UNIVERSITY OF Cincinnati department of Internal Medicine

Updates in Perioperative Medicine

AAP Conference Series

August 28, 2019

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Learning Objectives

- Manage perioperative medications in patients undergoing non-cardiac surgery
- Risk stratify patients for the likelihood of Major Adverse Cardiac Events (MACE) in the perioperative period
- Make appropriate use of preoperative diagnostic testing prior to non-cardiac surgery

A Preamble About Evidence…

- What was George Washington's most likely cause of death?

A. Smallpox
B. Epiglottitis
C. Tuberculosis
D. Exsanguination

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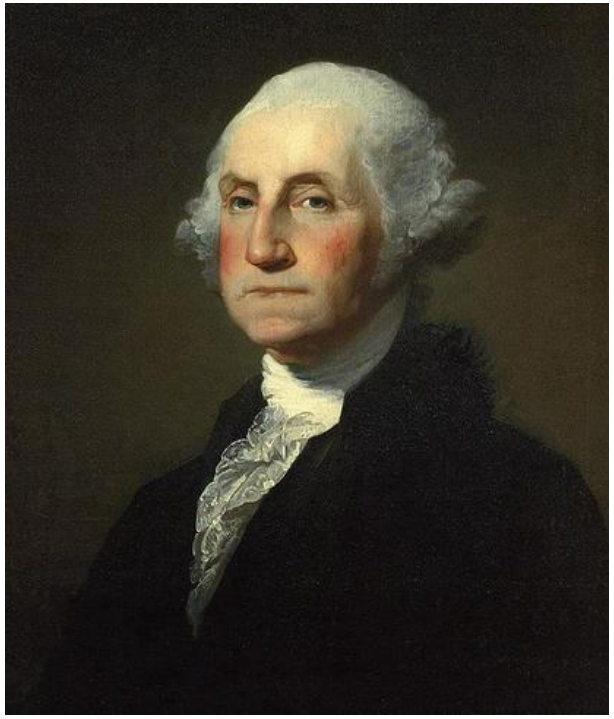
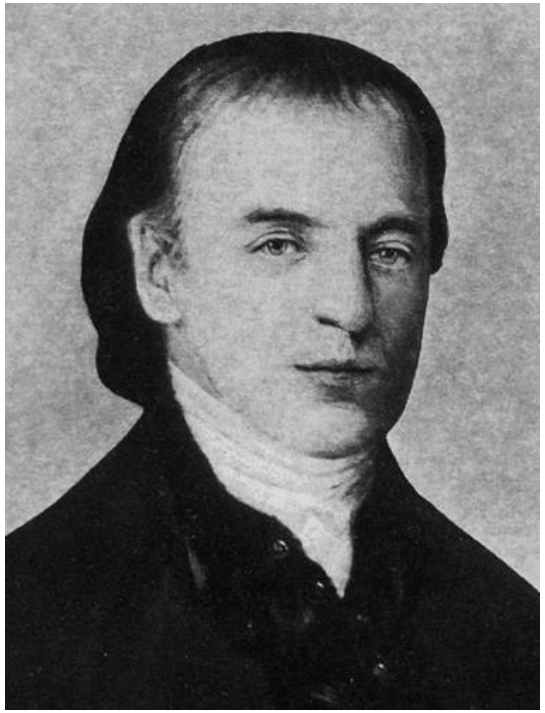
A Preamble About Evidence…

- December 13th, 1799



Washington



Craik

Question 1

- 55yo male with HTN, DM2, hyperlipidemia and CKD (serum Cr = 2.2) fell from a ladder and suffered a proximal femur fracture. Orthopedics would like to operate tomorrow morning. The patient takes ASA 81, atorvastatin, labetalol 200 TID, glargine 15 u. He is an active individual who regularly walks and engages in strenuous activity without dyspnea, fatigue, or chest pain.
  - VS: T 98.6, HR 95, BP 125/80
  - EKG: NSR with no e/o prior or current ischemia

- Which of the following management decisions is most appropriate?

A. Continue current therapy

B. Increase labetalol to control heart rate

C. Hold labetalol the morning of surgery

D. Change labetalol to metoprolol

Make your selection and we will discuss the correct answer a bit later in this presentation…

EBM = Evidence Based Murder?

Forbes

Larry Husten
Contributor

FOLLOW

I'm a medical journalist covering cardiology news.
full bio →

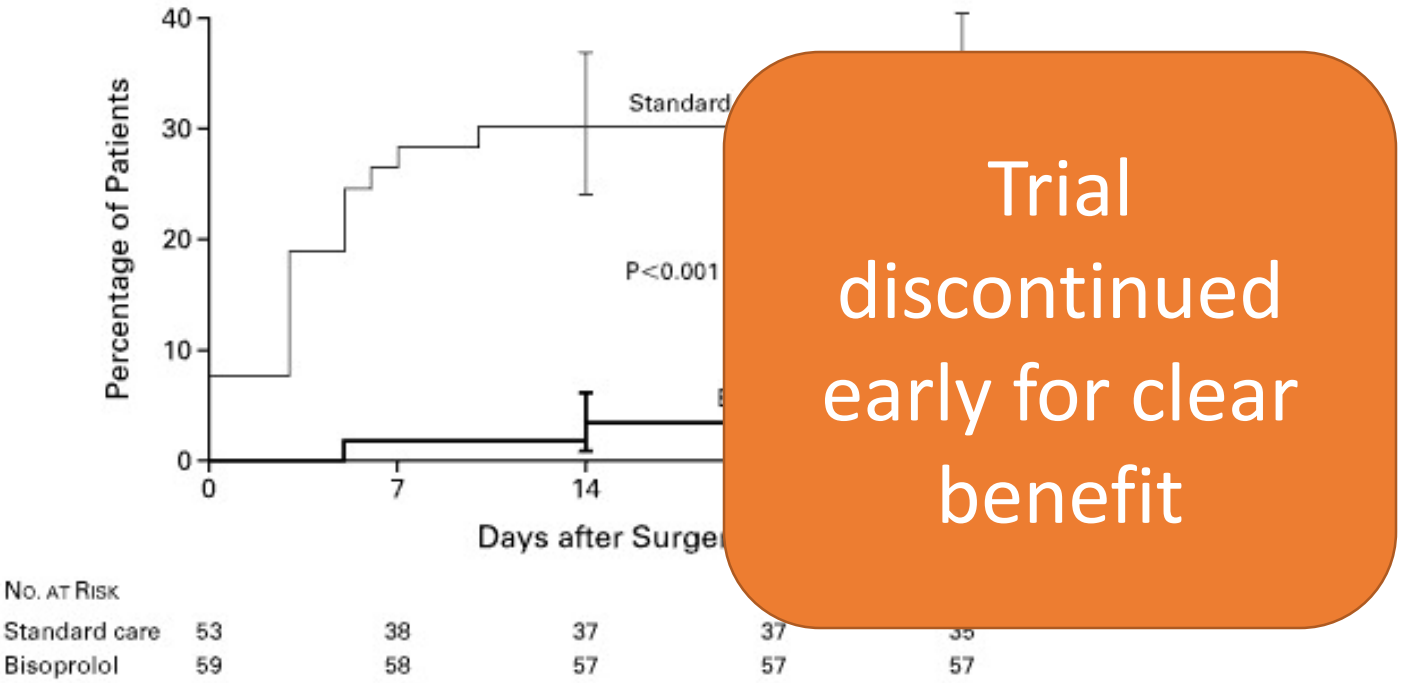
PHARMA & HEALTHCARE 1/15/2014 @ 12:37PM | 40,499 views

Medicine Or Mass Murder? Guideline Based on Discredited Research May Have Caused 800,000 Deaths In Europe Over The Last 5 Years

+ Comment Now + Follow Comments

1999: DECREASE-I

	Placebo	Bisoprolol	P value
Post-op cardiac death (%)	17	3.4	0.02
Post-op non-fatal MI (%)	17	0	<0.001



Trial discontinued early for clear benefit

Poldermans D et al. N Engl J Med 1999;341:1789-1794.

DECREASE-I Aftermath

- A handful of RCTs followed which showed neutral results
- Some non-randomized trials, underpowered trials, observational data, and some trials with zero events in either arm
- Studies were extremely heterogeneous with regard to patient populations, agents used, method of delivery, time of initiation, and duration of therapy post-op

Beta Blockers and Surgery

- 2007
  - ACC/AHA adopted Class IIb recommendation for pre-operative initiation of BB in high risk patients undergoing non-cardiac surgery

Circulation. 2007 Oct 23;116(17):e418-99. Epub 2007 Sep 27.
ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on PerioperativeCardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery.
Fleisher LA[1], Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Tarkington LG, Yancy CW.

POISE Trial

- Devereaux, et al. Lancet, 2008
- Multicenter RCT, N = 8351
  - Any (1) of the following:
    - CAD, PVD, CVA, CHF admission <3y
  - OR any (3) of the following:
    - IP/IT surgery, Hx CHF, TIA, DM, Cr >1.75, Age >70, emergent / urgent surgery
- Randomized to placebo vs. metoprolol succinate 100mg given 2-4h before surgery. A second dose of 100mg given 6 hours post-op. At 18 hours post-op, started on 200mg/d
  - End point: composite of CV death, non-fatal MI, non-fatal arrest

Lancet. 2008 May 31;371(9627):1839-47. doi: 10.1016/S0140-6736(08)60601-7. Epub 2008 May 12.
Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial.
POISE Study Group[1], Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, Xavier D, Chrolavicius S, Greenspan L, Pogue J, Pais P, Liu L, Xu S, Málaga G, Avezum A, Chan M, Montori VM, Jacka M, Choi P.

