Etiology	Investigation and Treatment
Hypomagnesemia	Refeeding syndrome Third spacing fluid losses	Magnesium can be replaced intravenously or orally, recognizing that oral magnesium can cause diarrhea. Magnesium Sulfate 2g IV is expected to increase serum Mg by 0.16 mmol/L.
Hypophosphatemia	Refeeding syndrome Third spacing fluid losses	Phosphate can be replaced orally or intravenously when the enteral route is not feasible. Intravenous Sodium Phosphate 15 mmol is expected to increase serum phosphate by 0.16 mmol/L. If oral, a typical dose is Sodium Phosphate 500 mg PO BID (each dose contains 16 mmol of phosphate).

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26. Approach to Pregnancy Disorders

Author: Yayi Huang MD FRCPC

Obstetric medicine is the management of maternal disorders in pregnancy. The scope includes preconception counselling, optimization of pre-existing conditions in pregnancy, and the diagnosis and management of diseases specific to pregnancy. Despite being an expected competency for internists, caring for pregnant patients is well known to cause anxiety and uncertainly even amongst the most experienced practitioners. Keeping the following frameworks in mind will help when faced with any consultation in a pregnant patient.

1. **Is the problem pregnancy related or unrelated?**

It is important to compartmentalize diseases into those that are pregnancy specific (e.g. preeclampsia, cholestasis of pregnancy, acute fatty liver) and those that occur in a patient who happens to be pregnant. More often than not, physicians fear the most sinister complications of pregnancy when the diagnosis is one commonly encountered in the general population. Always approach a consult with these two groups of differential diagnoses and do not allow your unfamiliarity with the pregnant patient distract you from the principles you know well. Just think "what would I do if this patient isn't pregnant?".

2. **A healthy mother is a healthy baby.**

The mantra of any obstetric internist. First coined by a renowned Toronto based rheumatologist who recognized the detriment of uncontrolled inflammatory diseases on the fetus over the potential harm of immunosuppressive treatments. If the mother is unwell due to an inadequately controlled illness, the fetus will inevitably suffer from poor outcomes. This concept allows one to undergo investigations and interventions when the risks to the fetus are unknown, considering the lack of robust evidence for many decisions in obstetric medicine. It is also useful when counselling patients as they understandably want to minimize harm to their baby at all costs.

3. **Know your pregnancy physiology.**

Pregnancy affects every bodily system and leads to a variety of physiologic symptoms. Being familiar with the common symptoms and laboratory changes in a normal pregnancy is helpful when counselling patients and recognizing pathology. Pregnancy can also impact a

chronic condition by either exacerbating or remitting it, therefore, one should anticipate for these changes and alter treatment as appropriate.

4. **What about the baby?**

Even though the focus of an obstetric internist in a high-risk pregnancy is on maternal health, it is crucial to always be mindful of the fetus. Many treatments need to be modified for fetal safety, since drugs, contrast, and maternal antibodies can readily cross the placenta into the fetal circulation. It is also important to predict fetal complications from maternal conditions that may arise throughout pregnancy or around delivery. This necessitates close collaboration with the obstetrician or maternal fetal medicine (MFM) specialist as they are the ultimate custodians of fetal health.

27. HYPERTENSIVE DISORDERS OF PREGNANCY

Authors: Maude Bouchard MD FRCPC, Yayi Huang MD FRCPC

Physiologic blood pressure changes in pregnancy

- Decreases to a nadir during the second trimester around 20 weeks (5–10 mm Hg below baseline), due to the vasodilatory effect of progesterone
- Begins to increase during the third trimester and returns close to preconception levels postpartum

Definition (Hypertension Canada 2018 & SGOC 2014)[1,2]

- Systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg
- On the average of at least 2 measurements taken at least 15 minutes apart
- Severe hypertension if ≥ 160 mmHg systolic or 110 mmHg diastolic – medical emergency in pregnancy

Classification

Table 1 – Classification of hypertension in pregnancy

Disorder	Characteristics
Pre-existing (chronic) HTN	• HTN diagnosed pre-pregnancy or developing < 20+0 weeks • Warrants tighter control (<130/80) if associated with comorbidities (diabetes, nephropathy, cardiovascular) • 20% risk of preeclampsia
Gestational HTN	• New onset HTN developing ≥ 20+0 weeks • 40% risk of preeclampsia
Preeclampsia	• Can be superimposed to pre-existing HTN, complicating gestational HTN or de novo • Develops ≥ 20+0 weeks to 6 weeks PP (5%) • Called early-onset preeclampsia if develops < 34+0 weeks • Defined as hypertension AND: - New or worsening proteinuria OR

	- ≥ 1 adverse conditions (e.g. headaches, visual symptoms, mild desaturation, mild creatinine elevation, abdominal pain, IUGR, oligohydramnios, …) OR - ≥ 1 severe complication (e.g. eclampsia, PRES, pulmonary edema, severe AKI, HELLP syndrome, abnormal doppler velocimetry)
Others: • White-coat hypertensive effect • Transient hypertensive effect • Masked hypertensive effect	• White-coat effect: 40% of women progress to gestational hypertension and 8% to preeclampsia

Management of hypertension (SOGC 2014)[1]

Non-severe hypertension (140-159/85-109 mmHg)

- If on antihypertensive drugs pre-pregnancy, switch to one of the following agents prior to conception.
- If ≥ 20 weeks, evaluate for preeclampsia (CBC, LFT's, urates, creatinine, electrolytes, urine PCR)
- As per new recommendations based on *CHIPS* trial[2], target diastolic BP of 85mmHg to reduce the risk of severe hypertension; no recommendations on systolic BP, generally target <140mmHg
- Avoid ACEi and ARBs during pregnancy (increases the risk of fetal malformations in second and third trimester)

Table 2 - Antihypertensives for non-severe hypertension

First line agent	Starting dose	Maximum dose
Labetalol	100mg PO BID to TID	300mg po QID
Nifedipine XL	30mg PO OD	60mg po BID
Methyldopa	250mg po BID	500mg po QID
Second line agent	**Starting dose**	**Maximum dose**
Hydralazine	10-25mg po TID to QID	50mg PO QID

Severe hypertension (≥ 160/110 mmHg)[1]

- Is a risk factor for strokes and accordingly, is considered an obstetrical emergency and required immediate management
- If ≥ 20 weeks, evaluate for preeclampsia (CBC, LFT's, urates, creatinine, electrolytes, urine PCR)
- Target 140-150/90-100 mmHg
    - *The goal is not to normalize BP, but to achieve a safer BP range to avoid loss of cerebral autoregulation and impairment of placental perfusion

Table 3 – Antihypertensives for severe hypertension

Agent	Starting dose	Subsequent dose
Labetalol	20mg IV	20-80mg IV q30 min OR 1-2mg/min IV (max 300mg)
Nifedipine IR	5mg PO	5-10mg IR q30
Hydralazine	5-10mg IV	5-10mg IV q30 OR 0.5-10mg/h IV

Management and Preeclampsia and Eclampsia (SOGC 2014)[1]

1. Hypertension
    - BP management as described above
    - Screen for all potential adverse conditions and severe complications

2. Eclampsia
    - Defined as new onset seizure in a patient with preeclampsia
    - Magnesium is indicated for eclampsia prevention if: ≥ 1 severe complication severe hypertension, headaches/visual symptoms, abdominal pain, platelet count <100,000, progressive renal insufficiency, and/or elevated liver enzymes.

Table 4 – Magnesium Sulfate dose for eclampsia prevention

Agent	Starting dose	Subsequent dose
Magnesium sulfate	4g IV in 20 to 30mins	1g/h IV x 24h

- All patients on a magnesium infusion need to be in a monitored setting, usually labor and delivery, and have a foley to monitor urine output as magnesium is renally cleared.
- Monitor for magnesium toxicity: CNS depression, decreased reflexes, respiratory depression, bradycardia, hypotension

- Treatment of toxicity:
    - STOP MgSO4
    - 10% Calcium gluconate 10 mL IV over 10 minutes
- Eclampsia is considered an obstetrical emergency and an indication for delivery.
- Treatment of eclampsia is also magnesium sulfate.

3. Delivery
    - Always liaise with obstetrics to assess best timing for delivery.
    - If no indication for immediate delivery, ensure close monitoring of BP and lab results

Prevention of Recurrent Preeclampsia

- ASA 162mg nightly started ≤ 16 week (usually 10-12 weeks) until 36 weeks (in anticipation of delivery)
- ASPRE trial[3] showed that Aspirin 150mg (two tablets of 75mg used in the UK) significantly decreased rates of preterm (<37 weeks gestation) preeclampsia
- Indicated if ≥ 1 of the following high-risk factors
    - Previous preeclampsia
    - Chronic hypertension
    - Type 1 or 2 diabetes
    - Chronic kidney disease
    - Systemic lupus erythematosus
    - Antiphospholipid syndrome
    - Multiple gestation
    - ≥ 2 moderate-risk factors (e.g. age >35, BMI >30, FHx, etc.)
- Other measures
    - Calcium 1000mg daily if dietary intake < 600mg
    - Moderate-intensity exercise 150 min/week

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28. VENOUS THROMBOEMBOLISM IN PREGNANCY

Authors: Maude Bouchard MD FRCPC, Yayi Huang MD FRCPC

Epidemiology

- Incidence in pregnancy: of 0.1%
- Increased risk 6 weeks post-partum (RR 20-80 vs nonpregnant) > third trimester (RR 9 vs nonpregnant) > first and second trimesters (RR 2 vs nonpregnant)
- Increased risk in pregnant woman with an inherited thrombophilia (RR 15 vs pregnant woman without thrombophilia)
- Other risk factors: sickle cell disease, smoking, multiple pregnancy, age > 35, obesity, cesarean section (especially emergency section)

Pathophysiology

Virchow's Triad in Pregnancy

1. Hypercoagulability: due to alteration of coagulation proteins with increased factors V, VII, VIII, X and vWF and decreased protein S
2. Venous stasis: due to mechanical compression of pelvic vessels by the gravid uterus, the relative and intermittent compression of the left common iliac vein by the right common iliac artery where they cross and the hormonal changes of pregnancy
3. Vascular damage: endothelial injury at the time of delivery

Clinical presentation

Table 1 - Comparison of VTE clinical presentation in a pregnant vs nonpregnant population

	Pregnant	Nonpregnant
DVT	• 80-85% in the left leg • In proximal veins (iliac and femoral) with distal extension of the thrombus • Groin/buttock/back pain > edema > skin change of color	• 55-60% in the left leg • In distal veins (popliteal) with proximal extension of the thrombus • Lower extremity pain, skin change of color, edema
Pulmonary embolism	• Desaturation (< 97%) • Sustained tachycardia (> 110) • Dyspnea, pleuritic pain, hemoptysis	• Desaturation (< 92%) • Sustained tachycardia (>100) • Dyspnea, pleuritic pain, hemoptysis

Diagnosis

Deep Vein Thrombosis (DVT):

- If there is a high clinical suspicion of DVT, anticoagulation should not be withheld while awaiting diagnostic results.
- Ultrasound is the test of choice in a patient presenting with symptoms of DVT. Always ensure there was at least an attempt at visualizing the proximal veins (i.e. femoral and iliac veins) although it may be difficult in later trimesters.
- If the first compression ultrasound is negative, it should be repeated within 3-7 days as a single ultrasound cannot rule out DVT in pregnant women.
- If the suspicion of proximal DVT is high and the ultrasound is repeatedly inconclusive, consider MRI.

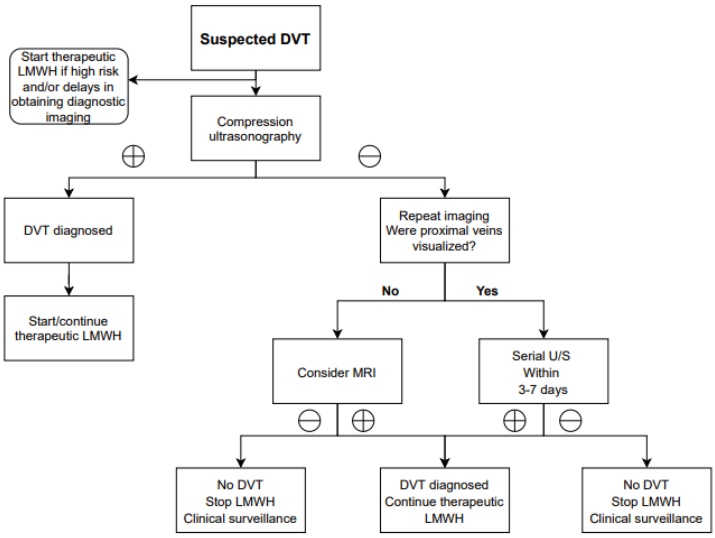

Figure 1. Diagnostic algorithm for DVT (Thrombosis Canada 2021 & SOGC 2014)[1,2]

Pulmonary Embolism:

- If high clinical suspicion of pulmonary embolism, empiric anticoagulation should be started.

- As per SOGC 2014 guidelines, bilateral leg compression ultrasonography remains the first line investigation when pulmonary embolism is suspected in an attempt to avoid further imaging and radiation if it's positive.
    - Still the current widespread practice
- As of September 2021, Thrombosis Canada adopted the Pregnancy-adapted YEARS algorithm from the Artemis study.[3] (see figure 3)
    - Differs from previous guidelines as it includes D-dimer and has CTPA as imaging of choice
    - Although it has been shown to reduce unnecessary diagnostic imaging in pregnant women, there is currently no unanimous consensus on whether d-dimer can safely rule out pulmonary embolism, so it should not replace physician clinical judgement.
- V/Q scan is generally preferred in pregnancy given lower rates of maternal breast radiation with slight increase in fetal radiation as compared to CTPA. Whether V/Q scan or CTPA is chosen in pregnancy depends on resource availability and patient preferences.

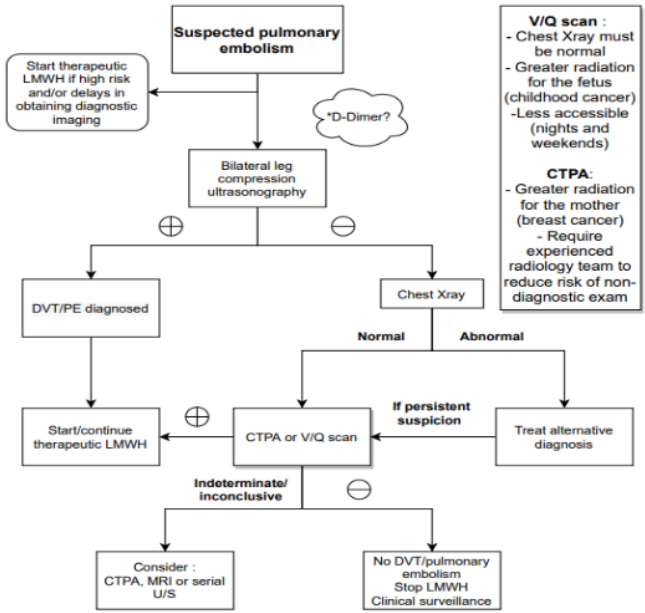

Figure 2. Diagnostic algorithm for pulmonary embolism (SOGC 2014)[1]

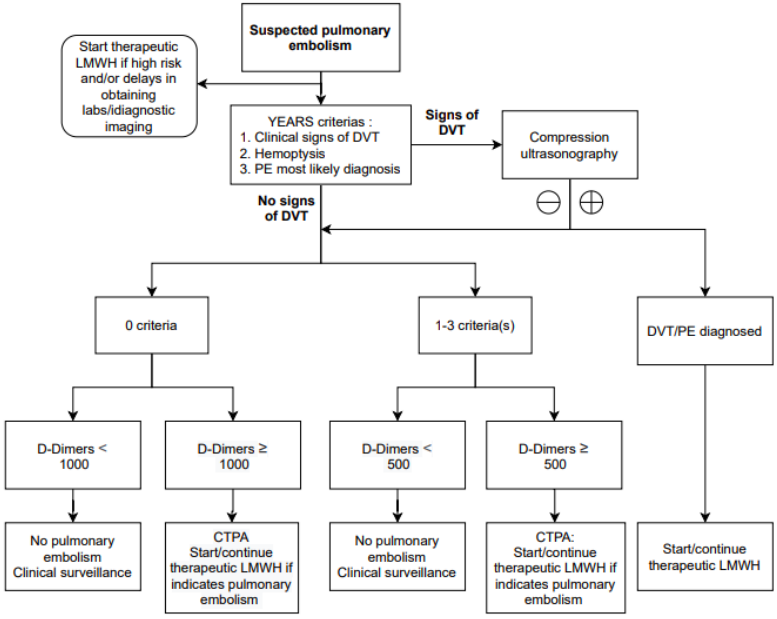

Figure 3. Pregnancy-adapted YEARS algorithm for diagnosis of pulmonary embolism in pregnant women (Thrombosis Canada 2021)[2]

Anticoagulation

Duration

- Total duration of therapy should be at least 3 months, but may be longer if VTE occurred early in pregnancy. Anticoagulation should continue for the remainder of the pregnancy and including the first 6 weeks postpartum.