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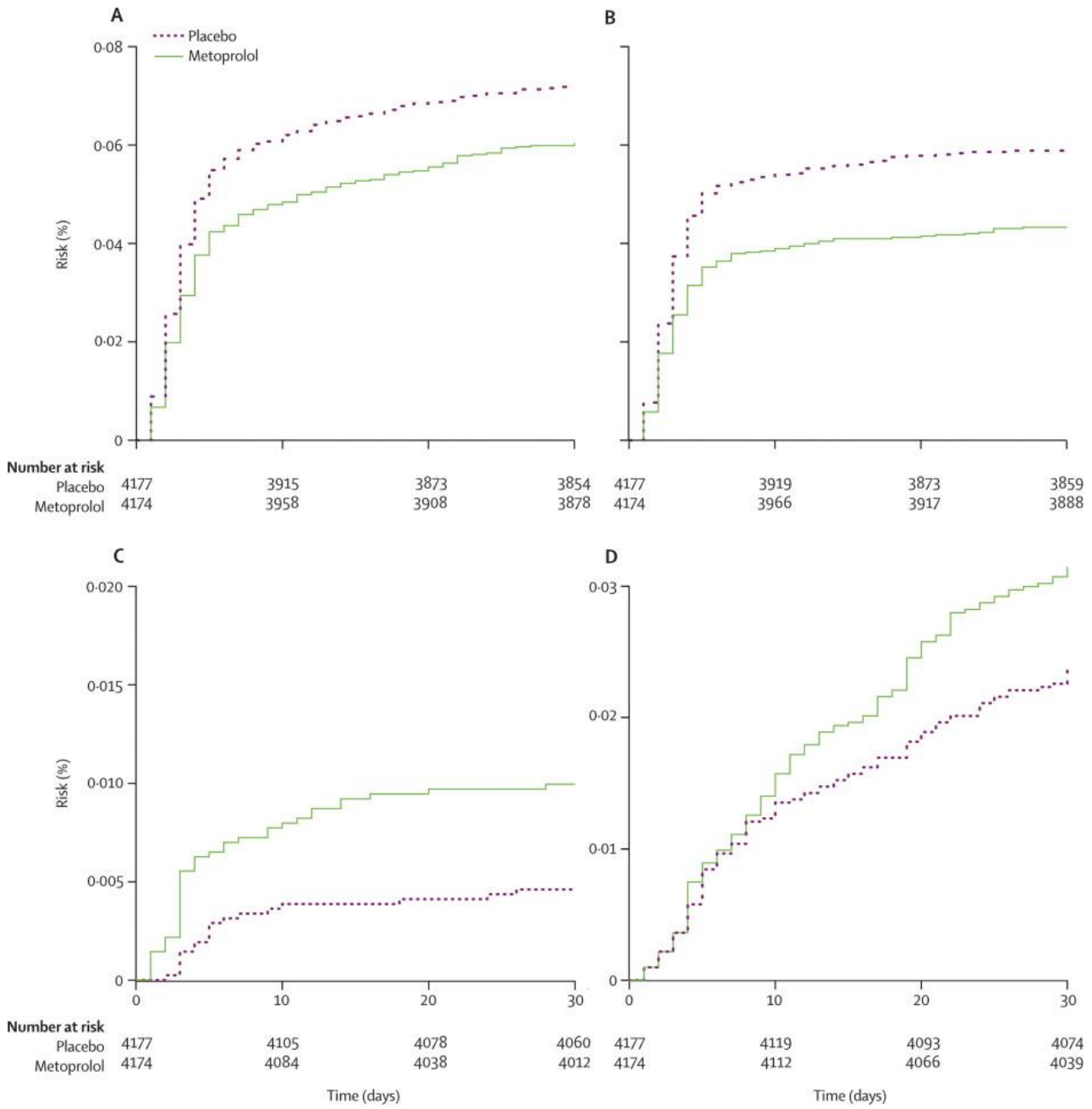
Primary outcome



MI

Stroke

Death

ESC & ACC Guidelines 2009

- European Society of Cardiology
  - Issued Class I recommendation for pre-operative beta blockade in high risk patients undergoing non-cardiac surgery
- ACC/AHA
  - Published focused update on the use of beta blockers to augment the 2007 guidelines
  - Class IIa recommendation for BB “titrated to HR and BP” for patients undergoing vascular surgery, or intermediate risk surgery with >1 risk factor

2009-2011

- Pre-op risk assessments during this time:
  - Urgency of the procedure
  - Risk attributable to type of procedure
    - High Risk = suprainguinal vascular, intraperitoneal, intrathoracic
    - Low Risk = plastic, eyeballs, and endoscopes
    - Intermediate = everything else
  - Clinical risk factors (RCRI)
    - If >1 RCRI points, we would start a beta blocker even if they were being actively wheeled to the OR

Auerbach, A and Goldman, L. Assessing and Reducing the Cardiac Risk of Noncardiac Surgery. *Circulation*. 2006;113:1361-1376.

2011

- Don Poldermans is fired by Erasmus University Medical Center for academic misconduct
- By this time, DECREASE had reached its 6th iteration, and DECREASE 1 cited >700 times
- Erasmus commissioned independent committee to review DECREASE trials
  - Falsified data & procedures, lack of rigorous blinding procedures and data security, lack of informed consent

2011-2013: Beta Blockers – Into the Void

2014: Updated ACA/AHA Guidelines

A hero emerges…

Fleisher LA, Fleischmann KE, Auerbach AD, et al. **2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines**. J Am Coll Cardiol 2014; 64:e77.

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Back to Question 1

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Issues

- Addressing chronic BB therapy (regardless of indication)
- Balancing current hemodynamic properties against chronic therapy
- Use of non-selective beta blocker / are all BB created equal?

Chronic BB Therapy

- *Beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically* (Class: I, LOE: B)
  - Several observational studies showed association with increased mortality with BB stoppage

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

Chronic BB Therapy

- *It is reasonable for the management of beta blockers after surgery to be guided by clinical circumstances, independent of when the agent was started* (Class: IIa, LOE: B)
- Consider current hemodynamics; keep HR 60-70, SBP >100 (ACC 2009, specific targets not addressed in 2014 guideline)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

Choice of Agent

- All RCTs showing perioperative mortality benefit use B1-selective drugs (metoprolol, atenolol, bisoprolol)
- Atenolol may have lower mortality vs metoprolol
- Bisoprolol may have lower stroke risk than either atenolol or metoprolol
- Non-selective BB (labetalol, carvedilol, propranolol)
  - Theoretical risk of higher pulmonary and peripheral vascular complications
  - More to come on this topic…

Wallace AW, Au S, Cason BA. Peri-operative beta-blockade: atenolol is associated with reduced mortality when compared with metoprolol. Anesthesiology 2011;**114**:824-836.

Ashes C, Judelman S, Wijeysundera DN, Tait G, Mazer CD, Hare GM, et al. Selective β1-Antagonism with Bisoprolol Is Associated with Fewer Post-operative Strokes than Atenolol or Metoprolol: A Single-center Cohort Study of 44,092 Consecutive Patients. Anesthesiology 2013;**119**:777-787.

Question 2

- 55yo male with HTN, DM2, CVA, and CKD (serum Cr = 2.2) fell from a ladder and suffered a proximal femur fracture. Orthopedics would like to operate tomorrow morning. The patient takes ASA 81, atorvastatin, amlodipine, glargine 15u. He is an active individual who regularly walks and engages in strenuous activity without dyspnea, fatigue, or chest pain.
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  - Exam: Normal
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- Which of the following management decisions is most appropriate?

A. Continue current therapy

B. Start metoprolol succinate 100mg daily

C. Start metoprolol tartrate 25mg twice daily

D. Further risk stratification with myocardial perfusion imaging

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When to Start BB?

- *In patients with 3 or more RCRI risk factors (e.g. DM, HF, CAD, CKD, CVA, high risk surgery), it may be reasonable to begin beta blockers before surgery* (Class: IIb, LOE: B)
- *In patients with intermediate or high-risk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers* (Class: IIb, LOE: C)
- *In patients in whom beta-blocker therapy is initiated, it may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, prefer- ably more than 1 day before surgery* (Class IIb, LOE: B)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

When to Start BB?

- "Beginning beta blockers <1 day before surgery is at a minimum ineffective and may in fact be harmful. Starting the medication 2 to 7 days before surgery may be preferred, but few data support the need to start beta blockers >30 days beforehand."
- *Beta-blocker therapy should not be started on the day of surgery* (Class III Harm, LOE: B)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

Question 2 Discussion

- Best answer: Continue current therapy (no beta blocker)
  - Reasoning: despite RCRI = 3, not enough time to monitor effect & titrate safely
  - *Maybe* start low dose metoprolol if the case can be safely delayed another day… the answer isn't crystal clear

BB Initiation

- Retrospective study of outcomes associated with preop BB initiation in diabetics undergoing non-cardiac surgery
- 50,952 BB users and 50,952 non-BB controls
  - 57% of study and control pts had CAD
- Stratified β–blockers:
  - Cardioprotective (atenolol, bisoprolol, metoprolol, carvedilol)
  - Other (propranolol, labetalol, etc)
- Two initiation time periods
  - >30 days preop OR ≤30 days preop

Impact of Beta-Blocker Initiation Timing on Mortality Risk in Patients With Diabetes Mellitus Undergoing Noncardiac Surgery: A Nationwide Population-Based Cohort Study. Chen RJ, Chu H, Tsai LW. J Am Heart Assoc. 2017 Jan 10;6(1)

BB Initiation

- Cardioprotective BB (compared to no BB):
  - Lower inpatient mortality (OR 0.75, 95% CI 0.68-0.82)
  - Lower 30-day mortality (OR 0.75, 95% CI 0.70-0.81)
- Timing of Initiation:
  - Cardioprotective BB for >30 d (compared to ≤30d):
    - Lower inpt mortality (OR 0.72, 95% CI 0.65-0.78)
    - Lower 30-day post-op mortality (OR 0.72, 95% CI 0.66-0.78)
    - Other BB were not associated with improved outcomes
  - Use ≤ 30 days before surgery: higher inpatient and 30d post-op mortality
- Cardioprotective BB for >30 days before surgery associated with lower mortality risk

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Estimating Clinical Risk of Peri-op MACE

- The "**intermediate**" category of risk no longer exists – please delete it from your brain!
- With the 2014 ACC/AHA guidelines, the differentiation has been simplified to "low" (<1%) risk, and "elevated" (≥1%) risk of **major adverse cardiac events** (**MACE**)
- RCRI (0-1 = low*)
  - http://www.mdcalc.com/revised-cardiac-risk-index-for-pre-operative-risk/
- ACS NSQIP Surgical Risk Calculator
  - http://www.riskcalculator.facs.org/PatientInfo/PatientInfo
- Gupta MICA Calculator
  - http://www.qxmd.com/calculate-online/cardiology/gupta-perioperative-cardiac-risk

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

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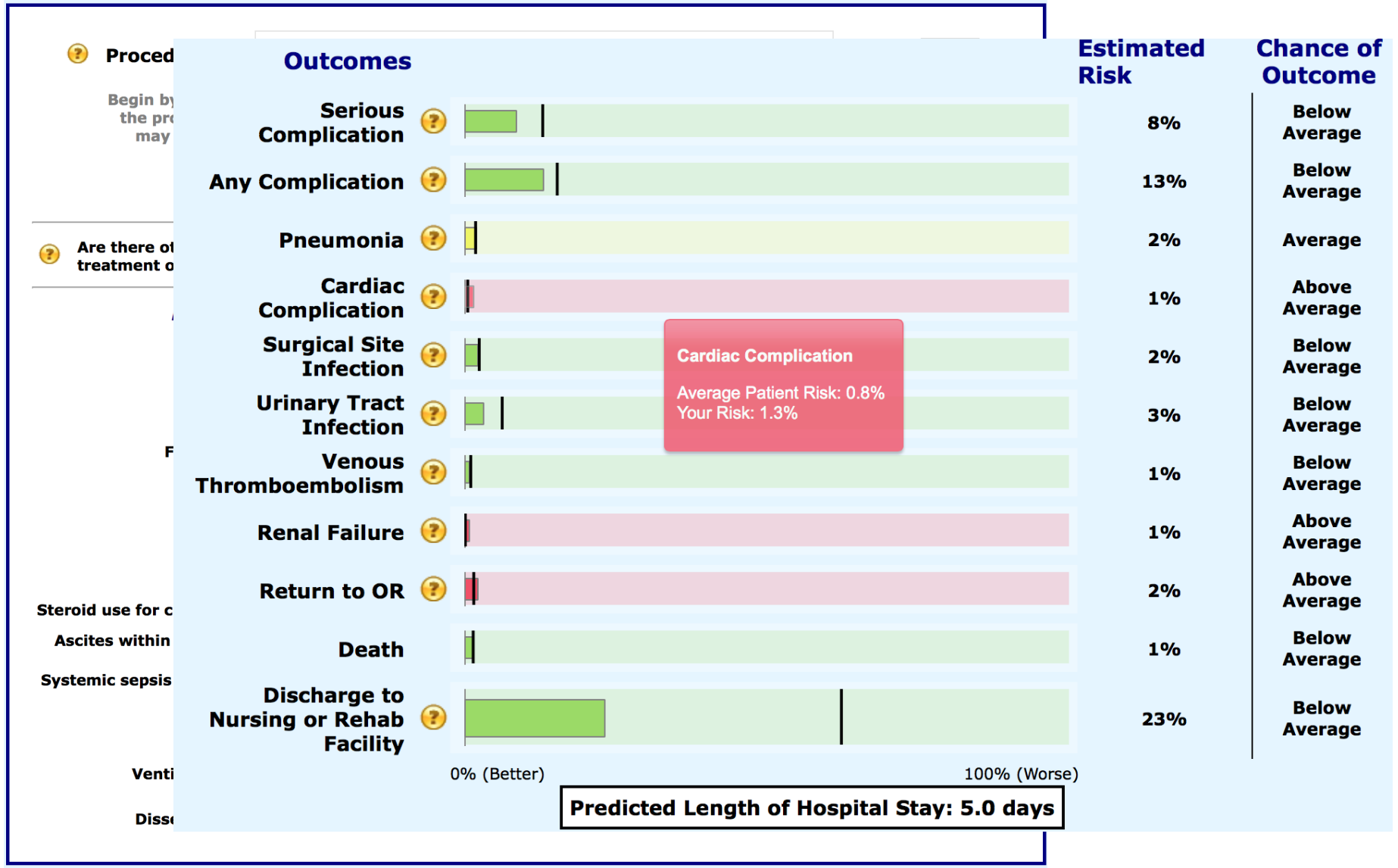
ACS NSQIP Risk Calculator



Estimating Risk of MACE

- CLASS IIa: *A validated risk-prediction tool can be useful in predicting the risk of perioperative MACE in patients undergoing noncardiac surgery* (Level of Evidence: B)
- CLASS III NO BENEFIT: *For patients with a low risk of perioperative MACE, further testing is not recommended before the planned operation* (Level of Evidence: B)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

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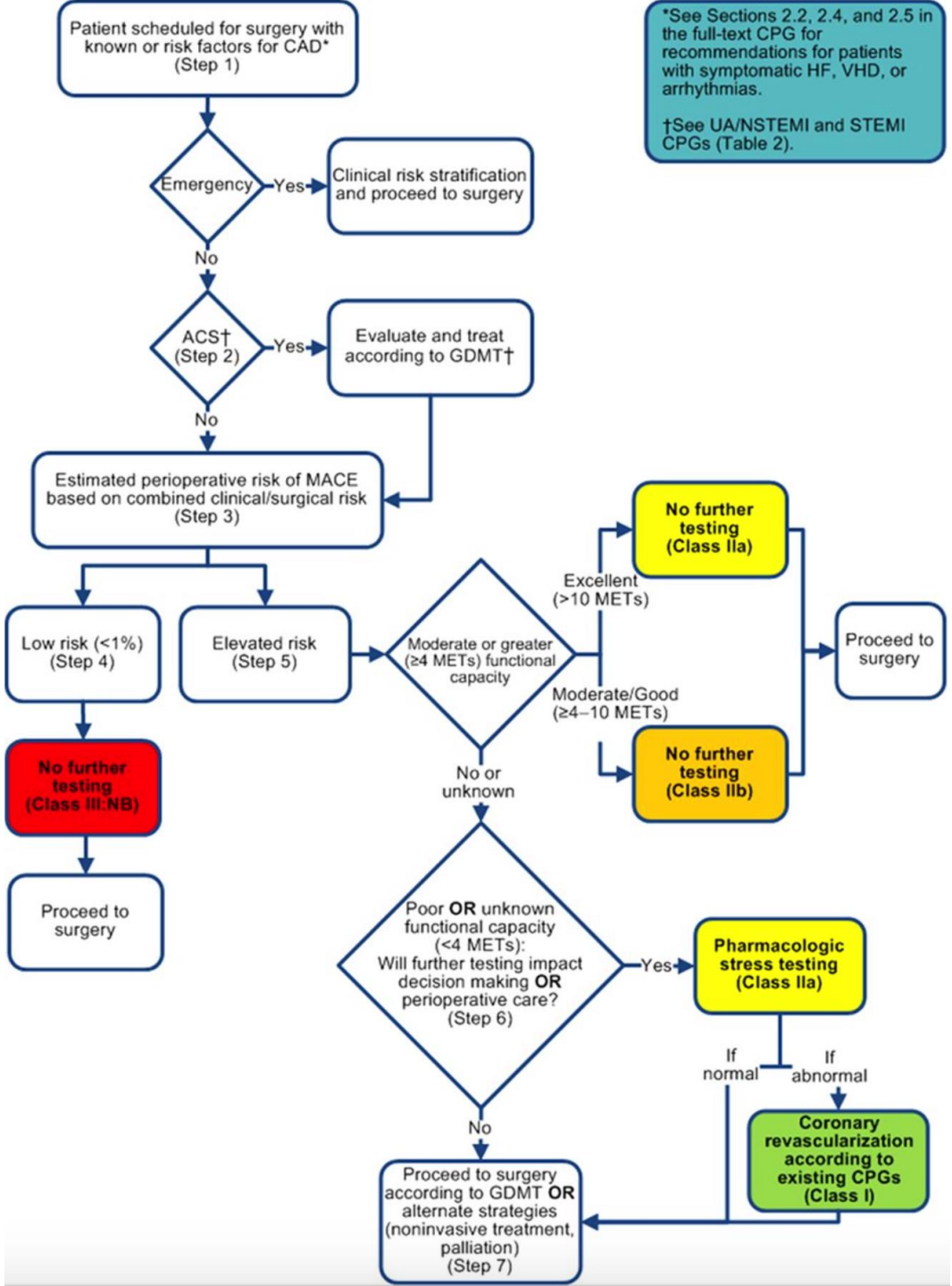
2014 Updated Preoperative Algorithm



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Question 3

- 62yo female with no PMH presents from home after a fall in which she sustained a hip fracture. Physical exam reveals +S3, JVD, peripheral edema, orthopnea. BNP is 550, and SCr 3.3. CXR shows mild pulmonary edema. BP is 180/92. Surgery is delayed for TTE, which reveals EF 25%, no WMAs.

- Which of the following management decisions is most appropriate?

A. Proceed to the operating room
B. Initiate BB and proceed to the operating room
C. Delay surgery for diuresis
D. Delay surgery for diuresis and BB initiation

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C. Delay surgery for diuresis
D. Delay surgery for diuresis and BB initiation

Question 3 Answer

- "C" – delay surgery for diuresis, then proceed to OR; expert consultation is advised for urgent settings
- The patient has an "active cardiac condition" (decompensated heart failure, ACS, arrhythmia) which needs to be medically optimized prior to surgery
- BB titration in heart failure patients takes weeks to be done safely
  - Abrupt start before the physiologic stress of surgery may result in unpredictable adverse events in this vulnerable category of patients
- Hip fracture literature would urge that she undergo repair <48h
  - Must weigh the risks and benefits for each patient

When to Stop the Line?