Therapeutic options

- Antepartum
    - LMWH is the anticoagulant of choice as it does not cross the placenta.
    - Warfarin should be avoided for the treatment of VTE because of the fetal risks: exposure between 6-9 weeks gestation is associated with a 5% risk of

"warfarin embryopathy", including midface hypoplasia, short proximal limbs, short phalanges. Use only if patient refuses LMWH, or if benefits outweigh risk (i.e., sometimes used in patients with mechanical heart valves, but only in the second trimester; LMWH in first and third trimester).
    - DOACs are contraindicated in pregnancy as studies showed major birth defects potentially related to DOAC exposure.
    - If there is an absolute contraindication to anticoagulation, temporary IVC filters can be considered. Similarly, if VTE occurs very late in pregnancy, or when the delivery is imminent (i.e., within 2 weeks of delivery), an IVC filter should be strongly considered.
    - Thrombolytic therapy needs to be considered in cases of massive pulmonary embolism and hemodynamic compromise, as it may be lifesaving. It is relatively contraindicated for 10 days postpartum, but has been used successfully as soon as 1 hour following vaginal delivery, and 10 hours following C-section. Eliminated in 24h.

- Postpartum
    - Breastfeeding: LMWH or warfarin
    - No breastfeeding: LMWH, warfarin, or DOACs

<u>Peripartum</u>

- Those on therapeutic anticoagulation should have a planned delivery via induction vaginal delivery or scheduled C-section (mode of delivery decided by the obstetrician for obstetric indications).
- Patients should be instructed to stop anticoagulant and present to hospital whenever contractions occur.

Table 2 - Anticoagulation management during labor/delivery and postpartum (Society for Obstetric Anesthesia and Perinatology 2018)[4]

Anticoagulant	Peripartum	Postpartum
Therapeutic LMWH	Last dose ≥24h before neuraxial procedure	If hemostasis achieved: Consider prophylaxis ≥8-12h postpartum Resume therapeutic 24-48h postpartum *Liaise with obstetric team to ensure hemostasis
Therapeutic IV heparin	Discontinue ≥6h with normal aPTT before neuraxial procedure	
Prophylactic UFH	Last dose 4-6h with normal aPTT before neuraxial procedure	If hemostasis achieved: ≥4h post catheter removal ≥6h post vaginal delivery ≥8-12h post C-section
Prophylactic LMWH	Last dose ≥12h before neuraxial procedure	

Thromboprophylaxis

Table 3 - Thromboprophylaxis indications in pregnancy (Thrombosis Canada 2020)[5]

History of VTE	Antepartum (In pregnancy)	Postpartum 6 weeks
Unprovoked VTE	Yes	Yes
Estrogen-related VTE (eg. OCP, previous pregnancy VTE)	Yes	Yes
Provoked non-estrogen VTE (eg. hip fracture)	No	Yes
High risk thrombophilia (homozygous factor V Leiden, homozygous prothrombin gene mutation, antithrombin III deficiency, compound thrombophilia)	Yes	Yes
Protein S/C deficiency	No	If family history: Yes If no family history: No
Low risk thrombophilia (heterozygous factor V Leiden, heterozygous prothrombin mutation)	No	No

- The need for prophylaxis in patients undergoing C-section remains controversial, and there are no randomized studies in this patient population.
- Thrombosis Canada[5] recommends postpartum thromboprophylaxis in women with at least one of the following additional risk factors:
    - Preeeclampsia with IUGR
    - Antepartum bedrest ≥7 days
    - Postpartum hemorrhage >1L requiring surgery
    - Medical conditions (heart disease, SLE, sick cell disease, cancer, inflammatory bowel disease)
    - Previous VTE
    - High risk thrombophilia (homozygous factor V Leiden, homozygous prothrombin gene mutation, antithrombin III deficiency)
    - Transfusion

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29. SURGERY IN OLDER ADULTS

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Older adults (age 65+) undergoing surgery face additional risk of postoperative complications and prolonged recovery. For this reason, additional consideration of geriatric contributors to risk (frailty, comorbidity, psychological conditions, and cognition), and goal directed therapy are needed to inform shared decision making.[1-5]

Assessing Capacity

Assess capacity for decision making. If patient is deemed not capable, identify and discuss surgical intervention goals with substitute decision maker (SDM), involving patient as appropriate given ability to participate.[6]

Defining Treatment Goals

Discuss treatment goals including[2]:

- Anticipated outcome of surgery: cure, quality of life
- Goals should be taken in context of overall life expectancy and life expectancy from surgery
- Document Advanced Care Directives, code status, and SDM

Preoperative: Assessing and Mitigating Risk[2,3]

As with younger adults, the goal of preoperative assessment is to identify risk factors to inform decision making as well as identify potentially reversible risk factors to provide optimization preoperatively. Among older adults, a 2018 meta-analysis found impaired cognition, frailty, depression, and smoking were associated with increased risk of postoperative complications.[7]

Assessment of the following is recommended by Geriatric and Surgical Perioperative management guidelines to inform on and mitigate risk:

<u>Comorbidities:</u>

1. Multi-morbidity: Consider Charlson Comorbidity Index as measure of overall comorbidity

- Ensure comorbidities are appropriately managed and stable prior to elective surgery.

2. Cardiac Risk: As per ACC/AHA. See Chapter 3.

3. Pulmonary Risk: See Chapter 12. Even without pulmonary disease, older adults are at higher risk for aspiration, atelectasis, and other pulmonary complications.

Recommendations:

- Postoperative incentive spirometry
- Individualized recommendations based on assessment of cardiac, pulmonary risk and comorbidities

Cognition and Mood:

4. Cognition: Preoperative screening is strongly recommended
    - History from patient and informants to document baseline cognition, if available
    - Cognitive screen such as the Mini-Cog

Table 1 - Mini-Cog[8] https://mini-cog.com

3 Word Registration "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember." Banana, Sunrise, Chair Maximum 3 repetitions	No points
Clock Draw Provide a circle. "Please draw a clock with all of the numbers" after complete "Set the time to 10 past 11" 1 point for numbers 1 point for hand placement	/2
Recall. "Please tell me the words I asked you to remember" 1 point for each word recalled without cueing	/3
A score <3 is a positive screen indicating need for further assessment	

5. Delirium Risk: (see Chapter 19)

6. Depression: Consider PHQ2 screen

Table 2 - PHQ2[2]

ASK THE PATIENT THE FOLLOWING QUESTIONS:
1. "In the past 12 months, have you ever had a time when you felt sad, blue, depressed, or down for most of the time for at least 2 weeks?"
2. "In the past 12 months, have you ever had a time, lasting at least 2 weeks, when you didn't care about the things that you usually cared about or when you didn't enjoy the things that you usually enjoyed?"
Yes to either question is a positive screen indicating need for further assessment

Recommendations:

- Consider further assessment by primary care provider (PCP), geriatrics, or psychiatry for those who screen positive with Mini-Cog and PHQ2 (or consider further screening with MMSE, MoCA, PHQ9)
- Delirium prevention (see Chapter 19)
- Leverage social supports, encourage families/supports to attend visits, visit postoperatively and engage in the surgical process along with older adult if possible

Function:

7. Falls: "Have you fallen in the past year"

8. Physical Function:

- ADL and iADL function (short screen Table 3)
- Use of mobility aid
- Consider chair rise, gait assessment, and Timed-Up and Go test

Table 3 - Short Simple Screening Test for Functional Assessment[2]

ASK THE PATIENT THE FOLLOWING QUESTIONS:
1. "Can you get out of bed or chair yourself?" 2. "Can you dress and bathe yourself?" 3. "Can you make your own meals?" 4. "Can you do your own shopping?"
If NO to any of these questions, more in-depth evaluation should be performed, including full screening of activities of daily living and instrumental activities of daily living.

9. Frailty: Measure of overall vulnerability

- Rockwood clinical frailty[9] (Appendix A, end of chapter)
- Frailty Screen: Frail Non-Disabled Survey and Clinical Frailty Scale, modified Fried score

10. Supports:

- "Who will support you after surgery?"

Recommendations:

- Consider pre-surgical OT and/or PT assessment "pre-habilitation"
- Consider referral for comprehensive falls assessment
- Leverage family support

Medications and Substances:

11. Substance Abuse:
    - Alcohol: CAGE questionnaire, consider the low-risk alcohol drinking guidelines for older adults (no more than 5 standard drinks per week for women, 7 for men)[10]
    - Smoking

12. Medication Review[11]

Recommendations:
- Counsel for smoking cessation prior to elective surgery
- Start thiamine 50-100mg daily for individuals exceeding recommended alcohol intake and plan for inpatient management
- Discontinue unnecessary medications with particular attention to risk for withdrawal, falls risk, delirium risk (see 2019 Updated Beers Criteria)
    - Taper benzodiazepine, non-benzodiazipine sedative hypnotics
    - Discontinue anticholinergics (diphenhydramine, dimenhydrinate)
- Continue essential medications
- Provide counseling around management of antihypertensives, anticoagulation (See Chapters 4, 5 and16)

Nutrition and Swallowing:

13. Malnutrition:
    - Screen for malnutrition by measuring weight, height, albumin and asking about unintentional weight loss
    - Patients are at high nutritional risk if:
      (1) body mass index (BMI) < 18.5 kg/m2
      (2) serum albumin < 3.0 g/dL (with no evidence of hepatic or renal dysfunction)
      (3) unintentional weight loss > 10-15% within six months

14. Swallowing:
    - Screen all patients by asking about coughing or choking with eating or drinking

Recommendations:
- Formal SLP assessment pre-op for all who screen positive
- Dietician assessment for all patients at high nutritional risk

- Consider perioperative nutritional supplementation

Palliative Care Referral

15. Palliative Care:
    - "Would I be surprised if the patient in question were to die in the next 12 months, even if surgery is performed?

Recommendation:
- Consider referral to palliative care if answer is "No"

Preoperative: Estimating Risk

Consider using a risk prediction tool such as ACS NSQIP surgical risk calculator: https://riskcalculator.facs.org/RiskCalculator/ to inform shared decision making.[12]

Consider providing a question prompt list to patient/family prior to appointment to encourage thoughtful discussion.[5]

Perioperative Recommendations[2]

Immediately Preoperative:

- Confirm goals of care, code status, and SDM
- Consider shortened fluid fast (clear fluids up to 2 hours before anesthesia)
- Best practices re: antibiotics and VTE prophylaxis
- Medication review: check that essential medications have been taken and non-essential medications held

Intraoperative considerations:

These primarily lie within the domain of surgery and anesthesia; however, one may wish to recommend the following for consideration:

- Consider regional anesthesia
- Multimodal pain management with minimization of benzodiazepines
- Additional considerations for those with high risk of delirium (Chapter 19)

Postoperative:

1. Cognition
    - Monitor for and treat delirium

- Routine delirium prevention: Remove foley, ensure devices (hearing aids, glasses, dentures) are accessible. (See Chapter 19)

2. Pain
    - Monitor pain
    - Multimodal individualized pain management: standing acetaminophen in addition to low dose opioid, consider COX2 inhibitor in select patients, consider regional anesthesia

3. Function
    - Early mobilization and/or PT assessment
    - Consider scheduled toileting
    - Resume diet as early as possible, consider SLP and dietician, and/or supplementation if indicated
    - Minimize tethers (bolus IVF/feeds whenever possible, remove foley, IV to saline lock)
    - Engage family and multidisciplinary team

4. Prevent Complications
    - Remove catheter
    - Chest physiotherapy and incentive spirometry
    - Aspiration precautions
    - Monitor for pressure ulcers

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Appendix A: Rockwood Clinical Frailty Score

Clinical Frailty Scale*

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 Managing Well – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 Vulnerable – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – **Completely dependent for personal care,** from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
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DALHOUSIE UNIVERSITY
Inspiring Minds

30. CANCELLING SURGERY

Authors: Ashley Jensen MD MPA, Anna Goulding MD FRCPC

Introduction and General Approach

Delaying or cancelling surgery has serious implications for patients, families, as well as surgical teams and hospital resources. However, when there are acute medical problems that need to be addressed prior to surgery or the risks of a proposed surgery outweigh benefits it is appropriate to delay or even cancel surgery.

Emergency Surgery

For emergency surgery for an immediate life or limb threatening condition do not delay surgery for risk assessment or testing. Treat any unstable conditions such as arrhythmias, heart failure or infection.

Urgent and Semi-Urgent Surgery

For urgent (eg. bowel obstruction, hip fracture) or semi-urgent (e.g. resection of cancer that has potential to metastasize or grow) surgery,[1] reasons to consider delaying include unstable cardiac conditions, suspected undiagnosed severe pulmonary HTN or severe obstructive cardiac disease, acute stroke or infection. In the case of semi-urgent surgery for patients with fresh cardiac stents, delay for at least one month post-PCI.

Elective Surgery

For elective surgeries (e.g. knee arthroscopy for osteoarthritis) you may delay surgery for recent cardiac stents (at least 3 months after PCI wherever possible) and for recent VTE, delay surgery for at least 3 months of anticoagulation.[2]

Communicating your recommendation to delay or cancel surgery

Once you have made the decision with your patient that surgery needs to be delayed or cancelled, clearly communicate this with the surgical and anesthesia team and any involved specialists (e.g. the patient's oncologist). Clearly state the reasons for the delay or cancellation, as well as the steps that need to be completed prior to proceeding to surgery and a proposed timeline. This information should also be clearly documented in your consultation note. In addition, plan the follow-up for the patient and make any referrals as appropriate.

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31. Perioperative COVID-19 Infection

Authors: Ian Downie MD, Yayi Huang, MD FRCPC

Introduction

Due to the dynamic nature of the COVID-19 pandemic, much of the management discussed in this chapter may require reassessment by the reader to see if the information is applicable to their current clinical situation. The continued emergence of SARS-CoV-2 variants, changing levels of population immunity and new evidence-based therapeutics may make previous literature less applicable as the pandemic progresses. In this chapter we aim to provide a practical, evidence-based overview of COVID-19 perioperative management that respects the evolving virus and ongoing study of it.