Table 2. Active Cardiac Conditions for Which the Patient Should Undergo Evaluation and Treatment Before Noncardiac Surgery (Class I, Level of Evidence: B)

Condition	Examples
Unstable coronary syndromes	Unstable or severe angina* (CCS class III or IV)† Recent MI‡ Bare-metal stent placement in the last 6 weeks§ Drug-eluting stent placement in the last year§
Decompensated HF (NYHA functional class IV; worsening or new-onset HF)	
Significant arrhythmias	High-grade atrioventricular block Mobitz II atrioventricular block Third-degree atrioventricular heart block Symptomatic ventricular arrhythmias Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR >100 bpm at rest) Symptomatic bradycardia Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient >40 mm Hg, aortic valve area <1 cm^2, or symptomatic) Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

CCS = Canadian Cardiovascular Society; HF = heart failure; HR = heart rate; MI = myocardial infarction; NYHA = New York Heart Association.
*According to Campeau.
†May include "stable" angina in patients who are unusually sedentary.
‡The American College of Cardiology National Database Library defines recent MI as >7 days but ≤1 month (within 30 days).
§Stent placement added by the authors of this module.
Fleisher et al. *Circulation*. 2007.*

Recent Cardiac PTCA/PCI

- 2016 ACC update on DAPT
  - DES
    - Elective surgery should optimally be delayed 6 months
    - May be considered after 3 months if the risk of further delay > expected risks of ischemia and stent thrombosis
  - BMS
    - Elective surgery should be postponed for at least 30 days
- 2017 ESC update on DAPT
  - Elective surgery requiring interruption of P2Y12-inh may be considered after 1 month, irrespective of the stent type, if aspirin can be maintained throughout the perioperative period
  - In patients with recent MI or other high ischemic risk features requiring DAPT, elective surgery may be postponed for up to 6 months
- Patients who have undergone PTCA without stent placement should not undergo non-emergent surgery within 2 weeks
- Always continue aspirin if surgeon will allow

Levine GN, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in PatientsWith Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016 Sep 6;68(10):1082-115.

Question 4

- 54yo male with HTN, smoker, CKD (Cr 2.1), hyperlipidemia seen in consultation before an aortobifemoral bypass in 2 weeks. He takes lisinopril 20, amlodipine 10, rosuvastatin 10. Works in a factory carrying heavy steel cable and denies angina or DOE. No prior cardiac history. Negative EKG. BP is 139/90, HR 85. Exam is unremarkable.

- Which of the following management decisions is most appropriate?

A. Obtain pharmacologic stress test
B. Initiate low dose metoprolol and operate as planned
C. Initiate low dose metoprolol and return in one week for titration
D. Proceed to surgery without additional interventions

Question 4

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Question 4 Discussion

- Proceed to surgery
  - 2014 guidelines recommend beta blocker initiation for RCRI ≥3 (his was 2, for supra-inguinal vascular surgery and creatinine >2)
  - Elevated risk of MACE, but good functional status
    - No need for stress test

To Stress or Not to Stress?

- If a patient is found to be at elevated risk of MACE for an elective procedure, the guidelines still recommend assessment of functional status as the next decision point
- <4 METs, or indeterminate, reasonable to obtain pharmacologic stress test (Class IIa) *if the results of such testing will change management*

Stress Testing Pitfalls

- Dobutamine Echo
  - Sn 85% Sp 70%; LR+ 2.8; LR- 0.21
  - False positives in setting of LBBB from septal wall motion abnormalities
- Myocardial Perfusion Imaging
  - Sn 83%, Sp 49%; LR+ 1.6, LR- 0.35
  - Dipyridamole or adenosine may cause bronchospasm and is usually avoided in patients with COPD (Regadenoson less so, but still avoided in patients with severe asthma/COPD)
- Both tests have marginal LR+ & LR-
  - Positive test does not significantly increase the likelihood of a low/intermediate risk patient having an event
  - Negative test will not reassure us that high-risk patient will *not* have an event
- **Predictive power of stress testing is poor** and does not accurately predict which patients will have a perioperative cardiac event
  - Consider only for clinically high-risk patients, where a positive test will lead to delay of surgery, revascularization, non-surgical treatment, or palliation

Kertai MD, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart. 2003 Nov;89(11):1327-34.

J Nucl Cardiol. 2012 Aug;19(4):681-92. doi: 10.1007/s12350-012-9547-4. Epub 2012 Apr 7.

A randomized, double-blind, placebo-controlled study assessing the safety and tolerability of regadenoson in subjects with asthma or chronic obstructive pulmonary disease.

Prenner BM[1], Bukofzer S, Behm S, Feaheny K, McNutt BE.

Question 5

- 68yo F with CVA 1y ago, HTN, CKD (SCr 2.5), DM on insulin (A1c = 12), CABG 2y ago, HFrEF with an EF of 35% 9 months ago, is in your clinic on Friday at 5pm for a pre-op exam prior to cataract surgery on Tuesday.
- She reports that her mobility is limited to going from bed to chair, but this is not changed from the time of her last stroke. She has 2-pillow orthopnea but this is also not changed over 12 months.
- She takes insulin, aspirin, carvedilol, lisinopril, atorvastatin, torsemide. Exam reveals normal vital signs, normal heart sounds, clear lungs, and trace ankle edema which the patient says is chronic.

- Which of the following diagnostic tests should be obtained prior to the patient going to surgery?

A. EKG
B. Echocardiogram
C. NTpBNP
D. Both A and C
E. Both B and C
F. All of the above
G. None of the above

Question 5 Answer

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G. None of the above

Question 5 Discussion

- Patient with “elevated risk” of MACE based on clinical risk factors, but no active cardiac conditions, going for low risk surgery should proceed to the operation without additional testing

Preoperative EKG

- CLASS IIa
  - *Preoperative resting 12-lead electrocardiogram (ECG) is reasonable for patients with known coronary heart disease, significant arrhythmia, peripheral arterial disease, cerebro- vascular disease, or other significant structural heart disease, except for those undergoing low-risk surgery*. (Level of Evidence: B)
- CLASS IIb
  - *Preoperative resting 12-lead ECG may be considered for asymptomatic patients without known coronary heart disease, except for those undergoing low-risk surgery*. (Level of Evidence: B)
- CLASS III: NO BENEFIT
  - *Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures*. (Level of Evidence: B)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

Preoperative Echocardiogram

- CLASS IIa
  - *It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function*. (Level of Evidence: C)
  - *It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function*. (LOE: C)
- CLASS IIb
  - *Reassessment of LV function in clinically stable patients with previously documented LV dysfunction may be considered if there has been no assessment within a year*. (LOE: C)
- CLASS III: NO BENEFIT
  - *Routine preoperative evaluation of LV function is not recommended*. (LOE: B)

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.

Preoperative BNP

- No official recommendation from ACC/AHA at this time regarding preoperative BNP/NTpBNP
  - "*Preoperative natriuretic peptide levels independently predict cardiovascular events in the first 30 days after vascular surgery and significantly improve the predictive performance of the Revised Cardiac Risk Index (RCRI)*."
- Canadian Cardiovascular Society:
  - "*We recommend measuring NTpBNP or BNP before non-cardiac surgery to enhance perioperative cardiac risk estimation in patients who are 65 years of age or older, are 45-64 years of age with significant cardiovascular disease, or have an RCRI score ≥ 1 (Strong Recommendation; Moderate-Quality Evidence)*."

Can J Cardiol. 2017 Jan;33(1):17-32. doi: 10.1016/j.cjca.2016.09.008. Epub 2016 Oct 4.
Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery.
Duceppe E[1], Parlow J[2], MacDonald P[3], Lyons K[4], McMullen M[5], Srinathan S[6], Graham M[7], Tandon V[8], Styles K[9], Bessissow A[10], Sessler DI[11], Bryson G[12], Devereaux PJ[13].

Preoperative BNP

Meta-analysis of 2179 patients from 18 studies

Risk of **death or myocardial infarction at 30 days** after non-cardiac surgery, based upon a patient's preoperative NT-proBNP or BNP result

Test result	Risk estimate, %	95% CI for the risk estimate
NT-proBNP < 300 ng/L or BNP < 92 mg/L	4.9	3.9%-6.1%
NT-proBNP value ≥ 300 ng/L or BNP ≥ 92 mg/L	21.8	19.0%-24.8%

Recommend closer postoperative surveillance with a postoperative ECG in the PACU and troponins for the first 48-72 hours

Can J Cardiol. 2017 Jan;33(1):17-32. doi: 10.1016/j.cjca.2016.09.008. Epub 2016 Oct 4.
Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery.
Duceppe E[1], Parlow J[2], MacDonald P[3], Lyons K[4], McMullen M[5], Srinathan S[6], Graham M[7], Tandon V[8], Styles K[9], Bessissow A[10], Sessler DI[11], Bryson G[12], Devereaux PJ[13].

Can't Cover it All…

- Perioperative statins (start 'em)
  - **Association of Perioperative Statin Use with Mortality and Morbidity After Major Noncardiac Surgery**. London MJ et al. *JAMA Intern Med*. 2017 Feb 1;177(2):231-242. PMID:7992624
- Perioperative ACE/ARB (stop 'em)
  - **Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery**. Roshanov PS, et al. *Anesthesiology*. 2017;126(1):16-27.
- Perioperative DOAC management (stop 'em, don't bridge 'em)
  - **2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation**. Doherty JU, Gluckman TJ, Hucker WJ et al. *J Am Coll Cardiol*. 2017 Feb 21;69(7):871- 898. doi: 10.1016/j.jacc.2016.11.024. Epub 2017 Jan 9.