Active COVID-19 Infection

Management of COVID-19 Infection

The therapeutic options available to treat perioperative COVID-19 infections are the same as in the non-perioperative setting. The Ontario COVID-19 Science Advisory Table maintains regularly updated clinical practice guidelines for treatment of COVID-19 infection in adults. This resource can be accessed via the QR code below:

The perioperative patient may influence the decision to use certain therapeutics. For example, full-dose anticoagulation may pose higher

risk of bleeding in a postoperative patient. For patients undergoing surgery to treat an infection, immunosuppressing medications used to treat COVID-19 may increase the risk of developing a more severe infection. Steroids may impair wound healing. The risk/benefit ratio must be weighed in each individual and incorporate the perspective of the surgical team and patient.

Deciding Whether to Recommend Postponement of Surgery

In a large international cohort study conducted by the *COVIDSurg Collaborative* group, patients with perioperative COVID-19 infection were found to have a **high rate of mortality and pulmonary complications**, especially for patients older than 70 years old, with extensive comorbidities (ASA class 3-5), undergoing cancer surgery or undergoing emergency/major surgery.[1] A planned sub-study of the this cohort found that perioperative COVID-19 infection was independently associated with increased incidence of postoperative venous thromboembolism.[2] An American retrospective study of patients with perioperative COVID-19 infection similarly found a higher risk of perioperative complications (pneumonia, respiratory failure, pulmonary embolism, sepsis) compared to a control group.[3] This study only included patients undergoing major elective surgery whereas the *COVIDSurg Collaborative* study included patients undergoing emergent, major, and minor procedures.

Given the apparent increased risk associated with undergoing surgery with an active COVID-19 infection, it may be beneficial to **delay non-emergent surgery**. Several factors must be considered and discussion with the patient and surgical team is crucial. The urgency and the extent (major vs. minor procedure) of surgery should be incorporated into the decision.

COVID-19 Infection Preceding Surgery

Timing of Surgery following COVID-19 Infection

Large cohort studies have found that patients who underwent surgery with a recent COVID-19 infection, had an increased risk of perioperative mortality and VTE for up to seven weeks from time of COVID-19 diagnosis.[2,4] Furthermore, patients *with ongoing symptoms* related to their COVID-19 infection had increased rate of mortality even if undergoing surgery after more than seven weeks from diagnosis.[4] Another study found **increased risk of perioperative complications** for patients undergoing surgery **up to 8 weeks after COVID-19 diagnosis.**[3]

Several perioperative physician groups have recommend delaying surgery after COVID-19 infection to minimize perioperative risk.[5,6,7]

There may instances where it may not be optimal for elective surgery to be postponed, such as patients with cancer requiring surgical treatment. The risks and benefits of proceeding with surgery again must be weighed with appropriate stakeholders to decide on surgical timing. In one cohort study of cancer patients with minimally symptomatic COVID-19 infection undergoing low-risk elective surgery after a minimum of 20 days from COVID-19 infection, there was not an increased rate of complications.[8]

Preoperative Evaluation of a Patient with Previous COVID-19 Infection

Following COVID-19 infection many patients continue to experience a wide variety of symptoms and sequalae from their illness. **Post-acute sequelae of SARS-CoV-2 infection (PASC)** has not been studied extensively in the perioperative setting but there have been reviews on the subject in the literature.[9] Given the known increased risk of mortality in patients with persistent symptoms even seven weeks after diagnosis, it is prudent to investigate patients with symptoms of PASC appropriately.

Cardiac

There are several cardiac conditions associated with PASC including prolonged tachycardia, POTS, orthostatic intolerance, heart failure, arrythmia, and myocardial infarction.[10,11] Given the association of these conditions with a previous COVID-19 infection, symptoms such as chest pain or palpations should be taken seriously and evaluated with further testing as per clinician judgement.

Respiratory

Persistent respiratory disease either radiographically or on pulmonary function testing appears to correlate with severity of illness during acute COVID-19 infection.[12] In an observational prospective cohort study of patients 100 days post-diagnosis of COVID-19, the most common persistent radiographic abnormalities were ground glass opacities with reticulation and the most common pulmonary function test (PFT) abnormalities were decreases in FEV1 or FVC, DLCO, or TLC.[13] 37% of patients in this cohort had ongoing mild-moderate hypoxia based on blood gas measurement.[13] It should be noted that there seems to be weak correlation between the severity of radiographic findings and pulmonary function abnormalities.[13] In the largest-to-date longitudinal cohort study that followed patients after COVID-19 infection, 22-56%

(depending on illness severity) of patients had persistent pulmonary abnormalities[12] at six months post-infection. In the same cohort at one year, a large proportion of patients continued to have radiographic or pulmonary function abnormalities, especially in those who had severe COVID-19 infections (requiring high flow oxygen delivery or intubation).[14]

Given these findings, clinicians may consider assessing for persistent respiratory disease in patients with previous COVID-19 who have persistent symptoms or in those who required high flow oxygen or mechanical ventilation during the acute infection. At a minimum patients should have their oxygen saturation assessed via pulse oximetry to detect ongoing hypoxemia. Imaging and PFTs can be considered depending on the clinical scenario. It is unclear the specific risk perioperatively related to post-COVID-19 radiographic or PFT abnormalities. One should remember that radiographic findings may not correlate with PFT testing. Unfortunately, there is no current evidence-based therapies for chronic respiratory changes following COVID-19 infection and it is also unclear whether patients with persistent abnormalities will further recover further after more than one-year post-infection.

Hematologic/Vascular

As explained above, the increased risk of thromboembolism persists following acute COVID-19 infection for up to seven weeks and so this should be factored into timing of surgery. There is no evidence-based guidelines to suggest management of VTE prophylaxis in patients requiring surgery shortly after COVID-19 infection and no clear data to suggest whether biomarker testing is useful to predict risk of VTE. An expert-panel survey did suggest consideration of intermediate dose VTE prophylaxis dosing or the addition mechanical thromboprophylaxis to standard chemical DVT prophylaxis for those requiring surgery within one month of COVID-19 infection.[15] Consider involving a local thrombosis expert in the care of patients requiring surgery shortly after COVID-19 infection.

Central Nervous System

New cognitive dysfunction has been associated with COVID-19 infection in both mild and more severe cases requiring hospitalization.[16,17] Caution should be taken to avoid delirium perioperatively in those with persistent impaired cognition.

Renal

In a retrospective observation study of patients admitted to hospital with COVID-19, 46% suffered an AKI and 35% of those who survived to discharge following COVID-19 with AKI did not recovery to their renal baseline.[18] For patients being assessed perioperatively it may be helpful to retest creatinine and electrolytes if these labs were not repeated after an admission for COVID-19 with an associated AKI.

Medication

One should assess whether a COVID-19 recovered patient is on anticoagulation or required an extended course of steroid therapy as this may affect preoperative medication planning.

Take Home Points

- Knowledge surrounding perioperative management of patients who have been infected with Sars-CoV-2 is evolving along with the pandemic.
- The current treatment for COVID-19 infections perioperatively is similar to the non-perioperative setting.
    - As of 2022, the Ontario COVID-19 Science Advisory Table produces up-to-date therapeutic guidelines for management of COVID-19.
- The risk of perioperative adverse events is increased compared to baseline in patients with active or recent (less than seven weeks from diagnosis) COVID-19 infection.
    - Therefore, there should be consideration for delay of non-emergent surgery.
- Even after seven weeks post-COVID-19 infection, if patients have ongoing symptoms (suggestive of PASC) they have an increased risk of perioperative adverse events.
    - Given this, ongoing symptoms following COVID-19 infection should be taken seriously and investigated as needed by the consulting clinician.

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32. Top 10 Trials in Perioperative Medicine

Authors: Leora Branfield Day MD FRCPC, Ariel Lefkowitz MD CM MEd FRCPC

1. BRIDGE

Bottom Line: In patients with low- and intermediate-risk atrial fibrillation who require interruption of warfarin for an elective procedure or operation, periprocedural bridging anticoagulation with LMWH does not reduce the risk of arterial thromboembolism but increases the risk of major bleeding.

Population and Methods: This multicentre double-blind placebo-controlled trial included patients older than 18 years old with atrial fibrillation or flutter and CHADS2 score ≥1 on warfarin therapy for ≥3 months. They were randomized to bridging anticoagulation with LMWH or placebo after perioperative interruption of warfarin therapy 5 days before an elective procedure or operation. The primary outcomes up to 30 days post-procedure were arterial thromboembolism (systemic embolism, stroke or transient ischemic attack) and major bleeding.

Results: 1884 patients were enrolled and randomized with a mean CHADS2 score of 2.3. Discontinuing warfarin without bridging anticoagulation was noninferior to bridging anticoagulation for the prevention of arterial thromboembolism (0.4% vs 0.3% respectively, P = 0.01 for noninferiority, P = 0.72 for superiority). Those in the placebo group had significantly lower rates of major bleeding compared to the bridging group (1.3% vs 3.2%).

Limitations and Critiques: Only 3% of patients had CHADS2 scores of 5-6, so these results may not apply to patients with a high CHADS2 score. These findings also do not pertain to those on DOACs.

Ramifications for practice: Based on the results of the BRIDGE trial, in patients with atrial fibrillation or flutter with CHADS2 score of 4 or less, it is safe to forego heparin bridging during interruption of anticoagulation for elective procedures.

Douketis JD, et al. "Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation". *The New England Journal of Medicine*. 2015. 373(9):823-33.

2. Measurement of Exercise Tolerance before Surgery (METS)

Bottom Line: In patients with ≥ 1 cardiac risk factors undergoing major noncardiac surgery, subjective assessment of functional capacity was not effective in identifying those at high risk for perioperative death or MI, but DASI scores (using the Duke Activity Status Index questionnaire) were predictive.

Population and Methods: This prospective cohort study conducted at 25 centres in 4 countries included those ≥40 years old with at least one cardiac risk factor going for major noncardiac surgery. All participants had their functional capacity subjectively assessed by the anesthesiologist seeing them in pre-op clinic, recording their assessment of their metabolic equivalents as poor (<4), moderate (4-10), or good (>10). Participants also completed the DASI questionnaire, underwent cardiopulmonary exercise testing (CPET), and had their pre-op NT-BNP and post-op troponins and creatinine measured. The primary outcome was death or MI within 30 days of surgery.

Results: 1401 patients were included in the cohort. Subjective assessment of functional capacity was not associated with risk of perioperative death or MI. In contrast, DASI scores had significant associations with risk of death or MI by 30 days post-op. Higher NT-BNP concentrations were also predictive of death or MI by 30 days. CPET was not helpful in predicting post-op cardiac complications, but peak oxygen consumption predicted in-hospital moderate to severe complications. NT-BNP and DASI scores only had a slight-to-fair correlation with one another.

Limitations and Critiques: Events occurred at a rate lower than expected, raising some doubts about adequate powering. The authors' decision to categorize patients whose subjective functional capacity could not be ascertained as "poor functional capacity" has been critiqued as well.

Ramifications for Clinical Practice: Subjective assessment of patients' preoperative functional capacity using metabolic equivalents is not predictive of a poor outcome as per this cohort trial, but the DASI questionnaire and measurement of NT-BNP may help estimate risk of death or postoperative MI. Furthermore, since the DASI questionnaire and NT-BNP measurements did not correlate with each other, authors hypothesized that using these measures together may enhance predictive capacity.

Wijeysundera DN, et al. "Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study". *Lancet*. 2018. 391(10140):2631-2640.

3. POISE-2: Aspirin in Patients undergoing Noncardiac Surgery

Bottom Line: In patients at risk of vascular complications who are undergoing noncardiac surgery, perioperative aspirin does not reduce the risk of mortality or non-fatal MI, but does increase the risk of perioperative bleeding.

Population and Methods: This double-blinded study randomized patients older than 45 years old at significant risk for perioperative vascular complications (e.g. prior CAD, CVA, PAD, or multiple risk factors) who were undergoing major noncardiac surgery. They were required not to take aspirin in the 72 hours prior to surgery. Patients were randomized to aspirin (200 mg x1 day then 100 mg PO daily) or placebo to be taken immediately before surgery and postoperatively. They were stratified according to whether they were already taking aspirin (continuation stratum) or not taking aspirin prior (initiation stratum). The study was conducted at 135 centres in 23 countries, and follow-up extended to 30 days.

Results: 10,010 patients were randomized. There was no significant difference in the primary outcome of all-cause mortality or non-fatal MI (7.0% in the aspirin group and 7.1% in the placebo group). However, patients in the aspirin group had more major bleeding events (4.6% vs 3.8%).

Limitations and Critiques: Only 4.7% of randomized patients had a history of PCI, so it is unclear whether these results apply to such patients. In addition, some have argued that the study was underpowered to detect a difference in rate of MI between the groups, which might have shown an important difference.

Ramifications for Clinical Practice: Based on POISE-2 ASA, clinicians should not initiate ASA in patients undergoing noncardiac surgery who are at risk for vascular complications. Indeed, they can safely hold ASA perioperatively in those already taking it, as POISE-2 ASA suggests it is safe to do so.

Devereaux PJ, et al. "Aspirin in patients undergoing noncardiac surgery". *The New England Journal of Medicine*. 2014. 370(16):1494-1503.

4. Preoperative N-terminal Pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery

Bottom Line: Preoperative NT-proBNP is strongly associated with postoperative cardiac complications within 30 days after noncardiac surgery and improves cardiac risk prediction when used together with the RCRI score.

Population and Methods: This prospective cohort study was conducted in 16 hospitals across 9 countries and enrolled patients ≥45 years old undergoing inpatient noncardiac surgery. Patients had NT-proBNP levels measured before surgery and then had troponin T levels measured daily for up to 3 days after surgery. Study personnel and health care providers were blinded to the NT-proBNP measurements. Troponin was measured 6-12 hours after surgery and daily for 3 days after surgery. The primary outcome was the composite of vascular death and MINS at 30 days.

Results: 10,402 patients were included in this study. Preoperative NT-proBNP values were independently associated with the composite outcome of vascular death or MINS at 30 days after surgery. The authors identified several thresholds for NT-proBNP where, at each increasing threshold, the risk of postoperative cardiac complications increased (<100 pg/mL, incidence 0.3%; 100-200 pg/mL, incidence 0.7%; 200-1500 pg/mL, incidence 1.4%; and ≥1500 pg/mL, incidence 4.0%). Adding the NT-proBNP to the RCRI score helped with risk prediction in 25% of patients.

Limitations and Critiques: This study may have missed MINS events in patients without ischemic symptoms after day 3. The NT-proBNP thresholds derived from this cohort for elevated major cardiac events and death also were not externally validated.

Ramifications for Clinical Practice: NT-proBNP is a cheap and simple intervention that can be used preoperatively to identify patients at risk for postoperative cardiac events after noncardiac surgery. Accordingly, the CCS guidelines recommend that a NT-proBNP/BNP should be ordered for patients undergoing elective noncardiac surgery requiring an overnight admission who are at risk for cardiovascular disease (age ≥65 years, RCRI ≥1, or age 45-64 years with known significant cardiovascular disease).

Duceppe E, et al. "Preoperative N-terminal Pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery: A cohort study". *Ann Intern Med*. 2020. 172(2):96-104.

5. Association of Preoperative Patient Frailty and Operative Stress With Postoperative Mortality

Bottom Line: In patients who underwent noncardiac surgery at Veterans Health Administration Hospitals, patients with high frailty scores who underwent low or moderate stress surgical procedures had very high rates of mortality.

Population and Methods: This retrospective cohort study was conducted using four years of data on noncardiac surgical cases from the Veterans Affairs Surgical Quality Improvement Program (VASQIP), 2010-2014, including those for whom data was available on whether or not the patient was alive at one year post-op. Each surgical case was given an Operative Stress Score (OSS, a score of 1-5 developed by the authors for this study); an example of a low risk procedure with OSS 1 is cystoscopy, whereas a laparoscopic cholecystectomy was considered a moderate stress surgery. Each patient undergoing surgery was given a frailty score using the Risk Analysis Index score (RAI, a validated tool that uses 14 variables, calculated 0-81, where higher numbers indicate greater frailty). The RAI score was used to divide the cohort into robust (RAI ≤ 20), frail (30-39), and very frail (≥ 40).

Results: 432 731 patients who underwent surgery during the cohort time frame were included in the study. Higher RAI correlated with higher mortality at 30 days, 90 days, and 180 days post-op. In robust patients, mortality rose with higher OSS, but mortality was generally low, 0.22% at 90 days post-op for OSS 1-2, and only 1-3% even for OSS 4 (high stress surgery) at 180 days post-op. In frail patients, mortality was high even for low stress procedures, 4-5% for OSS 1-2 and 10-13% for OSS 3-4 at 90 days post-op. In very frail patients, mortality at 30 days was 10% and at 90 days post-op was 22-23% for OSS 1-2, and for OSS 3-4, mortality was 18-22% at 30 days, rising to 34-35% at 90 days and 42-43% at 180 days.

Limitations and Critiques: Use of a sample of veterans limited the generalizability, since the population was 92.8% male. Limiting the sample to those undergoing surgery does not allow us to make conclusions on whether those foregoing surgery had higher, lower, or equal mortality compared to those undergoing surgery. As mortality was the only outcome measured, conclusions cannot be made about quality of life, level of function, or other patient-centred outcomes. Finally, the OSS was not validated prior to this study, which casts some doubt on the way procedures were stratified.

Ramifications for Clinical Practice: Patients with frailty may have a significantly elevated mortality after even minor surgeries or procedures, such as lap chole or cystoscopy, which may inform counseling around the risks and benefits of such procedures. The OSS may be helpful in grading the stress of surgeries, and the RAI is an effective tool to identify and quantify frailty in older adults.

Shinall MC, et al. “Association of preoperative patient frailty and operative stress with postoperative mortality”. *JAMA Surgery*. 2020. 155(1):e194620.

6. Are Incentive Spirometry, Intermittent Positive Pressure Breathing, and Deep Breathing Exercises Effective in the Prevention of Postoperative Pulmonary Complications After Upper Abdominal Surgery?

Bottom Line: In patients undergoing upper abdominal surgery, deep breathing exercises and incentive spirometry both were more effective than no physical therapy at decreasing pulmonary complications postoperatively.

Population and Methods: This meta-analysis conducted a database search for primary and review articles published between 1966 and 1992 that contained randomized control trial data comparing routine care with one or more of incentive spirometry (IS), deep breathing exercises (DBEX), and intermittent positive pressure breathing (IPPB) in the postoperative period after upper abdominal surgery. The outcome of interest was pulmonary complications, but was not uniformly defined across studies. Statistical analysis was performed to analyze for common odds ratio (COR), calculated using the uncorrected Mantel-Haenszel test. First, an overall analysis of any of the above interventions vs. control was conducted, then the studies were separated by intervention and re-analyzed.

Results: After searching the literature, 14 RCT studies were included in analysis. The overall COR between any of the studied treatments and control was not statistically significant for preventing pulmonary complications. Two studies were used in analyzing IS vs control (combined N = 212), and found a COR of 0.44 (95% CI = 0.18-0.99). Four studies were used in analyzing DBEX vs control (combined N = 564), and found a COR of 0.43 (95% CI = 0.27-0.63). In comparing different intervention modalities head-to-head, no intervention was found to be statistically significantly more effective than another.

Limitations and Critiques: Outcome measures between studies were quite heterogeneous, with measures of discerning pulmonary complications varying between chest X-rays, physical exam, PFTs, and ABGs; these outcomes were not clearly clinically significant, as it was not clear whether atelectasis or pulmonary infiltrate seen on CXR affected length of stay, trajectory of recovery, or mortality. Studies were judged by the authors to have overall low methodological rigour, with some not explicitly stating the method of randomization or patient adherence to study protocol.

Ramifications for Clinical Practice: Deep breathing exercises and incentive spirometry reduce the risk of pulmonary complications. Deep breathing exercises are easy and do not require equipment, and should be recommended to all patients undergoing surgery whenever possible.

Thomas, JA, & McIntosh, JM. “Are incentive spirometry, intermittent positive pressure breathing, and deep breathing exercises effective in the prevention of postoperative pulmonary complications after upper abdominal surgery? A systematic overview and meta-analysis”. *Physical Therapy*. 1994. 74(1):3–10.

7. Association of New-Onset Atrial Fibrillation After Noncardiac Surgery With Subsequent Stroke and Transient Ischemic Attack

Bottom Line: In patients undergoing noncardiac surgery, new onset atrial fibrillation (AF) was associated with a significantly increased risk of stroke or TIA compared to no AF.

Population and Methods: This retrospective cohort study involved patients in Minnesota (median age 75 year) who had their first-ever documented episode of AF within 30 days after undergoing noncardiac surgery. 452 patients with postoperative AF after noncardiac surgery were matched 1:1 on age, year of surgery, type of surgery, and sex, to patients with no diagnosis of AF in the first 30 days after surgery. The primary outcome was TIA or ischemic stroke. Secondary outcomes were all-cause mortality, cardiovascular mortality and subsequent documented AF. Cumulative incidence plots were used to visualize differences in occurrence of primary and secondary outcomes between those with and without postoperative AF. Cox proportional hazard regression models determined absolute risk differences.

Results: Over a median follow up time of 5.4 years, patients with postoperative AF had a significantly higher risk of stroke or TIAs compared to patients without postoperative AF (HR = 2.69). There was significantly higher risk of subsequent documented atrial fibrillation and all-cause death in patients with postoperative AF compared to those without.

Limitations and Critiques: Generalizability of these findings is limited as the study population was predominantly Caucasian. Investigators also were not able to classify strokes as cardioembolic vs being due to other causes, and the number and duration of subsequent AF episodes and whether they were persistent or paroxysmal were not known. The use of observational data means that residual confounding was possible despite statistical adjustments and matching of patient cohorts. Finally, as the study was not blinded, a finding of postoperative AF may have led to increased monitoring and therefore a bias towards greater frequency of detection of subsequent AF episodes in this group.

Ramifications for Clinical Practice: Postoperative AF after noncardiac surgery is not a transient, self-limited event and is associated with increased risk of arterial thromboembolism. However, it is not clear how these findings should impact clinical practice, and whether anticoagulation therapy is indicated in this population.

Siontis KC, Gersh BJ, Weston SA, et al. “Association of New-Onset Atrial Fibrillation After Noncardiac Surgery With Subsequent Stroke and Transient Ischemic Attack”. *JAMA*. 2020;324(9):871–878.

8. Effect of the Tailored, Family-Involved HELP on Postoperative Delirium and Function in Older Adults

Bottom Line: In older adults undergoing elective surgery, the use of a tailored, family-involved delirium prevention program decreased the risk of postoperative delirium.

Population and Methods: This single-blinded study randomized patients older than 70 years old who were admitted to 6 surgical wards in a hospital in West China. They were eligible to participate if they were scheduled for an elective surgery, had an estimated length of stay of at least 2 days, and were able to reliably complete cognitive testing. The primary outcome was postoperative delirium within 7 days of surgery, measured using the CAM criteria. The intervention was the tailored Family-Involved Hospital Elder Life Program (t-HELP), which was administered to the intervention group for 7 days post-op or until hospital discharge, and was comprised of 11 protocols, including:

- Regular communication of orientation
- The provision of cognitive stimulating activities
- Early mobilization protocol
- Pain management protocol with complementary therapies like backrubs or hand massage
- Sleep enhancement protocol with relaxation strategies
- Nutrition assistance and aspiration prevention protocol
- Fluid repletion and constipation protocols
- Vision and hearing enhancement protocols
- Polypharmacy mitigation protocol

Results: 281 patients were randomized. There was a significantly lower rate of postoperative delirium in the t-HELP group (4 cases, 2.6%, vs 25 cases, or 19.4%, in the control group), NNT 5.9. Secondary outcomes also showed significantly less postoperative physical and cognitive decline, as well as shorter mean length of stay (12.15 vs 16.41 days).

Limitations and Critiques: Since the trial was conducted only in China, analysis must take into account differences between Chinese and Canadian hospitals (e.g. in China there are lower nurse to patient ratios and longer lengths of stay, surgical patients are generally younger and less frail due to practice patterns, and families are generally more involved). Due to the nature of the intervention, double-blinding was not possible. The primary outcome was only measured up to 7 days, which may not capture all delirium events. Finally, studying the effectiveness of a set of protocols cannot elucidate which protocols are specifically helpful.

Ramifications for Clinical Practice: Using the t-HELP and similar protocols are effective in reducing postoperative delirium for older adults undergoing surgery.

Wang, Y.-Y., et al. “Effect of the tailored, family-involved hospital elder life program on postoperative delirium and function in older adults”. *JAMA Internal Medicine*. 2020. 180(1), 17.

9. Association of Postoperative High-Sensitivity Troponin with MINS and 30-Day Mortality in Noncardiac Surgery

Bottom Line: In patients undergoing noncardiac surgery, peak postoperative high-sensitivity troponin T (hsTnT) in the first 3 days after surgery was associated with a risk of 30-day mortality even in the absence of an ischemic feature (e.g. ECG changes, ischemic symptoms).

Population and Methods: This international prospective cohort study included patients ≥45 years undergoing inpatient noncardiac surgery. Patients had a hsTnT measured at 6-12 hours after surgery and daily for up to 3 days. The primary objective was to determine the relationship between perioperative hsTnT levels and 30-day mortality and potential diagnostic criteria for myocardial injury after noncardiac surgery (MINS). A modified Mazumdar approach was used to determine hsTnT thresholds associated with death. Regression analyses were used to evaluate whether postoperative hsTnT elevations required an ischemic symptom to be associated with 30-day mortality. Patients were excluded if peak hsTnT levels were from a nonischemic etiology (e.g, chronic elevation).

Results: 21,842 participants were included and only 1.2% died within 30 days. Elevated peak postoperative hsTnT predicted higher 30-day mortality and several nonfatal cardiac outcomes. Mortality increased at higher peak hsTnT levels. An increase in hsTnT of ≥5 ng/L was also associated with an increased risk of 30-day mortality (3%). Importantly, 93% of patients with hsTnT elevations predicting increased 30-day mortality had no ischemic features. Accordingly, MINS was defined as an elevated postoperative hsTnT judged as being due to myocardial ischemia without the requirement of an ischemic feature.

Limitations and Critiques: The incidence of MINS may have been overestimated among 60% of patients who did not have a preoperative hsTnT measured. There may have been an underestimation of non-ischemic etiologies for postoperative hsTnT measurements.

Ramifications for Clinical Practice: As most patients with MINS are asymptomatic, routine troponin monitoring can help identify those with increased risk of death. Adding to previous findings from the VISION Study, these findings helps to inform CCS guidelines, which recommend measuring troponin daily for 48-72 hours in patients undergoing noncardiac surgery who have a baseline risk >5% for cardiovascular death or nonfatal MI at 30 days.

Writing Committee for the VISION Study Investigators. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA*. 2017;317(16):1642–1651

10. Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery

Bottom Line: Withholding Angiotensin-converting enzyme inhibitors (ACEi)/Angiotensin II receptor blockers (ARBs) before noncardiac surgery is associated with a lower risk of 30-day mortality and postoperative vascular events.

Population and Methods: This was a secondary analysis of 4,802 patients on baseline ACEI/ARBs in the VISION study who were ≥ 45 years of age and undergoing noncardiac surgery requiring an overnight admission. Analyses compared outcomes of patients who did not take ACEi/ARBs within 24 hours before surgery to the outcomes in those who did. Multivariate regression models evaluated the relationship between holding ACEi/ARBs and their primary composite outcome of 30-day all-cause death, MINS and stroke after noncardiac surgery. Secondary outcomes were clinically important intraoperative and postoperative hypotension (sBP < 90mmHG requiring intervention) at days 0-3.

Results: 26% of patients withheld ACEi/ARB for 24 hours before surgery. Compared to patients who continued their ACEi/ARB before surgery, these patients were less likely to suffer the primary composite outcome of 30-day all-cause death, stroke, or myocardial injury (18% adjusted RRR, NNT = 116) and less likely to suffer from intraoperative hypotension (20% adjusted RRR). When adjusted for postoperative hypotension, intraoperative hypotension was not significantly associated with vascular events and mortality (possibly due to insufficient power). However, clinically important postoperative hypotension was independently associated with a risk of vascular events and death, though did not differ between the groups. There was only a modest association between decisions to withhold ACEi/ARBs and surgical and patient characteristics, suggesting that such choices were due to clinical discretion.

Limitations and Critiques: Due to limited statistical power, the authors could not account for the effects of withholding other antihypertensives or starting new medications, and were unable to study subpopulations (e.g. patients with CHF). Renal outcomes could also not be evaluated, though previous studies have shown a lower risk of kidney injury.

Ramifications for Clinical Practice: Clinicians should recommend that patients on chronic ACEi/ARBs withhold these medications for 24 hours before surgery.

Roshanov PS, et al. "Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery: An Analysis of the Vascular events In noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort". *Anesthesiology*. 2017. 126(1):16-2

33. RATIONAL CLINICAL EXAM

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Approach to Systolic Murmurs

A murmur is characterized by intensity (grade), timing, configuration (time course), frequency (pitch), and location.

- Most common causes for mid-systolic murmurs/systolic ejection murmur are benign/innocent flow murmurs (an increase in flow rate across a normal semilunar valve) and aortic sclerosis.
- Fixed aortic valve obstruction (e.g. aortic stenosis) is distinguished from dynamic subaortic outflow tract obstruction (e.g. HOCM) by changes in the murmur with maneuvers (see AS chapter for HOCM vs. AS). HOCM and AS are generally ejection or mid-systolic murmurs.
- Early systolic murmurs: acute severe or mild chronic mitral regurgitation, primary TR with normal RV pressures, large VSD or small muscular VSD
- Late systolic murmurs: MVP, murmur of ischemic MR is frequently late systolic
- Holosystolic murmurs: MR, TR, or small VSD

Table 1 – Distinguishing features of pathologic and physiologic systolic murmur (from highest LR+ to lowest)

Sign	LR+ (Positive Likelihood Ratio)	LR- (Negative Likelihood Ratio)
Systolic thrill	12	0.73
Holosystolic murmur	8.7	0.19
Loud murmur	6.5	0.08
Plateau-shaped murmur (maintain a relatively constant intensity)	4.1	0.48
Loudest at apex	2.5	0.84
Radiation to carotid	0.91	1.0

Bottom line

- Top physical examination signs to rule in a pathologic murmur: systolic thrill, holosystolic murmur, and loud murmur. Presence of these signs can also help rule out physiologic murmurs.

Mitral regurgitation

- Best heard in the left lateral decubitus position, mitral regurgitation (MR) is a blowing, holosystolic murmur heard at the apex with radiation to the axilla (NB: if MR jet is posterolateral, it can radiate to the posterior left thorax).
- S1 is generally soft and S2 may be diminished. May have a split S2 due to aortic valve closing prematurely in severe MR.
- MR is usually louder on expiration. It can be accentuated when LV filling increases (heart failure, leg raise, supine) or arterial pressure increases (squatting, isometric hand grip).
- In patients with ruptured chordae tendinae or primary involvement of posterior mitral leaflet with prolapse or flail, the regurgitant jet is eccentric and directed anteriorly, thus can be confused aortic stenosis murmur.
- Single or multiple systolic clicks can be heard if the cause of MR is mitral valve prolapse.