Perioperative Statins

- A subject of controversy and no official recommendation exists
  - RCTs of dubious security (DECREASE III/IV)
  - Observational data
  - Mixed result meta-analyses depending upon inclusion/exclusion of DECREASE
- **Association of Perioperative Statin Use with Mortality and Morbidity After Major Noncardiac Surgery**. London MJ et al. *JAMA Intern Med*. 2017 Feb 1;177(2):231-242. PMID:7992624
  - Retrospective observational study utilizing VA SQIP database
  - 96486 patients in propensity matched cohorts
  - +/- Statin exposure from day of, or day after non-cardiac surgery

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- Statin exposure in propensity-matched cohort had significant reduction in:
  - 30d all cause mortality
  - Cardiac arrest
  - Q-wave MI
  - Sepsis & wound infection
  - Respiratory complications
  - Any non-fatal complication

Table 4. 30-Day Postoperative Outcomes

	Statin Exposure, % of Patients							
	Entire Cohort				Matched Cohort			
Variable	Exposed (n = 56 939)	Nonexposed (n = 123 539)	*P* Value	All (N = 180 478)	Exposed (n = 48 243)	Nonexposed (n = 48 243)	*P* Value	All (n = 96 486)
30-d All-cause mortality	1.8	2.4	<.001	2.2	1.8	2.3	<.001	2.0
Cardiac complications								
Cardiac arrest	0.7	0.8	.03	0.8	0.7	0.9	.001	0.8
Q-wave MI infarction	0.5	0.4	<.001	0.4	0.5	0.6	.02	0.5
Composite	0.8	1.0	.03	0.9	0.8	1.1	<.001	1.0
CNS complications								
Cerebrovascular accident	0.5	0.3	<.001	0.4	0.4	0.5	.39	0.5
Coma	0.1	0.2	.10	0.1	0.1	0.1	>.99	0.1
Composite	0.4	0.4	.60	0.4	0.4	0.4	.38	0.4
Thrombotic complications								
DVT or thrombophlebitis	0.7	0.7	.02	0.7	0.7	0.8	.06	0.7
Pulmonary embolism	0.5	0.6	.07	0.5	0.5	0.5	.48	0.5
Graft failure	0.3	0.2	<.001	0.2	0.3	0.3	.47	0.3
Composite	1.3	1.2	.19	1.3	1.2	1.3	.07	1.3
Infection complications								
Sepsis	2.0	2.9	<.001	2.6	2.1	2.5	<.001	2.3
Organ space	0.5	1.0	<.001	0.9	0.6	0.6	.33	0.6
Deep wound	0.8	1.1	<.001	1.0	0.8	0.9	.01	0.9
Composite	2.8	4.2	<.001	3.8	2.9	3.4	<.001	3.2
Respiratory complications								
Failure to wean	1.8	3.2	<.001	2.8	1.9	2.6	<.001	2.3
Pneumonia	2.2	3.2	<.001	2.9	2.3	2.9	<.001	2.6
Reintubation	2.2	2.9	<.001	2.7	2.2	3.0	<.001	2.6
Composite	3.4	5.1	<.001	4.6	3.5	4.5	<.001	4.0
Renal complications								
Acute renal failure	0.5	0.6	.002	0.6	0.5	0.6	.08	0.5
Progressive renal insufficiency	0.8	0.8	.74	0.8	0.8	0.9	.052	0.8
Composite	1.0	1.2	.009	1.1	1.0	1.2	.005	1.1
Any nonfatal complication	6.9	9.2	<.001	8.5	7.0	8.5	<.001	7.7

Abbreviations: CNS, central nervous system; DVT, deep vein thrombosis; LOS, length of stay; MI, myocardial infarction.

Perioperative Statins

- Limitations in the VA study
  - Observational study, risk of selection bias
  - No measure of biochemical MI
  - Statin prescription was used as a surrogate for statin administration
  - Adverse effects of statins not measured

Perioperative ACEi/ARB

- **Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery**. Roshanov PS, et al. *Anesthesiology*. 2017;126(1):16-27
  - Prospective cohort study
  - 4800 patient subgroup of ACE/ARB users at baseline
  - 1245 (25.9%) patients had medication witheld 24 hours prior to surgery
    - Characteristics of these patients similar to those who continued therapy, with the exception that they were less likely to have very high preop BP
  - 18% reduction in the relative risk of the composite outcome of death, stroke, or MINS (adjusted relative risk [aRR], 0.82; 95% CI, 0.70 to 0.96; $P = 0.01$)
  - 20% reduction in the relative risk of intraoperative hypotension (aRR, 0.80; 95% CI, 0.73 to 0.88; $P < 0.001$)

Perioperative ACEi/ARB

- **Nielson et al, J Hosp Med 2014**
  - Retrospective review, 922 patients undergoing spinal fusion, TKR, or THR
    - 343 received ACE or ARB (37%) prior to surgery
  - Higher rates of post-induction hypotension (SBP<80), 12.2% vs. 6.7%
  - 798 patients had both pre- and post-op creatinine documented
    - Post-op AKI 8.3% in ACE group vs. 1.7% (remained significant after adjustment for hypotension)
  - Post-op AKI increased mean LOS more than 2 days

Perioperative Anticoagulation

- **2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation**. Doherty JU, Gluckman TJ, Hucker WJ et al. *J Am Coll Cardiol*. 2017 Feb 21;69(7):871- 898. doi: 10.1016/j.jacc.2016.11.024. Epub 2017 Jan 9.
- Pay attention to population restriction for this guideline – NVAF only
- Busy but functional algorithm
- Great teaching reference

Perioperative Anticoagulation

- VKA or DOAC therapy
  - Step 1: Whether to interrupt
    - Assess patient-specific bleeding risk (increased if any are present)
      - Major bleed or ICH within past 3 months
      - Platelet abnormality (including ASA use)
      - Supratherapeutic INR
      - Prior bleed during bridging or similar surgical procedure
    - Assess procedure-specific bleeding risk
  - Step 2: When to interrupt
    - For VKA, therapy stopped 3-5 days prior depending upon INR, repeat INR 24 hours before procedure
    - For DOAC
      - Based on bleeding risk and creatinine clearance