Table 2 – Features of severe MR

Sign	LR
Radiation to anterior axillary line	LR+6.8 for moderate or worse MR
Known MV prolapse, absence of holosystolic or late systolic murmur (according to cardiologist)	LR- 0-0.8 for moderate or worse MR
Loudness: Grade 4 or more	LR+ 14
Loudness: Grade 3	LR+ 3.5
Loudness: Grade 0-2	LR+ 0.12

Resources

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2. Panidis IP, McAllister M, Ross J, Mintz GS. Prevalence and severity of mitral regurgitation in the mitral valve prolapse syndrome; a Doppler echocardiographic study of 80 patients.
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4. Talley, Nicholas J, and Simon O'Connor. Clinical Examination: A Systematic Guide to Physical Diagnosis. 8th Ed. Oxford: Blackwell Science, 1996. Print.
5. Harrison's Cardiovascular Medicine, 3e Ed. Joseph Loscalzo. McGraw Hill, 2016.

Approach to Aortic Stenosis

Aortic stenosis (AS) is the narrowing of the aortic valve due to bicuspid aortic valve, calcific degeneration, or rheumatic disease. Severe aortic stenosis is defined as an aortic valve area of <1.0cm^2, mean transvalvular gradient > 40mmHg, and peak jet velocity of >4m/sec. See Chapter 9 on Aortic Stenosis.

Practical tip: Effort syncope with a systolic murmur has a LR of 1.3 for AS, LR- of 0.76. Absence of syncope is not helpful (negative LR 0.76).

Prognosis and mortality:

1. Aortic stenosis and angina: 50% 5-year mortality
2. Aortic stenosis and syncope: 50% 3-year mortality
3. Aortic stenosis and dyspnea: 50% 2-year mortality

Physical Examination

- Carotid pulse: plateau/anacrotic pulse. Could have parvus (weak) et tardus (delayed) in severe AS.
- Palpation: hyperdynamic apex beat that may be displaced, +/- thrill over the aortic area.
- Auscultation: narrowly split or reversed S2, harsh mid-systolic ejection murmur, maximal over aortic area and may radiate to clavicle and carotid arteries. Loudest sitting up and in full expiration. Loudness of the murmur does not predict severity. Murmurs may be less intense in patients with superimposed HF.
- Gallavardin phenomenon: the murmur may disappear over the sternum and reappear at the apex as a holosystolic murmur, leaving a false impression that mitral regurgitation is present.

Use Table 3 to help you with identifying severe aortic stenosis on physical examination.

Table 3 – Features of moderate and severe AS (from highest LR+ to lowest).

Physical Examination Finding	LR+	LR-
Late-peaking systolic murmur	101	0.31
Delayed carotid upstroke	9.2	0.56
Murmur radiates to the right carotid artery	8.1	0.29

Decreased intensity or absent S2	7.5	0.5
Brachioradial delay	6.8	0
Murmur over right clavicle	3	0.1
Any systolic murmur	2.6	0
S4	2.5	0.26
Diminished carotid pulse	2	0.64

Aortic stenosis vs. aortic sclerosis

- Lack of radiation of murmur to right clavicle – LR 0.1 for AS, which virtually rules out mod-severe AS
- If radiates to right clavicles, use the following other signs to guide you: reduced S2, reduced carotid volume, slow carotid upstroke, murmur loudest in 2nd and right intercostal space
    - If 0 - 1 associated findings, then **LR 1.76 for AS**
    - If 3 -4 associated findings, then **LR 40 for AS**

Table 4 – Maneuvers to distinguish between HOCM and AS.

Maneuver	HOCM	AS
Valsalva strain phase (decreased preload)	Louder	Softer
Squatting/leg raise (increased preload)	Softer	Louder
Hand grip (increased venous resistance/afterload)	Softer	Softer

Examination of Hypertrophic Obstructive Cardiomyopathy (HOCM)

- Murmur decreases in intensity with passive leg elevation (LR+ 8.0). If murmur does not decrease, the negative LR is 0.22.
- If murmur decreases or remain unchanged with standing to squatting, LR+ is 4.5. If murmur increases, the likelihood is significantly reduced (LR- 0.13).

Resources

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3. Etchells E, Bell C, Robb K. Does This Patient Have an Abnormal Systolic Murmur? *JAMA*. 1997;277(7):564–571. doi:10.1001/jama.1997.03540310062036
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5. Harrison's Cardiovascular Medicine, 3e Ed. Joseph Loscalzo. McGraw Hill, 2016.

Approach to Volume Examination

Jugular venous pressure examination

- *Normal:* JVP is 6 to 8 cm above the right atrium
- *Abnormal/elevated:* JVP is > 9 cm above the right atrium (> 4 cm above the sternal angle)
- Jugular venous distension had the best combination of sensitivity (81%) and specificity (80%), predictive accuracy 81% for elevation of PCWP (>8mmHg)

Table 4 - JVP waveforms and associated conditions.

Elevated central venous pressure (CVP)	RV failure, tricuspid stenosis/regurgitation, pericardial effusion/constrictive pericarditis, SVC obstruction, fluid overload, hyperdynamic circulation
Dominant a wave	Tricuspid stenosis, pulmonary stenosis, pulmonary HTN, tricuspid regurgitation (LR+ 10.9)
Cannon a waves	Complete heart block, paroxysmal nodal tachycardia with retrograde atrial conduction, VT with retrograde atrial conduction/AV dissociation
X descent	Absent: atrial fibrillation Exaggerated: acute cardiac tamponade, constrictive pericarditis
Y descent	Sharp: severe tricuspid regurgitation, constrictive pericarditis Slow: tricuspid stenosis, right atrial myxoma
Large CV waves	Tricuspid regurgitation, constrictive pericarditis

Tips for volume status examination – VOLUME DEPLETED

- The presence of moist membranes, tongue and axilla make extracellular fluid contraction less likely.
- Dry mucous membranes without tongue furrows: LR- 0.3
- Dry axillary skin only mildly increases the probability of ECF contraction (LR+ of 2.8)

Tips for volume status examination – VOLUME OVERLOADED

Table 5 – Tests characteristics for hypervolemia

	LR+	LR-
Heart rate >100 bpm at rest	5.5	NS*
Abdominojugular reflux test	6.4	0.79
Lung crackles	2.8	0.5
JVP elevated	5.1	0.66
S_4	NS	NS
Apex displaced lateral to mid-clavicular line	5.8	NS
S3	11	0.88
Any murmur	2.6	0.81
Edema	2.3	0.64
Wheezing	0.22	1.3
Ascites	0.33	1.0

*NS – non-significant

- S_3 – high LR+ of 11 for HF in patients with dyspnea, however low negative predictive valve for high pulmonary capillary wedge pressure (PCWP >20mmHg). Sensitivity and specificity of S_3 were 51% and 90% for low EF (<50%) – therefore only useful when present.
- Pulmonary crackles – only mildly increased the probability of HF in patients with dyspnea (LR+ 2.8)

Resources

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Cirrhosis Signs

- Palmar erythema: due to excess estrogen associated with reduced breakdown of sex steroids within the liver
- Spider nevi: isolated telangiectasia that fill from a central feeding vessel found in the distribution of SVC on the upper trunk, arms and face, due to excessive estrogen
- Gynecomastia: can occur in men, with loss of body hair and testicular atrophy
- Leukonychia: white nails, caused by hypoalbuminemia, may also occur in protein calorie malnutrition/kwashiorkor, protein-losing enteropathy or prolonged proteinuria (nephrotic syndrome)
- Clubbing: may be associated with liver disease (see section on Clubbing)

Use the following signs to help identify the presence of absence of cirrhosis

Table 6 – Likelihood ratios for cirrhosis

Sign	LR+	LR-
Leukonychia	16-22	0.57-0.58
Gynecomastia	5.8-35	0.43-0.84
Decreased body hair	9	0.65
Facial telangiectasia	5.9-10	0.2-0.32
Testicular atrophy	5.8	0.84
Palmar erythema	5	0.59
Spider nevi	4.3	0.61
Jaundice	3.8	0.82

Table 7 – Likelihood ratios for portal hypertension

Sign	LR+	LR-
Distended abdominal veins	11	0.72
Encephalopathy	10	0.86
Ascites	7.2	0.69
Splenomegaly	3.5	0.74
Peripheral edema	3.0	0.71

Tips for examination of patients with liver disease

- Distended abdominal veins, encephalopathy, ascites, and spider nevi were most frequently studied findings with positive LRs of more than 4.0.

- Ascites and spider nevi may be the most reliable because they had the narrowest confidence interval.
- Hepatomegaly has LR of 2.4 and LR- of 0.37. Obesity has LR+ of 1.3 and LR- 0.76.
- Jaundice
    - Detectable on physical exam when level > 42 – 50 umol/L
    - For bilirubin > 50, sensitivity of exam is 78.4% and specificity is 68% (LR+ 2.5, LR- 0.31)
    - For bilirubin >256 umol/L, sensitivity of physical exam for jaundice is 96.4.
- Splenomegaly
    - Castell method: percussing at the lowest intercostal space in the left anterior axillary line in both expiration and inspiration. LR+ of 4.8 and LR- of 0.21.
    - Traube space: sixth rib superiorly, mid-axillary line and left costal margin inferiorly. LR+ 4.3 and LR- 0.26 (non-obese, fasting).
    - Nixon maneuver: right lateral decubitus, percussion initiated midway along the left costal margin and continued upwards along a line perpendicular to the costal margin. If upper limit of dullness extends >8cm above the costal margin: splenomegaly (sensitivity 59%, specificity 94%).

Bottom line

- Best rule in tests for hepatocellular dysfunction
    - Leukonychia, gynecomastia, decreased body hair, facial telangiectasias
- Best rule in tests for portal hypertension
    - Distended abdominal veins, encephalopathy, ascites

Resources

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Approach to Ascites

Background

- Ascites is free fluid in the abdomen
- Symptoms to elucidate include increased abdominal girth, recent weight gain, and ankle swelling
- Obtain history including causes such as liver and heart failure

Table 8 – Likelihood of ascites based on history

Focused History	LR +	LR -
Change in abdominal girth	4.2	0.17
Weight gain	3.3	0.47
Underlying liver disease	3.2	0.8
Recent ankle edema	2.8	0.1
Congestive heart failure	2.04	0.73

Physical Examination

- General assessment: lymphadenopathy, volume status, stigmata of chronic liver disease
- Cardiovascular and respiratory assessment
    - If JVP is elevated, consider heart failure as cause of ascites
- Abdominal examination
    - Inspection – ensure patient is supine and inspect from the foot of the exam table for bulging flanks
    - Percussion
        - Shifting dullness: starting at the umbilicus, percuss towards the flanks noting change from tympanic (gas in bowel) to dullness (free fluid). Note location of note change, then ask the patient to assume right lateral decubitus position, wait approximately 2 minutes and mark new location of dullness (closer to midline).
        - Fluid wave or 'thrill': better for large volume ascites (at least 2-3 liters) involves having the patient place the ulnar surface of their hand on the umbilicus to block wave transmission through skin. Place your left hand on left flank and flick with your right hand. Positive if you feel distinct impulse with left hand.
    - Examine the liver and spleen (see previous section on Cirrhosis exam)

Table 9 – Likelihood of ascites based on exam

Focused Physical Exam	LR +	LR -
Fluid wave	2.8 - 9.6	0.2 - 0.6
Shifting dullness	1.9 - 5.8	0.2 - 0.5
Bulging flanks	1.4 - 2.4	0.1 - 0.5
Percussion for flank dullness	1.3 - 2.6	0.2 – 0.3

Bottom line

- Best **rule out** tests
    - History: lack of ankle edema, lack of increased abdominal girth
    - Exam: absence of bulging flanks (LR+ 2.4, LR– 0.3), flank dullness (LR+ 2.6, LR- 0.3), or shifting dullness (LR+ 5.8, LR- 0.5)

- Best **rule in** tests
    - Positive fluid wave (LR+ 9.6, LR-0.6), shifting dullness, or peripheral edema
    - Puddle sign (LR+ 1.6, LR- 0.8) and auscultatory percussion not recommended

Resources

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2. Talley, Nicholas J, and Simon O'Connor. Clinical Examination: A Systematic Guide to Physical Diagnosis. 8th Ed. Oxford: Blackwell Science, 1996. Print.

Approach to Clubbing

Background

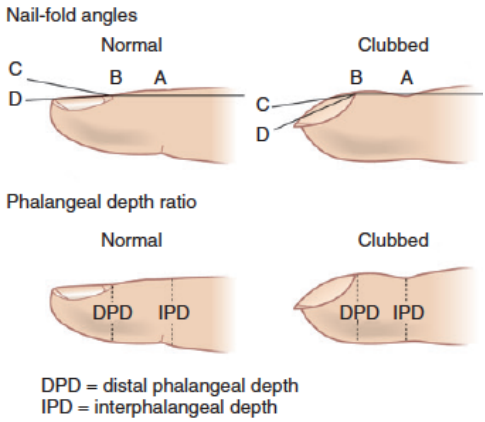
- Uniform swelling of the soft tissue of the distal phalanx of the fingers or toes
- Pathogenesis related to increase in vascular connective tissue, capillary damage, and megakaryocyte deposition
- Approximately 80% of patients with clubbing have an underlying disease
- Caused by lung (lung cancer, lung abscess, cystic fibrosis, pulmonary fibrosis, bronchiectasis), cardiac (cyanotic heart disease, infective endocarditis), or GI (cirrhosis, inflammatory bowel disease) conditions
- History and examination can help confirm clubbing and elucidating underlying etiology

Physical Examination

1. Inspect the appearance of fingers and toenails. Of note, the inter-observer agreement is variable (kappa = 0.36-0.90)[1] when clinicians make global assessments of clubbing at bedside.

2. Nail-fold angle

- ❑ Profile = ABC
  167.2° = mean normal angle (angle above 180° associated with clubbing)
- ❑ Hyponychial = ABD
  180° = mean normal angle (angle above 192° associated with clubbing)



3. Phalangeal depth ratio (DPD:IPD)

Ideally use calipers to measure, but visual estimates should suffice

- ❑ 0.9 = mean ratio
- ❑ >1.0 = abnormal, regardless of age, sex, or ethnicity

4. Schamroth's sign

- Oppose dorsal surfaces of similar fingers and watch for obliteration of diamond-shaped window (normally formed by Lovibond's angles)
- Used primarily as a quick screening test. Not validated but appears to reliably identify clubbing

5. Palpation for spongy nail bed

- Use your thumb and middle finger to grip the sides of your patient's finger, exert downward pressure with your index finger, use the nail at bed as a fulcrum and rock the distal and proximal ends of the patient's nails. A spongy nail bed feels like nail floating within distal phalanx (on autopsy > 2mm thick)

Note: The finding of clubbing in a patient with COPD has a LR+ 3.9 of predicting lung cancer; The finding of clubbing in patients with inflammatory bowel disease has a LR+ 2.8 in patients with Crohn's and 3.7 in patients with ulcerative colitis of indicating active disease.

Resources

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2. Talley, Nicholas J, and Simon O'Connor. Clinical Examination: A Systematic Guide to Physical Diagnosis. 8th Ed. Oxford: Blackwell Science, 1996. Print.
3. Tadesse, Abilo. (2016). Clinical Methods: Physical Examination And Clinical History Taking. Image –Nail Clubbing: Obliteration of hyponychial angle. https://www.researchgate.net/profile/Abilo-Tadesse/publication/334697259/figure/fig3/AS:784835681480706@1564130816111/Nail-clubbing-Obliteration-of-hyponychial-angle-Nail-fold-angle-180-0-and_Q640.jpg

Approach to Cerebellar Testing

The cerebellum directs our balance, muscle tone, and coordination. Therefore, signs of cerebellar disease can appear from head to toe.