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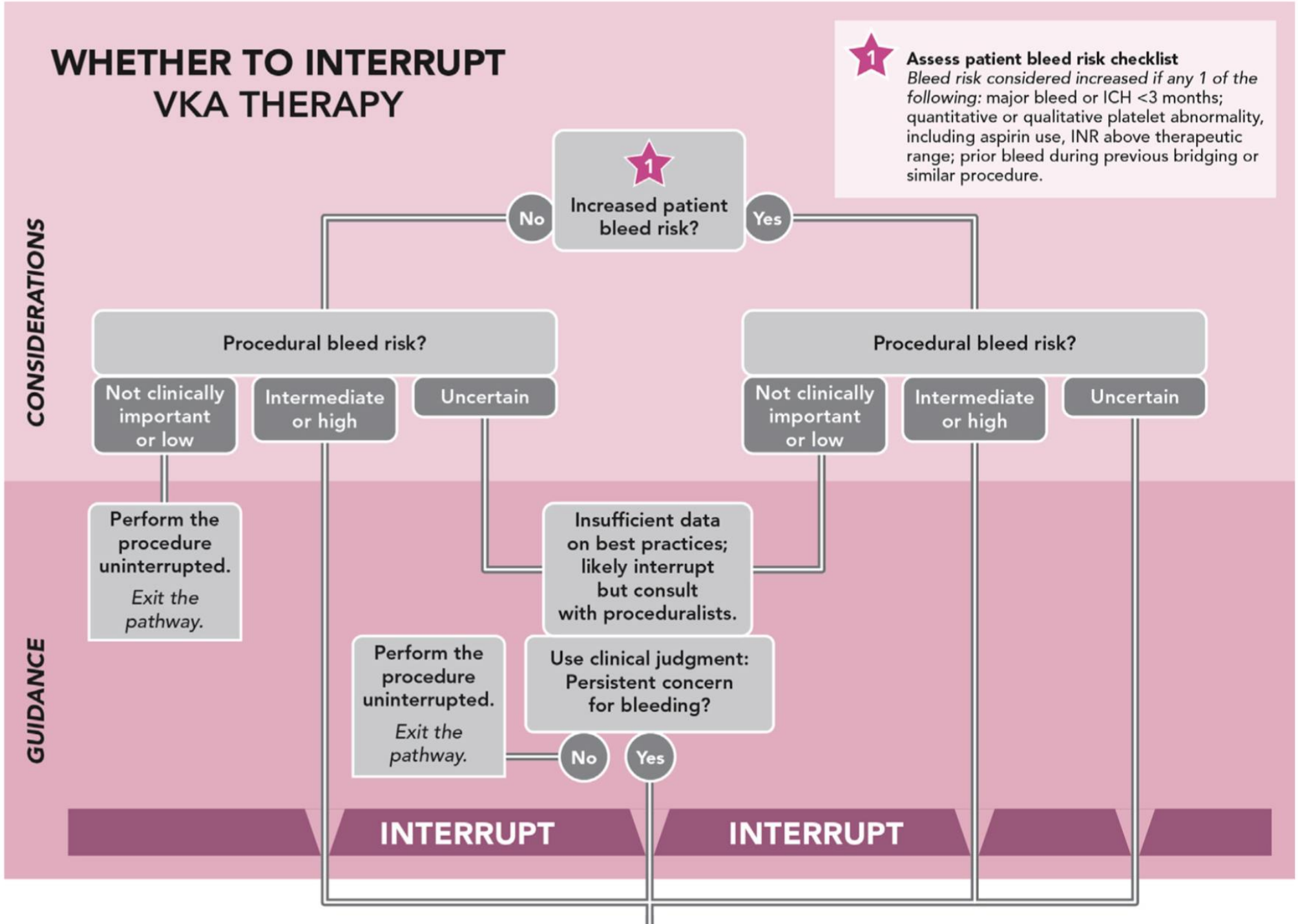
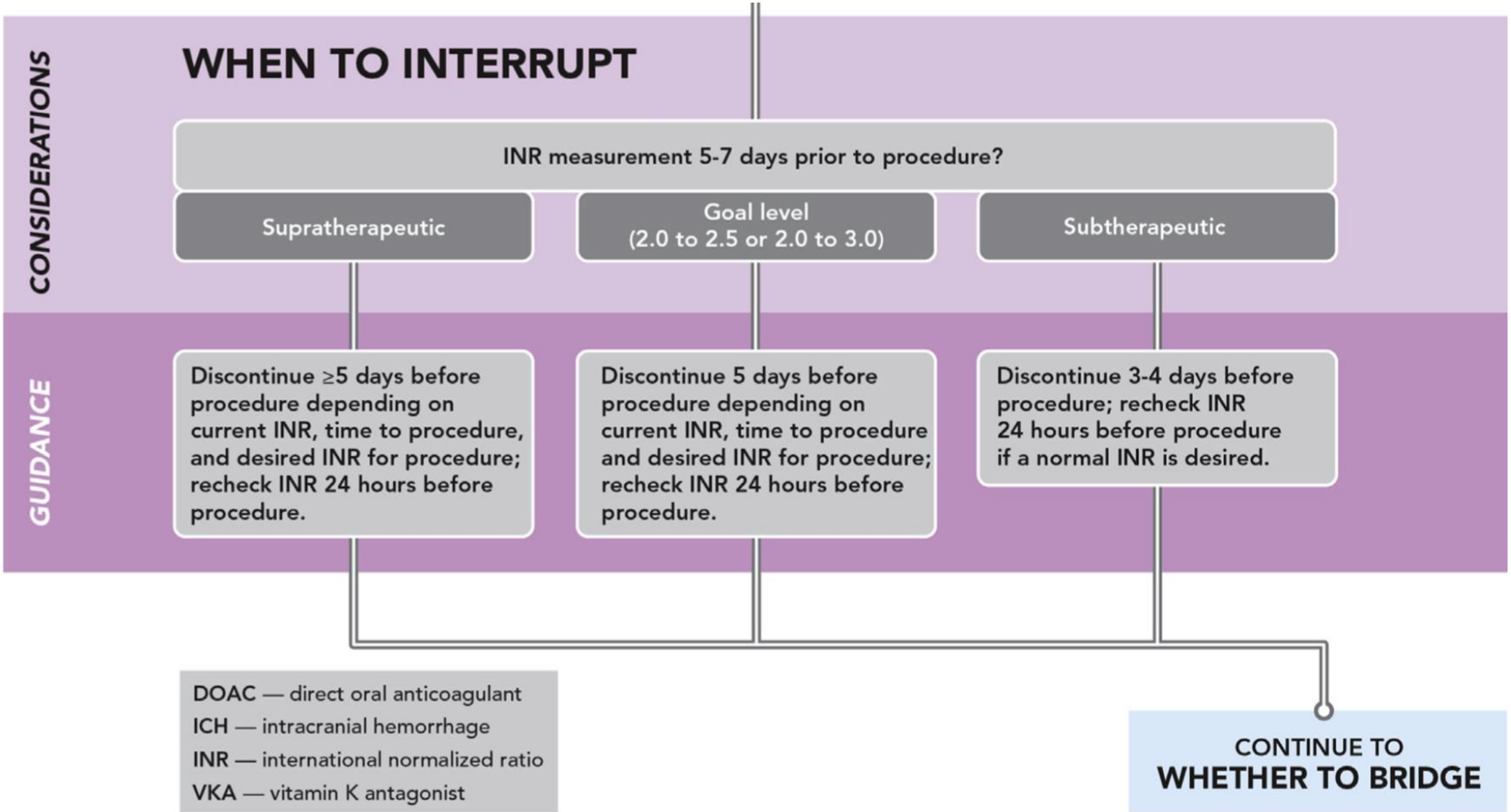
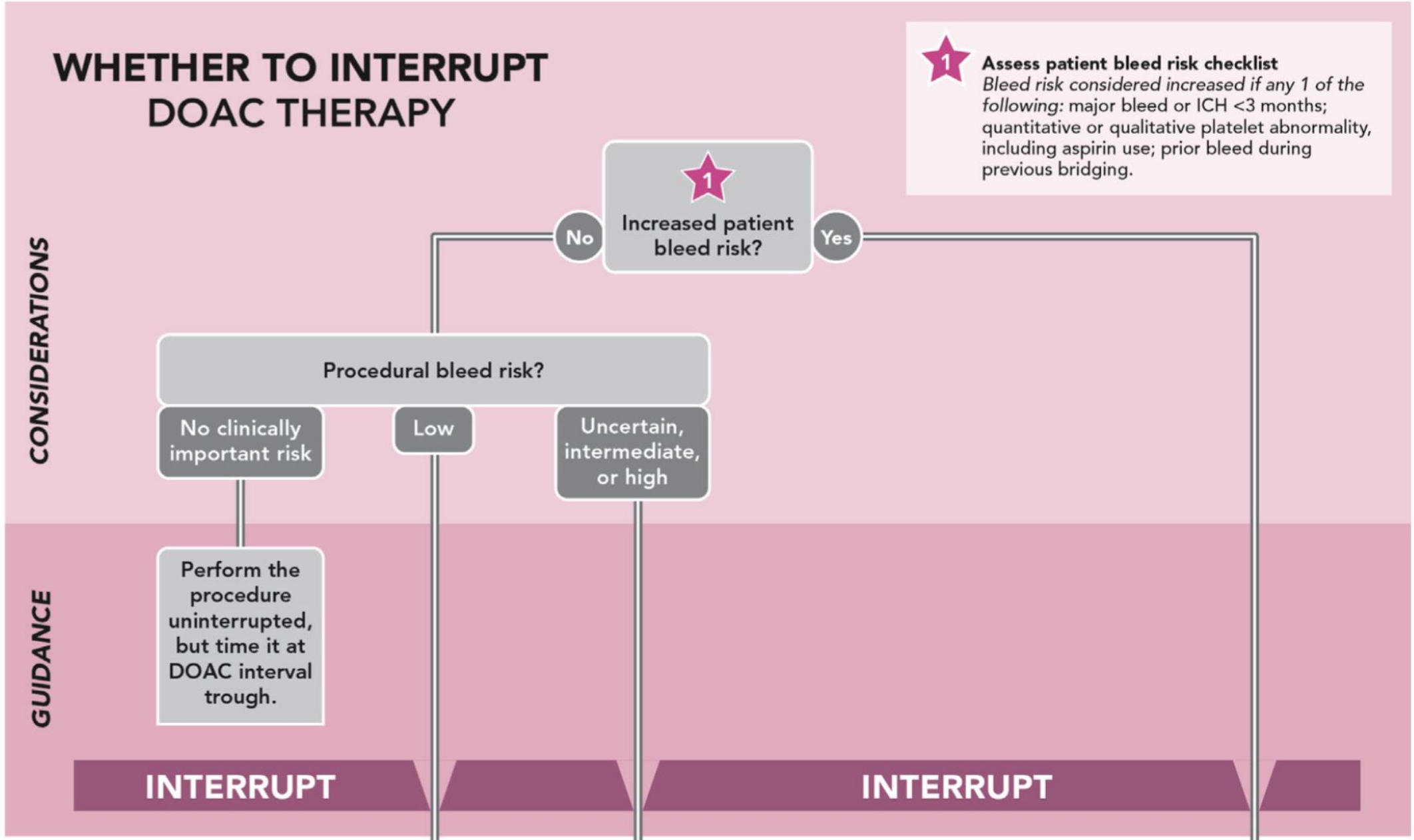
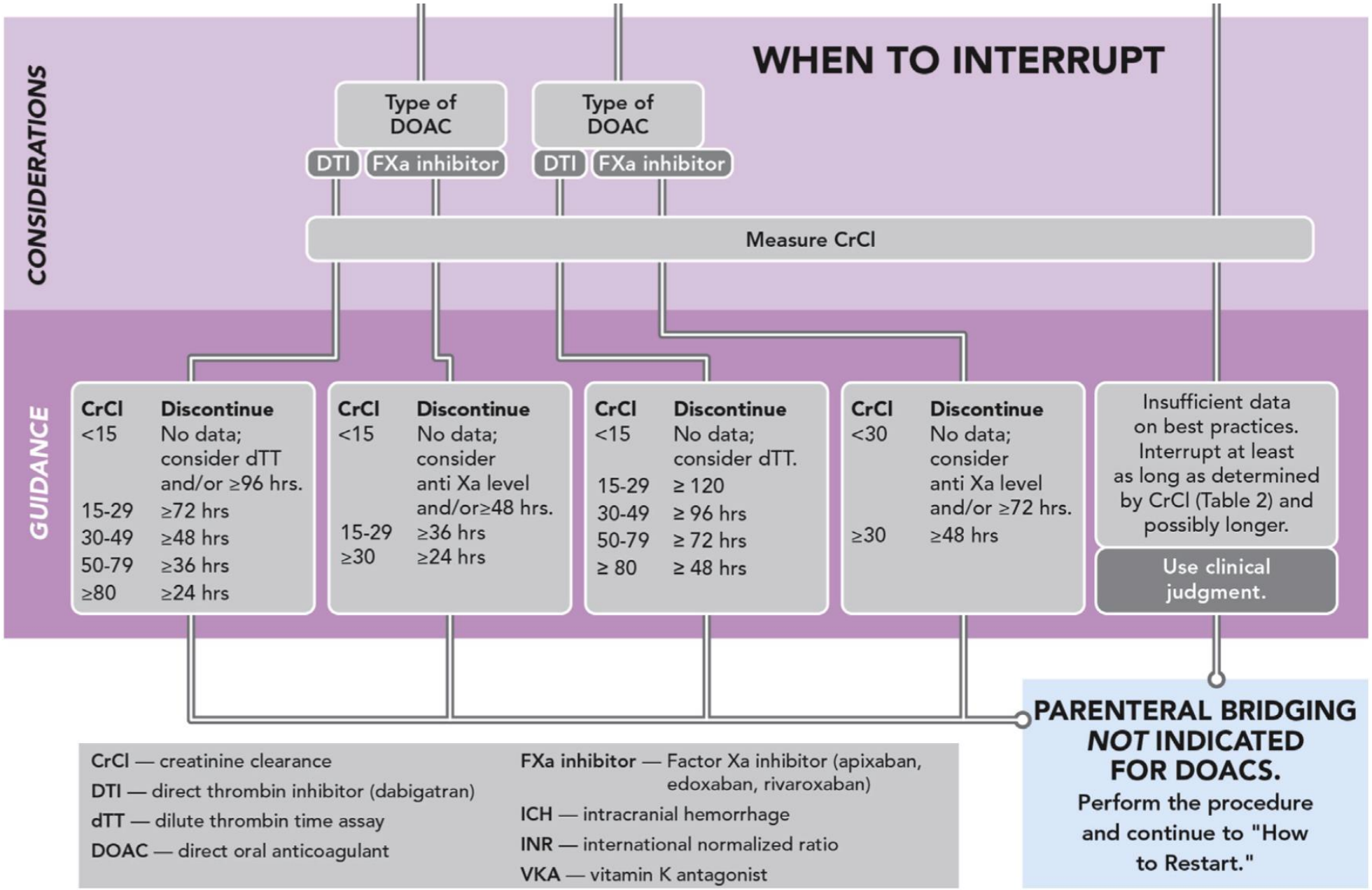
WHETHER TO INTERRUPT VKA THERAPY