1. Eyes

- Observe for resting nystagmus (in primary gaze)
- Assess extra-ocular movements and note any breakdown of smooth pursuit, nystagmus (horizontal, vertical, rotatory). Fast phase is towards the side of the cerebellar lesion.

2. Speech (say "British Constitution")

- Scan speech for inappropriate emphasis on syllable, pitch, explosiveness, pace, irregularity
- Test for dysarthria – say ka-ka-ka, ta-ta-ta, cu-cu-cu

3. Upper Limbs

- Tone
    - Flex or extend elbow with resistance then release and assess for overcompensation (rebound phenomenon)
- Dysmetria (hypermetria or hypometria)
    - Finger to nose – monitor for intention tremor (side-to-side or up and down) and past pointing (terminal limb dysmetria) where the patient overshoots the target or their nose
- Dysdiadochokinesis
    - Rapid alternating movements – patient taps alternatively the palm and back of one hand to the other hand
- Dysrhythmokinesis
    - Fingers – touch fingertips with thumb, play piano, tap fingertips
- Pronator Drift – pronation and upward motion indicates a cerebellar disease, pronation and downwards is associated with upper motor neuron or proprioception loss.

4. Lower Limbs

- Tone
- Dysmetria
    - Heel to shin – slide heel of one foot along sharp part of the opposite shin from mortise to knee (look for accuracy of fine movements)
- Dysrhythmokinesis

- Foot tap – tap each foot rapidly on a firm surface

For both upper and lower limbs test for pendular reflexes (more than three oscillations) of the triceps and patella.

5. Examine the trunk - Ask the patient to sit up without their arms and observe for truncal ataxia which can indicate a midline cerebellar lesion. Then sit down next to the patient and watch for swaying.

6. Test for gait by having the patient walk in a straight line then in tandem and assess for irregularity of rate, range and direction. Note wide-based, falling towards either side in random distribution (midline distribution) or falling towards one side (disease of cerebellar hemisphere) gaits.

To perform the **Romberg test**, ask patients to stand with their feet together, arms close to their body, and eyes closed. A positive Romberg test is when a patient has loss of balance or falling (denoting proprioception issue) with their eyes closed.

Table 10 – Summary of cerebellar disease findings.

	CEREBELLAR DISEASE
EYES	Nystagmus (rotatory, pendular, multidirectional)
SPEECH	Scanning or explosive speech
ARMS	Decreased tone Rapid alternating movements: Dysdiadokinesis Finger-nose: Dysmetria (overshoot) Rebound phenomenon
LEGS	Decreased tone Pendular reflexes Heel-to-shin dysmetria; Foot tap irregular
SENSORY	Normal
ROMBERG	Negative (fall with eyes open)
GAIT	Truncal ataxia Wide-based gait (very irregular; unable to stand with feet together)

References:

1. Gudlavalleti A, Tenny S. Cerebellar Neurological Signs. [Updated 2021 Nov 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556080/
2. Hui, D., Leung, A. K. C., & Padwal, R. (2011). Approach to internal medicine: A resource book for clinical practice. New York: Springer.
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4. Stanford Medicine 25. Cerebellar Exam. https://stanfordmedicine25.stanford.edu/the25/cerebellar.html

Approach to Vertigo

It is important to clarify what is meant by "dizziness":

- Vertigo: false sense of motion or spinning sensation
- Dysequilibrium: feeling off balance, wobbly, or unsteady
- Presyncope: feeling of imminently losing consciousness usually associated with position change

Table 11 – Peripheral vs central vertigo

Central Vertigo	Peripheral Vertigo
Gradual onset, minimal nausea/vomiting	Abrupt onset, severe nausea/vomiting
Can be abrupt if stroke or cerebellar bleed	Worse with position Worse in the morning
Severe imbalance, inability to walk	Mild-moderate imbalance, ability to walk
Associated with cranial nerve or focal neurologic deficits	Associated with hearing loss, tinnitus, and ear fullness

Physical Examination

1. Vital signs: check for an orthostatic drop

2. Neurologic Examination:
   - Nystagmus – spontaneous (central or vestibular neuronitis); gaze evoked
     - **Peripheral** - inhibited by visual fixation (increases when looking away from lesion)
     - **Central** - no change with visual fixation (increases when looking toward lesion)
   - Cranial nerves – look for palsies (Ramsay-Hunt syndrome, central problem)
   - Peripheral motor and sensory – look for focal weakness and decreased sensation in the feet
   - Reflexes – any asymmetry
   - Gait and posture – Romberg (positive with peripheral lesions)

3. Examine tympanic membranes with otoscope and assess hearing with Rinne and Weber tests

4. **Dix-Hallpike maneuver**
   - Ensure patient is sitting with gaze forward. The examiner grasps the patient's head and quickly guides them to a supine position with the head rotated to 30° and the head ending up 30° slightly below the horizontal. The examiner looks at the eyes of the patient for at least 15 seconds to see if rotatory nystagmus has been induced. It is repeated with rotating the head 30° to the opposite side. A positive test suggests a

peripheral cause of vertigo known as benign positional paroxysmal vertigo (BPPV).

5. **H**ead **I**mpulse-**N**ystagmus-**T**est of **S**kew (**HINTS exam**)
    - Head Impulse
        - Patient to maintain gaze midline and fixed on the examiner's nose. Quickly rotate head 20 degrees to the left and right. A normal response is eyes maintaining position (VOR vestibular ocular reflex intact). If the eyes are dragged off the target with the head turn or followed by a corrective saccade back to the target, it is suggestive of a peripheral lesion.
    - Nystagmus
        - Primary or lateral gaze, with unidirectional or bidirectional, vertical, or torsional nystagmus
        - Bilateral nystagmus which changes direction on eccentric gaze or vertical nystagmus is indicative of a central lesion. Direction-fixed horizontal nystagmus suggests a peripheral lesion.
    - Test of Skew
        - Patient to cover one eye and maintain gaze of the other eye on you. Uncover the eye as you move to cover the other and note any refixation. Abnormal test suggests a central lesion.

The acronym **INFARCT** are central findings on the *HINTS* exam:
- head **I**mpulse is **N**ormal
- **F**ast-phase **A**lternating or bidirectional nystagmus
- **R**efixation on **C**over-**T**est

The HINTS test was found to be 100% sensitive and 96% specific for the presence of a central lesion when applied to patients with vertigo and nystagmus and at least one stroke risk factor.[2]

Bottom Line
- Vertigo, positive Dix-Hallpike and/or vomiting → non-urgent peripheral disorder **(LR+ 7.6)**
- Young patient with vertigo but no neurological deficit → non-urgent cause of dizziness (**LR+ 1.5**)

Resources

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2. Kattah, J. C., Talkad, A. V., Wang, D. Z., Hsieh, Y. H., & Newman-Toker, D. E. (2009). HINTS to diagnose stroke in the acute vestibular syndrome three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke, 40(11), 3504-3510. DOI:10.1161/STROKEAHA.109.551234.
3. Talley, Nicholas J, and Simon O'Connor. Clinical Examination: A Systematic Guide to Physical Diagnosis. 8th Ed. Oxford: Blackwell Science, 1996. Print.

34. PERIOPERATIVE MEDICATIONS SUMMARY

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Introduction to this Guide

There are few clinical or evidence-based guidelines regarding perioperative management of medications. This guideline is largely based on literature of review papers, expert opinion, pharmacokinetic data, and manufacturer recommendations. Most medications taken for minor disorders that do not have systemic effects can be safely continued without incident.

The following approach is recommended for assessing the benefit versus risk of continuing or discontinuing medications for individual patients.

General preferences regarding drug administration

- Avoid non-essential medication on the morning of surgery so that the gastric load is minimized and the risk of aspiration is reduced.
- Essential oral medications should be given at least 2 hours preoperatively to ensure some absorption and to minimize gastric content.

If considering continuing a medication, evaluate:

- Whether the drug could adversely affect cardiovascular hemodynamics or electrolyte homeostasis
- Whether there are any potential drug interactions with intraoperative agents, particularly anesthetic agents
- Whether it could increase the risk of complications (e.g., bleeding, infections, venous thromboembolism, wound healing)

If considering discontinuing a medication, evaluate:

- The risk of a withdrawal reaction
- Whether tapering is required
- If and how fast the disease is likely to worsen without therapy and whether that could interfere with the surgery

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Acid suppressants			
Antacids - Aluminum hydroxide - Calcium carbonate - Magnesium hydroxide	Hold AM of surgery	Restart once patient is able to tolerate NG/PO intake, and symptom relief needed.	Not needed during surgery. Not known to reduce the risk of acid aspiration.
Histamine-2 receptor antagonists (H2RA) - Cimetidine* - Famotidine - Nizatidine - Ranitidine	Continue		Benefit shown in reducing the risk of acid aspiration by decreasing gastric volume contents and increasing gastric pH. *Special caution warranted with cimetidine as it is a weak inhibitor of multiple P450 enzymes. The inhibitory effect may last for days following cessation of cimetidine.
Proton pump inhibitors - Dexlansoprazole - Esomeprazole - Lansoprazole - Omeprazole - Pantoprazole - Rabeprazole			*References 100, 101*
Analgesics			*References 1, 14, 57, 72*
NSAIDS (COX-1) - Diclofenac - Ibuprofen - Indomethacin - Ketoprofen	Hold 4 days prior to surgery.	Resume when bleeding risk diminished, adequate hemostasis at surgical site, tolerating oral/NG intake.	When even minor bleeding can have serious consequences, such as in retinal and intracranial surgery, NSAIDS should be stopped for a minimum of 2 weeks.
- Naproxen - Meloxicam - Sulindac	Hold 7 days prior to surgery.		

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
NSAIDs (COX-2) - Celecoxib	Hold AM of surgery, unless ordered as pre-operative pain medication Hold for 2 days pre-op when the patient is at risk for renal dysfunction, myocardial ischemia or reperfusion injury.	Resume when tolerating oral intake Post-bowel surgery – do not start if patient has an anastomosis	Little or no effect on platelets. *References 1, 14, 57, 72*
Methadone	Continue (drink at least 3 hours before scheduled time of surgery)	Resume as soon as possible.	For methadone maintenance program or for pain management. Avoid fluctuation in drug level. If 3 days are missed, and the usual maintenance dose is methadone 30 mg or less, the usual dose may be restarted. If the usual maintenance dose is greater than 30 mg then start the dose at 30 mg or up to half the usual maintenance dose. The dose can then be titrated. *References 55, 56*
Buprenorphine-containing products: - Suboxone - Probuphine - Sublocade - BuTrans	Continue (all doses for all types of surgery)	Resume as soon as possible. If inadequate analgesia persists despite higher opioid doses, consider dose reduction of Suboxone	Consider preemptive analgesia (acetaminophen, NSAIDs, gabapentin). Strongly consider regional anesthesia techniques, and when possible peripheral or neuraxial catheter for post-operative use. Titrate short-acting potent opioids to effect (fentanyl, morphine, hydromorphone) and maximize use of non-opioid analgesics. *Reference 91*
Narcotics	Continue	Resume when tolerating oral/NG intake	Ensure patient takes dose on morning of surgery if they take high doses of narcotics or a long-acting preparation.
Nabilone	continue		

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Naltrexone Oral	Hold 3 days pre-op	start 7-10 days after discontinuing opioids	May be more sensitive to narcotics, requiring lower doses Note: this does not apply to Low Dose Naltrexone (LDN), which is a compounded product used as an adjunct in chronic pain and may be continued perioperatively. *Reference 98*
Direct Oral Anticoagulants Direct Xa inhibitors - Apixaban - Rivaroxaban - Edoxaban Direct thrombin inhibitor - Dabigatran	Hold prior to surgery, longer for patients with hepatic or renal impairment (see Chapter 17).	Resume when adequate hemostasis is achieved; avoid while epidural is in place; resume at least 6-12 hours after epidural removal (24 hours for traumatic procedures; longer for patients with renal impairment). *See preprinted order sheet at Mount Sinai Hospital - MS 817 Pre-Operative Management of Non-Warfarin Oral Anticoagulants.* *Reference 92, 105*	
Fondaparinux (for prophylaxis, 2.5 mg/day)	Hold 48 hours for low bleeding risk surgery Hold 4 days for high bleeding risk surgery Drug clearance is prolonged with renal impairment and in elderly.	ASRA guidelines make no recommendation on pre-op administration, but recommend that fondaparinux should not be administered for post-op thromboprophylaxis after difficult neuraxial procedures (i.e, more than one needle pass, difficulty threading a neuraxial catheter). Wait at least 6 hours after neuraxial catheter removal before giving 1st dose. *Reference 92, 105*	
Heparin IV (or SUBCUT treatment) doses greater than 5000 units, SUBCUT bid	Hold 4 to 6 hours prior to surgery.	Resume after 12 hours following major surgery; after 2 hours after minor surgery provided there is adequate hemostasis at surgical site / no obvious bleeding. Avoid while epidural catheter is in place; restart 2 hours after catheter removal	For emergency reversal use 1 mg of protamine per 100 units of heparin or fresh frozen plasma. *Reference 1*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Heparin SUBCUT BID or TID less than 5,000 units	Hold AM dose and check PTT/aPTT prior to surgery.	Hold AM dose prior to catheter removal, check PTT PRN; restart 2 hours after catheter removal	For emergency reversal use 1 mg of protamine per 100 units of heparin or fresh frozen plasma. *Reference 1*
Low-Molecular Weight Heparin (LMWH)	If dosed Q12H, hold 12 hours pre-op. If dosed Q24H, hold 24 hours prior to surgery.	Resume 12 – 24 hours postoperatively provided adequate hemostasis at surgical site / no obvious bleeding.	Hold AM dose prior to catheter removal, check PTT PRN; restart 2 hours after catheter removal *Reference 1*
Warfarin	Hold 5 days prior to surgery. Does not have to be discontinued for cataract surgery.	Resume when tolerating oral/NG intake provided adequate hemostasis at surgical site / no obvious bleeding.	Inhibits the synthesis of vitamin K dependent clotting factors. Use Fresh Frozen Plasma if urgent reversal is required. *Reference 1*
Antiplatelet agents			
ASA	Assess risk vs benefit If holding therapy is necessary, hold 5-7 days prior to surgery	Resume when tolerating oral/NG intake provided adequate hemostasis at surgical site / no obvious bleeding.	Thrombosis Canada 2021 recommends holding Aspirin for 5 to 7 days. In high risk patients (e.g. unstable coronary syndromes or cerebrovascular disease) it may not be feasible to stop therapy. Discuss risk with cardiologist and/or surgical team. *References 1, 5, 11, 72*
Clopidogrel	Assess risk versus benefit. If holding therapy is necessary, hold 5-7 days prior to surgery.	Resume when tolerating oral/NG intake provided adequate hemostasis at surgical site / no obvious bleeding.	Irreversibly inhibits platelet aggregation. For patients with recent cardiac stents (<6 months) and/or high cardiovascular risk, call cardiologist to discuss the risks of stopping. Note acute restenosis of stent is catastrophic.
Ticagrelor			Reversibly and noncompetitively binds to the adenosine diphosphate (ADP) P2Y12 receptor on the platelet surface which prevents ADP-mediated activation of the GPIIb/IIIa receptor complex, thereby reducing platelet aggregation.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Prasugrel	Assess risk vs benefit If holding therapy is necessary, hold 7 to 10 days prior to surgery.	Consider restarting as soon as possible for patients with a very high risk for cardiovascular disease	Active metabolite irreversibly blocks P2Y12 component of ADP receptors on the platelet. *Reference 93*
Aggrenox (ASA/ dipyridamole)	Assess risk vs benefit If holding therapy is necessary, hold 7 to 10 days prior to surgery.		Irreversibly inhibits platelet function for 7 to 10 days until new platelets can be generated. In high risk patients (e.g. unstable coronary syndromes or cerebrovascular disease) it may not be feasible to stop therapy. Discuss risk with cardiologist and/or surgical team. *References 1, 5, 11, 72*
Bisphosphonates			
- Alendronate - Etidronate - Risedronate	Hold AM of surgery	Resume when tolerating oral/NG intake (minimum 6 – 8 oz water) and is able to sit upright for a minimum of 30 minutes.	
Cardiovascular drugs			
Amiodarone	Continue	Resume when tolerating oral/NG intake and no bradycardia.	Monitor closely when restarted, as these may cause ↑ QT, ↑ ventricular arrhythmias which are enhanced by changes in electrolytes. IV form available if oral intake not possible for an extended period of time.
Other antiarrhythmics: - Disopyramide - Flecainide - Procainamide - Propafenone - Quinidine - Sotalol	Continue		Should be continued particularly if the indication is a serious heart arrhythmia that causes hemodynamic instability (e.g. sustained ventricular tachycardia). If a parenteral formulation is required, procainamide can be used as an alternative.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Angiotensin converting enzyme (ACE) inhibitors - Enalapril - Lisinopril - Perindopril - Ramipril - Trandolapril **Angiotensin II Receptor Blockers (ARBs):** - Candesartan - Irbesartan - Losartan - Olmesartan - Telmisartan - Valsartan* **Neutral Endopeptidase Inhibitor / ARB** Sacubitril / Valsartan (Entresto®)	Hold on the day of surgery for all patients, except surgeries under local anesthesia (i.e. local plus). May consider holding dose the night before surgery if taken at night. Only patients for whom the anesthesiologist believes the risks of hypertension outweigh the risks of hypotension will be asked to take them on the day of surgery.	Resume when tolerating oral/NG and hemodynamically stable. Check renal function before resuming.	Associated with intra-operative hypotension. The risk of clinically important hypotension is greatest within 24 hours of surgery, consider restarting ACEI/ARB on day 2 after surgery in patients receiving chronic ACEI/ARB therapy, if the patient is hemodynamically stable and able to tolerate NG/PO. Hold all combinations of ACEIs or ARBs (e.g. amlodipine/perindopril) *Reference 9, 102*
Antilipemic agents - Niacin - Fibrates - Bezafibrate - Clofibrate - Fenofibrate - Gemfibrozil	Hold AM of surgery	Resume when tolerating oral/NG intake.	Caution with creatine kinase increases or rhabdomyolysis
HMG-CoA reductase inhibitors/statins - Atorvastatin - Simvastatin - Pravastatin - Lovastatin - Fluvastatin	Continue		Some pleotropic (anti-inflammatory, vasodilatory and antithrombotic effects). Growing evidence that perioperative statin therapy is safe and beneficial in reducing morbidity and mortality in the perioperative period; with the greatest benefit in patients at higher risk for cardiovascular complications. *Reference 106*
Ezetimibe	Hold AM of surgery		
PCSK9 inhibitors - Evolocumab	Hold AM of surgery		May considering resuming at home, if patient expected to be discharged within 7 days of scheduled dose

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Bile acid sequestrants - Cholestyramine - Colestipol	Hold AM of surgery		Bile acid sequestrants bind some medications and therefore lower their bioavailability. Preferable to avoid in the immediate post-operative period when some oral agents may be administered.
Alpha1-Blocking Agents - Terazosin - Prazosin Doxazosin	Continue		(see separate entry for tamsulosin)
ß-Adrenergic Blocking Agents - Acebutolol - Atenolol - Bisoprolol - Carvedilol - Labetalol - Metoprolol - Nadolol - Pindolol - Propranolol - Sotalol - Timolol	Continue	Restart as soon as possible, provided hemodynamically stable. If possible, no interruption in course of therapy.	ß-blockers should be continued in patients undergoing surgery who are receiving them to treat cardiac conditions such as angina, symptomatic arrhythmias, hypertension. There is a risk for withdrawal syndrome if therapy is discontinued abruptly. Abrupt discontinuation has been associated with an increased risk of perioperative infarction. If oral intake not possible, IV formulation can be used postoperatively. <u>Metoprolol</u> Bioavailability = 50%. Theoretical IV to PO ratio is 1:2.5. Due to rapid maximum beta-blockade with IV dosing, see suggested conversion below: If less than 50 mg PO convert to 2.5 mg IV q6h. If needed, increase dose by 2.5 mg IV q6h and titrate to effect If <u>greater than</u> 50 mg PO convert to 5 mg IV q6h. If needed, increase dose by 5 mg IV q6h and titrate to effect. *Note: higher dosages such as 10-15 mg IV q4h may be required to achieve adequate beta blockade.* *References 1, 17, 53, 54*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Calcium Channel Blockers **Dihydropyridines** - Amlodipine - Felodipine - Nifedipine **Non-dihydropyridines** - Diltiazem - Verapamil	Continue	Resume when tolerating oral/NG intake and hemodynamically stable (i.e. no bradycardia) and able to tolerate NG/PO.	Do not use short acting sublingual nifedipine to treat postoperative hypertension. For arrhythmias controlled with CCBs consider IV diltiazem or verapamil if patient unable to take NG/PO medications. Diltiazem may be preferred since it has less negative inotropic/ chronotropic effects therefore less likely to cause pulmonary edema or heart failure. *Reference 7* If taking long-acting formulations of diltiazem (e.g., Cardizem CD, Tiazac XC) or verapamil (e.g., Covera-HS, Isoptin SR) and able to take via NG, determine the total daily dose, divide QID and use immediate-release formulation.
Digoxin	Continue	Resume when tolerating oral/NG intake and hemodynamically stable (i.e. no bradycardia) and able to tolerate NG/PO.	IV form available if oral intake not possible for an extended period of time. Consider decreasing dose by 20-25% when converting from PO to IV. Serum levels taken perioperatively. A trough level should be taken 5 – 7 days after reinitiating therapy if no loading dose was given, 2 days after reinitiating therapy if a loading dose was given, and 1 – 3 weeks after reinitiating therapy if renal impairment is suspected. Normal therapeutic range: 1.0 – 2.6 nmol/L Dosage adjustments maybe required postoperatively if renal function changes. *References 1, 7, 11, 93*
Diuretics - Furosemide - Chlorthalidone - Hydrochlorothiazide - Indapamide	Hold AM of surgery Continue if used for control of chronic congestive heart failure.	Resume when tolerating oral/NG intake and hemodynamically stable (no hypotension)	Potential for hypokalemia, intravascular volume depletion and hypotension. Monitor electrolytes and fluid status closely. *Reference 10*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Hypotensive Agents - Clonidine	Continue	Resume when tolerating oral/NG intake and hemodynamically stable (i.e. no bradycardia)	In general, hypotensive agents should be given on the morning of surgery. Of note, clonidine is an central alpha-2 agonist Abrupt cessation of central agonist may cause dangerous rebound hypertension. If oral intake is not possible, parenteral agents such as esmolol, propranolol, hydralazine, diltiazem, nitrates are options. When the discontinuation of clonidine is required and beta blockers are being used in combination, stop the beta blocker first to avoid unopposed alpha stimulation which can potentiate rebound hypertension. Giving labetalol an alpha 1 and beta-adrenergic blocking agent may be useful. *Reference 1, 12, 17*
Nitrates - Isosorbide dinitrate (ISDN) - Isosorbide mononitrate (ISMO)	Continue	If oral intake not possible postoperatively, ointment or patches can be used.*	Should be continued during the perioperative period if used as an antianginal to avoid compromising the stability of cardiac disease. *Do not substitute with patches or ointment in the preoperative period, intraoperative transdermal absorption not reliable. *References 1, 7*
Neurological and psychiatric medications			
Cholinesterase inhibitors - Donepezil - Galantamine - Rivastigmine	Continue	Resume when tolerating oral/NG intake Restart carefully and titrate to avoid the risk of a cholinergic crisis.	May exaggerate the muscle relaxation effect of succinylcholine during anesthesia and inhibit the effect of non-depolarizing neuromuscular blocking agents. Rivastigmine has a relatively shorter half-life. Give on morning of surgery if it coincides with patient's usual regimen. *Reference 72*
Anticonvulsants			

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
- Carbamazepine - Ethosuximide - Gabapentin - Phenobarbital - Phenytoin - Pregabalin - Primidone - Topiramate - Valproic Acid - Divalproex sodium - Levetiracetam - Oxcarbazepine	Continue	Resume when tolerating oral/NG intake Give phenytoin administered via the NG route 1 hour before or 2 hours after feeds or any medications containing calcium, magnesium or aluminum.	Risk of convulsion, hypoxia, aspiration pneumonia if withdrawn. If patient unable to take oral doses postoperatively for an extended period of time then preoperative conversion to a drug with an IV form is suggested for those treated with drugs which only have an oral form. Postoperative level suggested where applicable.
Antidepressants			
Monoamine Oxidase Inhibitors (MAO-I)	Continue	Resume when tolerating oral/NG intake	Consider 'MAO-I safe' anesthesia. Drug interaction with ephedrine can cause hypertensive crisis by releasing huge amounts of stored noradrenaline. Drug interaction with meperidine, fentanyl, alfentanil, sufentanil and dextromethorphan can cause an excitatory reaction similar to serotonin syndrome. Symptoms include agitation, headache and hemodynamic instability which can lead to pyrexia, seizure, coma and death. Proper discontinuation of MAO-I drugs require a 2 week taper. These agents are usually used where depression is refractory to conventional treatments. Therefore the risk of relapse is a reality. At doses greater than 10mg selegiline becomes non-selective (i.e. MAO-I Type A and B). *References 1, 7, 9, 72*
Non Selective (Type A, B) - Phenelzine - Tranylcypromine	Continue		
Selective (Type A) - Moclobemide **Selective (Type B)** - Selegiline - Rasagiline	Continue		
Selective Serotonin Reuptake Inhibitors (SSRI) - Citalopram - Fluoxetine - Fluvoxamine - Paroxetine - Sertraline	Continue	Resume when tolerating oral/NG intake	Continue during the perioperative period no reports of interactions with anesthetics. Withdrawal syndrome can occur after just one day of stopping therapy. Symptoms of this syndrome include dizziness, agitation, lethargy, nausea, chills, myalgias, gait instability, SOB, and impaired short-term memory. *References 1, 7*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Tricyclic antidepressants (TCA) - Amitriptyline - Desipramine - Doxepin - Imipramine - Nortriptyline Tetracyclic agents - mirtazapine	Hold AM of surgery	Resume when tolerating oral/NG intake	Can be taken with caution during perioperative period. Sympathomimetic activity of isoproterenol, phenylephrine, norepinephrine, epinephrine and amphetamines may be potentiated causing risk of hypertension and arrhythmias. Rare adverse effects include sedation, delirium, reduced cardiac conduction and arrhythmias. If withholding is warranted, taper over 7-14 days due to their long half-life and potential for withdrawal syndrome. *References 7, 10, 13*
Other antidepressants - Venlafaxine XR - Desvenlafaxine - Duloxetine - Vortioxetine - Bupropion	Continue		Risk of withdrawal symptoms if not continued in the perioperative period *Reference 94, 95*
Lithium	Hold AM of surgery	Restart once tolerating NG/PO intake.	May prolong the effects of neuromuscular blocking agents. At toxic levels may cause delirium, coma and arrhythmias. If renal clearance is affected monitor serum drug level. Normal therapeutic Range 0.4 – 1.2 mmol/L. Reference 7
Antidiabetic agents			*References 1, 4*
Metformin	Hold AM of surgery	Resume once patient eating full diet or tolerating NG feeds. Monitor blood glucose.	Lactic acidosis has rarely been associated with metformin use. Lactic acidosis is a serious and potentially avoidable complication: renal failure is a major factor contributing to lactic acidosis. Other factors include sepsis, acute myocardial infarction, liver impairment and respiratory conditions leading to hypoxemia.
GLP-1 receptor agonists - Liraglutide - Semaglutide - Dulaglutide - Exenatide - Lixisenatide	Hold day of surgery	Resume once patient eating full diet or tolerating NG feeds. Monitor blood glucose.	Day of surgery: If weekly dose is due on morning of surgery, delay until later in day after surgery is complete. *Reference 96*
SGLT2 inhibitors - Canagliflozin - Dapagliflozin - Empagliflozin	Hold 3 days prior to surgery (for major surgery)		Risk of euglycemic ketoacidosis See Health Canada Review *Reference 97, 107*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Oral hypoglycemic - Acarbose - Gliclazide - Glyburide - Glimepiride - Repaglinide - Pioglitazone **DPP4 inhibitors** - Sitagliptin - Saxagliptin - Linagliptin - Alogliptin	Hold (duration of hold depends on half-life of drug). For DPP4 inhibitors, hold on AM of surgery. For short acting agents, hold evening and morning dose as patient will be fasting. For long acting agents (e.g. Diamicron MR, hold 24 hours prior to surgery if susceptible to hypoglycemia or on restricted diet i.e. clear fluids). May need supplemental insulin PRN. Insulin supplemental scale may be required postoperatively until the patient is able to tolerate oral intake or NG feeds. If insulin is needed for more than 48 hours, start basal insulin (NPH) to promote smoother control. Start at 0.1 units/kg every 12 hours and continue supplemental Q6H insulin. Resume once patient eating or tolerating NG feeds. Monitor blood glucose. For patients undergoing ambulatory surgeries for which no more than one meal is expected to be omitted, no interruption may be acceptable. Resume once patient eating full diet or tolerating NG feeds. Monitor blood glucose. *Reference 96*		
Insulin	See Chapter 18 Diabetes for details. Depending on the severity of diabetes, daily insulin doses may be modified requiring the usage of perioperative SC or IV insulin and intraoperative IV insulin. If an IV insulin infusion is used, supplemental SC insulin should be continued postoperatively until the patient is able to tolerate oral/NG intake. DM Type 1, consider using IV insulin infusion • Start IV (D5W or 2/3 - 1/3) unless the patient is very hyperglycemic. (greater than 15 mmol/L) • Patients with Type 1 Diabetes should **NOT** have their insulin infusion stopped due to the risk of ketoacidosis DM Type 2, usually treated with insulin • Reduce usual insulin by 50-75% pre-surgery. • Check BG every 6 hours. • Add supplemental fast-acting or rapid-acting insulin scale Very insulin-resistant/deficient patients (> 100 units/day) may be managed as Type 1 DM above with insulin infusion.		
Antiparkinsonian drugs			
Dopaminergic agents: - Levodopa/ Carbidopa, - Levodopa/ Benserazide	Continue	Restart as soon as possible post-operatively to avoid the return of	Withdrawal has been associated with symptoms similar to Neuroleptic Malignant Syndrome. Benefits of continued treatment outweighs risk of possible arrhythmias due to interaction with anesthetic.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Dopamine agonists: - Bromocriptine - Pramipexole - Ropinirole		Parkinsonian symptoms.	
Anticholinergic agents: - Benztropine - Ethopropazine - Procyclidine - Trihexyphenidyl			
COMT Inhibitors: - Entacapone			Withdrawal of entacapone has been associated with a neuroleptic malignant-like syndrome.
Antipsychotics			
- Aripiprazole - Brexpiprazole - Clozapine - Chlorpromazine - Flupentixol - FluphenazineHaloperidol - Lurasidone - Olanzapine - Paliperidone - Quetiapine - Risperidone - Ziprasidone - Zuclopenthixol	Hold AM of surgery	Resume when tolerating oral/NG intake	Can be continued with caution during the perioperative period. Consider neuroleptic malignant syndrome if patient develops hyperthermia, muscle rigidity and dysregulation of autonomic nervous system postoperatively. These symptoms are similar to malignant hyperthermia, which sometimes occur after anesthesia. May be given to patient on am of surgery in some conditions. *Reference 7*
Gastrointestinal agents			
5-ASA products - ASACOL - MESASAL - MEZAVANT - PENTASA - SALOFALK	Hold AM of surgery	Resume when tolerating oral/NG intake and if drugs still indicated post-operatively.	In most cases holding one dose perioperatively will have minimal impact on the disease management. May continue perioperatively if needed. *References 73 to 78*
Ursodiol	Hold AM of surgery	Resume once tolerating oral/NG intake	