CONSIDERATIONS
WHEN TO INTERRUPT
INR measurement 5-7 days prior to procedure?
Supratherapeutic
Goal level (2.0 to 2.5 or 2.0 to 3.0)
Subtherapeutic
GUIDANCE
Discontinue ≥5 days before procedure depending on current INR, time to procedure, and desired INR for procedure; recheck INR 24 hours before procedure.
Discontinue 5 days before procedure depending on current INR, time to procedure and desired INR for procedure; recheck INR 24 hours before procedure.
Discontinue 3-4 days before procedure; recheck INR 24 hours before procedure if a normal INR is desired.
DOAC — direct oral anticoagulant
ICH — intracranial hemorrhage
INR — international normalized ratio
VKA — vitamin K antagonist
CONTINUE TO
WHETHER TO BRIDGE


WHETHER TO INTERRUPT DOAC THERAPY
1
Assess patient bleed risk checklist
Bleed risk considered increased if any 1 of the following: major bleed or ICH <3 months; quantitative or qualitative platelet abnormality, including aspirin use; prior bleed during previous bridging.
CONSIDERATIONS
1
Increased patient bleed risk?
No
Yes
Procedural bleed risk?
No clinically important risk
Low
Uncertain, intermediate, or high
GUIDANCE
Perform the procedure uninterrupted, but time it at DOAC interval trough.
INTERRUPT
INTERRUPT


WHEN TO INTERRUPT
CONSIDERATIONS
Type of DOAC
DTI
FXa inhibitor
Type of DOAC
DTI
FXa inhibitor
Measure CrCl
GUIDANCE
CrCl Discontinue
<15 No data; consider dTT and/or ≥96 hrs.
15-29 ≥72 hrs
30-49 ≥48 hrs
50-79 ≥36 hrs
≥80 ≥24 hrs
CrCl Discontinue
<15 No data; consider anti Xa level and/or≥48 hrs.
15-29 ≥36 hrs
≥30 ≥24 hrs
CrCl Discontinue
<15 No data; consider dTT.
15-29 ≥ 120
30-49 ≥ 96 hrs
50-79 ≥ 72 hrs
≥ 80 ≥ 48 hrs
CrCl Discontinue
<30 No data; consider anti Xa level and/or ≥72 hrs.
≥30 ≥48 hrs
Insufficient data on best practices. Interrupt at least as long as determined by CrCl (Table 2) and possibly longer.
Use clinical judgment.
PARENTERAL BRIDGING NOT INDICATED FOR DOACS.
Perform the procedure and continue to "How to Restart."
CrCl — creatinine clearance
DTI — direct thrombin inhibitor (dabigatran)
dTT — dilute thrombin time assay
DOAC — direct oral anticoagulant
FXa inhibitor — Factor Xa inhibitor (apixaban, edoxaban, rivaroxaban)
ICH — intracranial hemorrhage
INR — international normalized ratio
VKA — vitamin K antagonist

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DOAC Half Lives and Interruption Guide

TABLE 2 **Recommended Durations for Withholding DOACs Based on Procedural Bleed Risk and Estimated CrCl When There Are No Increased Patient Bleed Risk Factors**

	Dabigatran					Apixaban, Edoxaban, or Rivaroxaban		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13	15	18	27	30 (off dialysis)	6–15	Apixaban: 17 Edoxaban: 17 Rivaroxaban: 9	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk								
Low	≥24 h	≥36 h	≥48 h	≥72 h	No data. Consider measuring dTT and/or withholding ≥96 h.	≥24 h	≥36 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥48 h
Uncertain, intermediate, or high	≥48 h	≥72 h	≥96 h	≥120 h	No data. Consider measuring dTT.	≥48 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥72 h.	

NOTE: The duration for withholding is based upon the estimated DOAC half-life withholding times of 2 to 3 half-lives for low procedural bleeding risk and 4 to 5 drug half-lives for uncertain, intermediate, or high procedural bleeding risk (46,60-67).

CrCl = creatinine clearance; DOAC = direct-acting oral anticoagulant; dTT = dilute thrombin time.

VKA Interruption

- CHA_2DS_2-VASc ≤ 4, and no stroke, TIA, or arterial clot
  - Interrupt without bridge
- CHA_2DS_2-VASc 5-6, or stroke, TIA, or arterial clot ≥ 3 mos old
  - Increased bleeding risk
    - Interrupt without bridge
  - Average bleeding risk
    - With stroke, TIA, or arterial clot ≥ 3 mos ago → bridge
    - Without prior stroke, TIA, or arterial clot → no bridge
- CHA_2DS_2-VASc ≥ 7 or stroke, TIA, arterial clot ≤ 3 mos old
  - Bridge unless major bleed or ICH within 3 months

DOAC Interruption

- “Given the short-half lives of DOACs, bridging with a parenteral agent is rarely, if ever, needed prior to procedures. Reinitiation of these agents after the procedure, however, may need to be delayed owing to the risk of postprocedural bleeding.”
- If patient is unable to tolerate oral medication, consider bridging parenteral anticoagulant (full or prophylactic dose depending upon risk of bleeding)

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WHETHER TO BRIDGE

2 Assess patient thrombotic risk definitions:

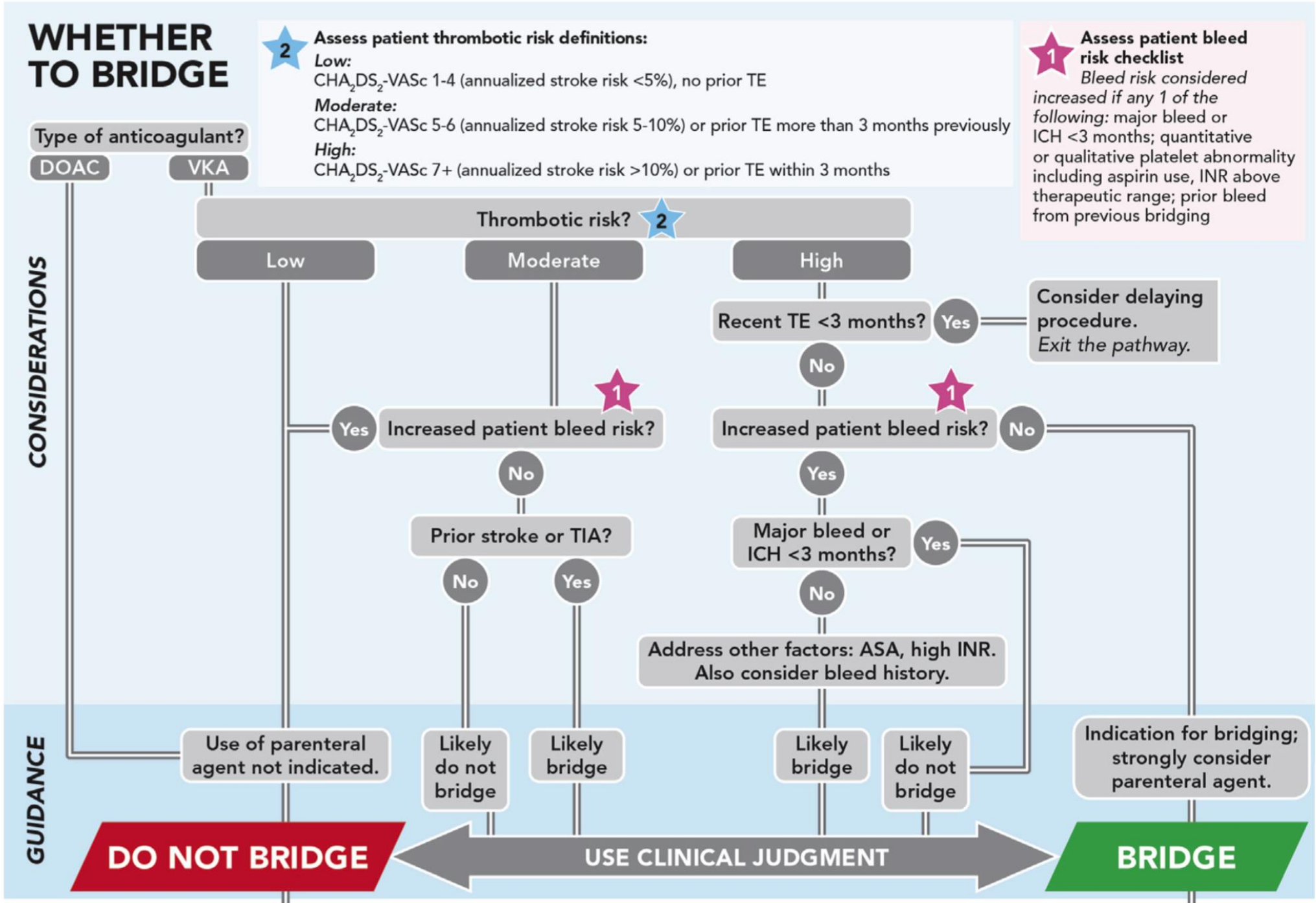
Low:
CHA_2DS_2-VASc 1-4 (annualized stroke risk <5%), no prior TE