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Corticosteroids			*References 58 to 72, 104*
Oral Corticosteroids - Betamethasone - Budesonide - Dexamethasone - Prednisone - Fludrocortisone - Hydrocortisone - Methylprednisolone - Prednisolone - Prednisone - Cortisone	Continue (daily dose plus supplemental stress dose if applicable)	Resume oral glucocorticoids once tolerating NG/PO intake. Dose dependent on previous steroid usage and postoperative status.	See below for determination of whether supplement steroid is required.
	Perioperative adrenal insufficiency is an uncommon complication of surgery. For steroid stress dosing, see Chapter 22.		
Rectal Corticosteroids Budesonide enema (2 mg/dose)	Hold rectal steroids AM prior to surgery. Routine supplemental steroid coverage is NOT recommended for budesonide.		Rectal budesonide is a potent glucocorticoid with high topical potency and weak systemic effects. At recommended dose, budesonide enema causes no or minimal adrenal suppression.
	Consider supplemental steroid coverage for hydrocortisone rectal enema		30-90% systemic absorption of hydrocortisone (even greater if rectal/colon mucosa is inflamed). 30-90% absorption of hydrocortisone 100 mg = prednisone 7.5 -22.5mg
Hormones and hormone modifiers			
Aromatase inhibitors - Anastrozole - Letrozole - Exemestane	Continue	Resume when tolerating oral/NG intake	
Bicalutamide			
Hormone Replacement Therapy (HRT)	Risks and benefits of continuing or stopping HRT in the perioperative period must be assessed for individual patient. Estrogen doses are generally 20-25% of that contained in the oral contraceptives. Meta-analysis of 8 observational studies and 9 randomized controlled studies by Canonico et.al, showed a pooled odds ratio for oral estrogen for VTE = 2.4 and for transdermal estrogen = 1.2.		
	<u>Low risk or Transdermal HRT:</u> Continue	Resume post-operatively	Transdermal HRT is associated with less risk of VTE than oral HRT. *References 86, 90*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
	High risk: Hold 4 weeks prior to surgery	Resume when patient is fully mobile and able to tolerate oral intake. DVT prophylaxis recommended if appropriate.	Hold for 4 weeks prior to surgery particularly if the patient has multiple VTE risk factors. *Reference 81*
Megestrol	Continue	Resume when tolerating oral/NG intake	Synthetic progestin. Has weak glucocorticoid activity. There have been a few reports of adrenal suppression with megestrol.
Oral Contraceptive Pill (OCP)	Whether or not to stop the oral contraceptives before surgery is a controversial issue. Estrogen interferes with the production and action of clotting factors. There is a concern that patients taking OCPs will have a further increase in thromboembolic risk. The decision to continue or stop OCP before surgery must balance the risk of not using OCP (i.e. pregnancy, or excessive menstrual bleeding) against the risk of thromboembolism. The incidence of VTE in young women who are non-OCP user is approximately 1-3 per 10,000 per year. Using OCP will increase the risk of VTE by 3-4 folds. The adverse effects associated with estrogen are dose dependent. *Reference 90*		
	Low risk of VTE: continue	Resume when tolerating oral/NG intake. DVT prophylaxis recommended if appropriate	If the patient is to have a low risk surgery and will soon be ambulating without any immobile extremities, consideration should be made to continue OCP since the medical complications of an unplanned pregnancy may outweigh the risk of venous thromboembolism.
	High risk of VTE: hold 4 weeks prior to surgery	Continue holding for at least 2 weeks or for duration of immobility. To be restarted with 1st day of menses. DVT prophylaxis recommended if appropriate.	Recommended to discontinue if undergoing high-risk surgery. High-risk surgeries are defined as orthopedic surgery of the lower extremities and surgeries where long periods of immobility are required. Must use alternative form of contraception or progesterone only pills and ensure pregnancy status prior to OR.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Raloxifene	Low risk of VTE: hold AM of surgery High risk of VTE: hold 72 hours prior to surgery	Restart when patient is fully mobile and able to tolerate oral intake. DVT prophylaxis recommended if appropriate.	Risk of VTE increased by 1.6 fold.
Tamoxifen	Low risk of VTE: hold AM of surgery High risk of VTE: hold 72 hours prior to surgery	Resume when patient is fully mobile and able to tolerate oral intake. DVT prophylaxis recommended if appropriate.	Risk of DVT and PE is increased approximately 2 fold. Oncologist should be consulted prior to discontinuation especially if used for breast cancer management to discuss risk/benefit ratio.
Myasthenia Gravis agents			
Neostigmine	Continue	Resume as soon as possible. If oral intake is not possible, consider parenteral form.	Withholding therapy may cause muscle weakness that would slow down discontinuation of mechanical ventilation and surgical recovery *Reference 7*
Pyridostigmine			
Respiratory agents, inhaled			*References 1, 12*
Inhaled	Continue	Resume as soon as possible. Use nebulizers if unable to use metered dose devices.	Administer just prior to surgery. For patients with asthma and chronic obstructive pulmonary dysfunction, use spacer postoperatively. Lung function is often affected in abdominal or thoracic surgeries.
Anticholinergics			
Beta-adrenergic agonists			Extra doses may be given preoperatively to increase pulmonary function
Corticosteroids			
Respiratory agents, oral			*References 1, 12*
Theophylline	Continue Serum level preoperatively.	Resume when tolerating oral/NG intake	Optimize perioperative pulmonary stability. Continue despite narrow therapeutic window and high potential for drug interactions. Normal concentration: 55–110 μmol/L.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Leukotriene inhibitors - Montelukast - Zafirlukast	Continue		
Lipoxygenase inhibitors - Zileuton	Continue		
Endothelin Receptor Antagonist Bosentan	Continue	Continue	*Reference 108*
Respiratory agents, intravenous or subcutaneous			*References 1, 12*
Monoclonal Antibody, anti-asthmatic - Omalizumab - Mepoliqumab - Reslizumab - Benralizumab - Dupilumab	Continue. If dose due day of surgery, reschedule dose to day prior to surgery.		
Thyroid and antithyroid agents			
Anti-thyroid agents for hyperthyroidism - Methimazole - Propylthiouracil	Continue	If not undergoing thyroidectomy, resume once tolerating NG/PO intake.	In hyperthyroid patients, thyroid storm is a major complication in the perioperative period. An overactive thyroid must be controlled. Methimazole is preferred over propylthiouracil for long surgeries due to its long half-life and once daily dosing. Beta blockers can be used to control symptoms of hyperthyroidism.
Levothyroxine	Continue	Resume when tolerating oral/NG intake.	Missing 1 to 2 doses unlikely to be a problem due to its very long half-life of about 7 days. IV form available if patient unable to tolerate oral intake for an extremely long period of time.

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Biologics and immunosuppressives			
A general approach to immunosuppressants / modulators: relative to most other therapies, there are few data on the perioperative risks of immunosuppressants and modulators. Primary concerns are impaired wound healing and risk of infection. There is also concern that changes in drug clearance intra- and post-operatively will result in drug accumulation and cause drug toxicity. General considerations: 1. Consultation with the prescriber of the immunosuppressant/modulator is warranted to determine the risk of loss of disease control if the therapy is interrupted. 2. In the absence of clear evidence, weigh the individual's risk of wound infection and impaired wound healing with loss of disease control. If the patient's disease control and there is a high baseline risk of post-operative infection, this would weigh in favour of holding the drug for a minimum of 5 half-lives preoperatively. Conversely if the patient's disease is modestly controlled but improved on the therapy and the baseline risk of infection is low, this would weigh in favour of continuing the drug perioperatively. 3. Unless the therapy is being used as an adjunct to surgery, there is no need to administer the therapy on the day of surgery. For drugs with serious adverse effect profiles, monitoring for changes in drug clearance intra- and post-operatively should be considered. If drug clearance is impaired, holding therapy post-operatively until clearance normalizes is advisable.			
Azathioprine	Hold AM of surgery	Resume when tolerating oral/NG intake.	*References 25-29*
Cyclosporine A	Continue If elect to discontinue because of concerns with wound healing, stop Sandimmune for 6 days and Neoral for 4 days prior to surgery	Resume when tolerating oral/NG intake.	Ensure patient is well hydrated. If renal clearance is affected, monitor serum drug level. IV form available if oral intake not possible for an extended period of time.
Hydroxychloroquine	Continue	Resume when tolerating oral/NG intake.	No association with perioperative complications.
Imatinib	Discuss with prescriber. If elect to discontinue preoperatively, should stop ~ 8 days preop (half-life of active metabolite = 40 hours).	Resume when tolerating oral/NG intake.	If the surgery is related to the tumour, imatinib may be used deliberately throughout the perioperative period to reduce tumour burden; there are preliminary data showing benefit preoperatively. Coordinate the decision with the patient's oncologist. Watch for thrombocytopenia. *Reference 35*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Methotrexate	Continue Can hold day of surgery to reduce pill burden.	Resume once tolerating oral/NG intake. If parenteral, may resume immediately post-operatively.	Data on interrupting methotrexate perioperatively weigh in favour of (consensus to) continuing through the perioperative period. Flares after stopping methotrexate would be expected to occur if methotrexate was stopped for several weeks; 1-2 days of treatment interruption would be unlikely to result in disease flares. *References 30-35*
Mycophenolate - **Mycophenolate mofetil (CellCept)** - **Mycophenolate sodium (Myfortic)**	Discuss with prescriber If elect to discontinue preoperatively, hold for 3 days prior to surgery	Resume once tolerating oral/NG intake	Impairs wound healing but may be preferably to other options if an immunosuppressant must be used perioperatively. Formulations not interchangeable. Mycophenolate mofetil 500 mg = mycophenolate sodium 360 mg IV mycophenolate mofetil available if oral intake not possible for an extended period of time. *Reference 37*
Rituximab	Ideally hold for a minimum of 6 months (1/2 year) prior to surgery in order to let B-cell counts recover If surgery must be done prior to 6 month period, assess need for additional antibiotic coverage and increase post-operative monitoring for infection	Rituximab re-treatment should not be given until complete healing is achieved/absence of infection	Depletes B-cells. *Reference 38-40*
Sulfasalazine	Hold AM of surgery	Resume when tolerating oral/NG intake provided hemodynamically stable and drugs still indicated post-operatively.	In most cases holding one dose perioperatively will have minimal impact on the disease management. May continue perioperatively if needed. *References 73 to 78*

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Tacrolimus	Discuss with prescriber If elect to discontinue preoperatively, hold for 7 days prior to surgery	Resume when sutures/staples can be removed	Few data are available. Similar rates of impaired wound healing to cyclosporine in transplant patients. *Reference 23*
TNF-alpha antagonists adalimumab etanercept infliximab golimumab ustekinumab vedolizumab	Hold one treatment cycle prior to surgery. Users anxious about stopping treatment perioperatively may elect to continue perioperatively.	Resume when sutures/staples can be removed	May consider continuing treatment perioperatively for IBD patients. Best evidence failed to find a statistically significant association with post-operative infection, but was associated with wound dehiscence. *References 41-51*
Tofacitinib (Xeljanz)	Hold 7 days before surgery	Resume 14 days after surgery	*Reference 103*
Phosphodiesterase-5 enzyme (PDE-5) inhibitors			
Erectile dysfunction - Sildenafil (Viagra) - Tadalafil (Cialis) - Vardenafil (Levitra)	Hold for minimum 24h pre-op (48h for tadalafil due to longer half-life)		PDE-5 inhibitors may enhance the vasodilatory effect of vasodilators. t½ = 4h (sildenafil) t½ = 15-17.5h (tadalafil) t½ = 4-6h (vardenafil) *Reference 93*
Pulmonary hypertension - Sildenafil (Revatio) - Tadalafil (Adcirca)	Continue		Assess risk versus benefit with anesthesia.
Miscellaneous agents			
Memantine	Continue	Resume once tolerating oral/NG intake	NMDA receptor antagonist *Reference 72*
Pentoxifylline	Hold 2 days before surgery	Resume once tolerating oral/NG intake	

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Triptans - Almotriptan - Eletriptan - Frovatriptan - Naratriptan - Rizatriptan - Sumatriptan - Zolmitriptan	Hold AM of surgery		Some triptans have routes of metabolism that include monoamine oxidase A, CYP3A4, CYP2D6, and CYP1A2, and hence the consensus was to avoid these medications on the day of surgical procedures and use an alternative treatment for acute headache, if needed. *Reference 99*
Tamsulosin (Flomax)	Hold minimum 14 days prior to cataract surgery (earlier if possible)	Resume once tolerating oral/NG intake	Correlation between Floppy Iris Syndrome and tamsulosin during cataract surgery. Tamsulosin should be clearly documented if the patient has taken this medication anytime up to one year prior to their scheduled cataract surgery. *Reference 16*
Vitamin E	Hold for a minimum of 7 days prior to surgery	Resume once tolerating oral/NG intake and adequate hemostasis at surgical site	Inhibits platelet aggregation. *Reference 13*
Vitamins, other	Hold AM prior to surgery	Resume once tolerating oral/NG intake	If considered essential and patient's oral intake not possible for extended period of time consider IV multivitamin. *Reference 1*
Herbals			*References 1, 7, 8*
- Danshen - Dong Quai - Ginger - Fever Few	Hold 7 – 14 days prior to surgery	Do not restart if possible	Interferes with warfarin action by prolonging clotting time.
Echinacea			Long-term use may suppress the immune system. Theoretical potential for problems with postoperative wound healing and opportunistic infections.
- Garlic - Fish oil - Cod liver oil - Turmeric			Inhibits platelet aggregation. Postoperative bleeding a potential problem with the ingestion of large amounts.
Ginkgo Biloba			Inhibits platelet aggregation via inhibition of platelet-aggregation factor. Spontaneous postoperative bleeds reported including cases of intracranial bleeding

DRUG CLASS	PRE-OP	POST-OP	COMMENTS
Ginseng			Inhibits platelet aggregation, possibly irreversibly. One case report of a significant drug interaction decreasing warfarin's effect.
Kava	Hold immediately; a minimum of 24 hours prior to surgery		Increase sedative effects of anesthetic. Linked to severe liver injury.
Ma Huang (Ephedra)			Can cause increased blood pressure, tachycardia and arrhythmias. Effects are dose dependent. Drug interactions with other sympathomimetics (e.g combination with halothane) can cause ventricular arrhythmias. Endogenous catecholamines depleted with long term use, risk for intraoperative hemodynamic instability.
St. John's Wort	Hold 7 – 14 days prior to surgery		Induces cytochrome P-4503A4 enzymes therefore potential to affect metabolism of multiple drugs.
Valerian	Taper dose a few weeks prior to surgery Alternative – continue use until surgery and benzodiazepines can be sued for withdrawal symptoms.		Can increase sedative effects of anesthetics. Has the potential to cause an acute benzodiazepine like withdrawal if stopped abruptly.
Other herbals	Hold 7-14 days prior to surgery		Interactions and effects unknown.

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