Moderate:
CHA_2DS_2-VASc 5-6 (annualized stroke risk 5-10%) or prior TE more than 3 months previously

High:
CHA_2DS_2-VASc 7+ (annualized stroke risk >10%) or prior TE within 3 months

1 Assess patient bleed risk checklist

Bleed risk considered increased if any 1 of the following: major bleed or ICH <3 months; quantitative or qualitative platelet abnormality including aspirin use, INR above therapeutic range; prior bleed from previous bridging



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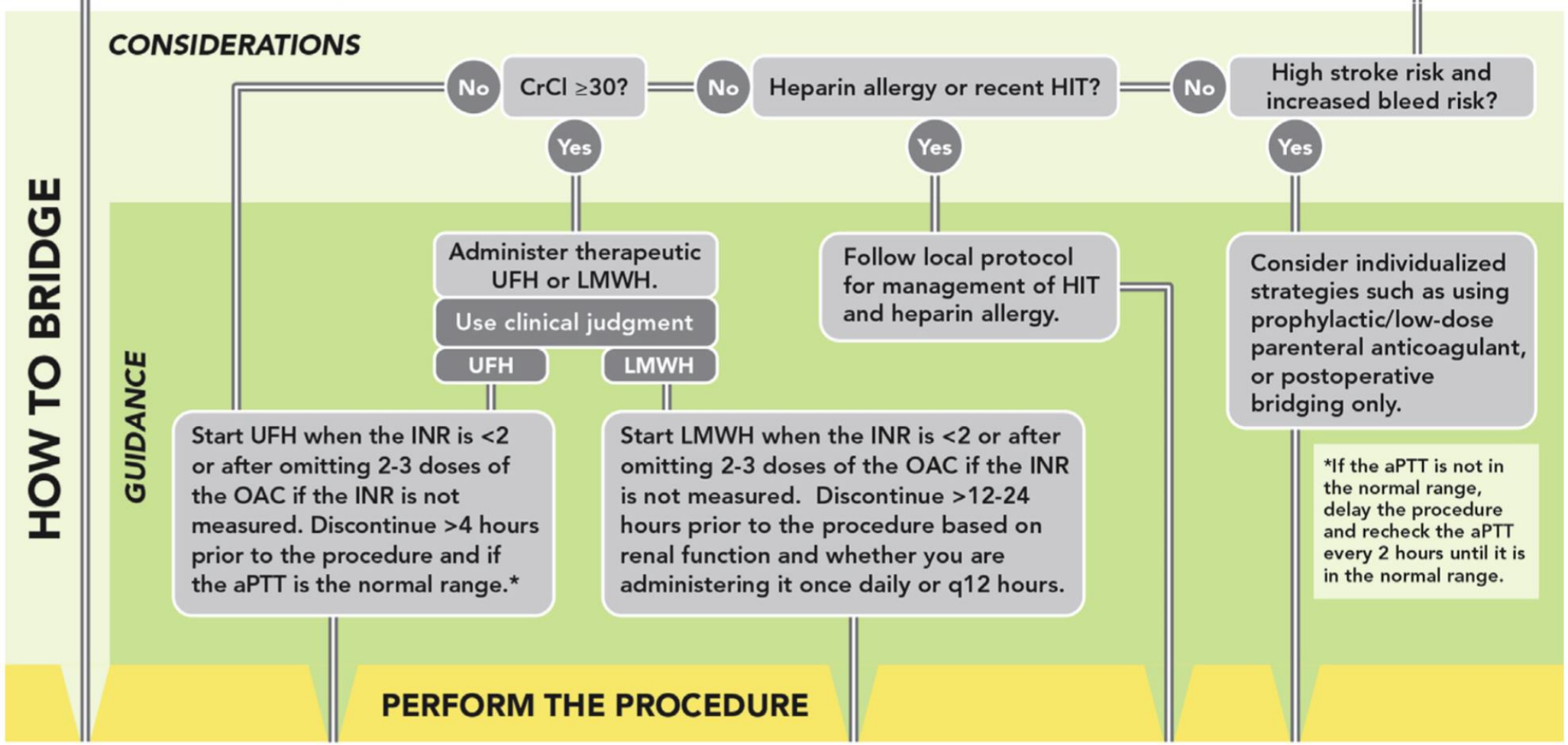

Restarting Anticoagulation

- Attention paid to:
  - Procedural site hemostasis
  - Consequences of bleeding
    - Intracranial, spinal, intraocular
  - Patient factors
    - Coagulopathy, platelet function

Restarting Anticoagulation

- VKA
  - In most cases, can be resumed within 24 hours at patient's usual dose
  - If moderate/high risk of thrombosis, consider post-procedural bridge
    - Low bleeding risk → start parenteral anticoag at 24 hours
    - High bleeding risk → delay parenteral anticoag to 48-72 hours
- DOAC
  - Treat like parenteral anticoagulation
    - Low bleeding risk → start at 24 hours
    - High bleeding risk → delay 48-72 hours
  - Dose according to post-procedural renal function

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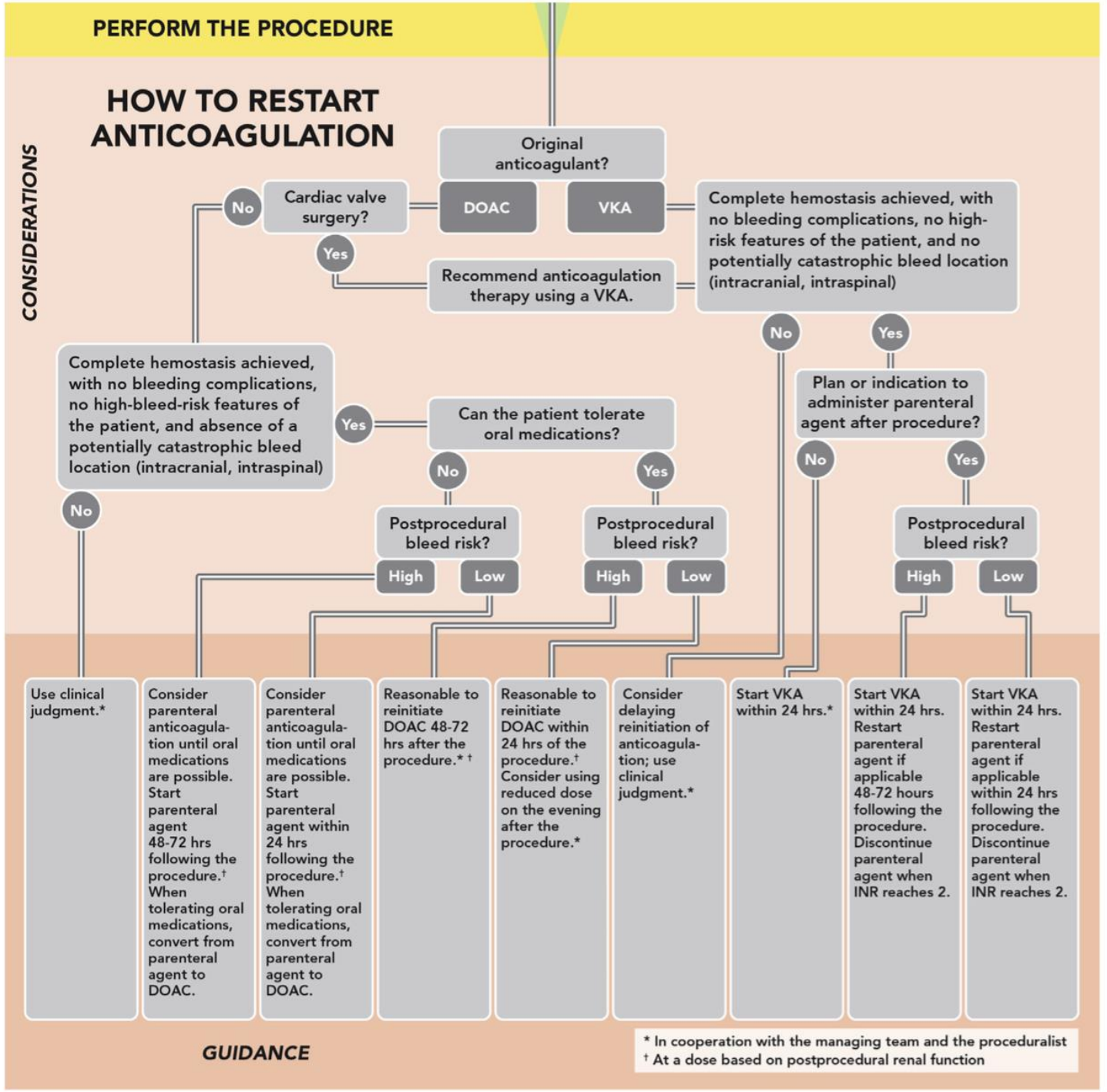
- Barf…



Learning Objectives

- Manage perioperative medications in patients undergoing non-cardiac surgery
- Risk stratify patients for the likelihood of Major Adverse Cardiac Events (MACE) in the perioperative period
- Make appropriate use of preoperative diagnostic testing prior to non-cardiac surgery

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Thank You!

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