

Updates & Controversies in Perioperative Medicine

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Perioperative Medicine Workshops

12:40 – 2:00:

Preoperative Cardiac & Pulmonary Evaluation

- Clinical assessment, preoperative testing, and approaches to risk reduction

2:10 – 3:30:

Tough Cases in Perioperative Medicine

- Common questions and dilemmas in the management of medical problems in surgical patients

Updates in Perioperative Medicine

1. Screening & treatment for postoperative myocardial injury
2. Anticoagulating postoperative atrial fibrillation
3. Managing medications around surgery
 - Stress-dose steroids
 - ACE-inhibitors & ARBs
 - Direct-acting oral anticoagulants

Screening for Myocardial Injury

You get signout about a patient with CAD and HFpEF who had a colectomy last week. Your fellow hospitalist tells you:

“He had no cardiac symptoms, but I checked a postop troponin anyway because his RCRI was 3. It peaked at 0.2 ng/mL, but I didn’t do anything based on this result.”

How do you respond?

1. I wouldn't have ordered a screening troponin
2. I'll just optimize his secondary risk reduction regimen
3. I'll order a stress test or refer to cardiology for possible cath
4. I'll start long-term anticoagulation
5. Meh – I'll ignore it too and inform the PCP

Perioperative Myocardial Injury

Findings from POISE (beta-blocker) trial:

- 5% of these “elevated risk” patients had postop MI, defined as elevated biomarker + ECG changes
- Most MI occurred by POD #3 (74% within 48 hr)
- Postoperative MI predicted 5-fold mortality
- Majority of postoperative MI were asymptomatic
- Silent MI had similar mortality as symptomatic MI

Postop Biomarkers Predicts Mortality

Study	Biomarker	Outcome
POISE (2011)	Troponin or CK-MB	2.5x mortality with isolated biomarker elevation
VISION (2012)	Troponin-T	4x mortality with any Tn-T elevation
Meta-analysis of 14 earlier studies (2011)	Troponin	3x mortality with elevation

1. Ann Intern Med. 2011;154(8):523-528.
2. JAMA. 2012; 307(21):2295-2304.
3. Anesthesiology 2011; 114(4): 796-806.

Arguments Against Screening

Insufficient Sensitivity:

- Screening only identified 21% of patients who died in POISE

Too late to do anything:

- Nearly 2/3 of deaths in patients with MI occurred by POD 3
- Many deaths in MI patients are not cardiac-related
- Elevated troponin just identifies obviously crashing patients

No known effective intervention:

- Don't order the test unless it will change management



Non-FDA Approved Indication

MANAGE Trial

Question: Does the direct thrombin inhibitor dabigatran improve outcomes in patients with elevated postop troponin?

Patients: 1754 patients who evidence of myocardial injury after noncardiac surgery (MINS), defined as elevated postop troponin either with clinical, ECG or imaging evidence of new ischemia or no other explanation (e.g., PE, sepsis, atrial fib)

Intervention: Dabigatran 110 mg bid vs. placebo for *up to 2 yrs*

Outcome: CV mortality, nonfatal MI, stroke, peripheral arterial thrombosis, and symptomatic PE

Amputation and symptomatic proximal DVT added *post hoc*

MANAGE Trial Outcomes

Outcome	Dabigatran	Placebo	NNT
Primary cardiac or vascular outcome	11%	15%	25 (p = .012)
Mortality – CV	6%	7%	NS
Mortality – All cause	11%	13%	
Myocardial Infarction	4%	5%	NS
Bleeding complications	3%	4%	NS

Screening for Myocardial Injury

Limitations of MANAGE trial:

- Design problems (changing sample size & outcomes)
- Outcomes too broad and individually no significant effect
- Comparison group was placebo
- Just too weird -- very different from usual practice

So now what?

Screening for MINS?: US guidelines ambivalent; Canadian guideline endorses it.

Statin & ASA: Association between their use and lower mortality in patients with MINS or postop MI (retrospective study only)

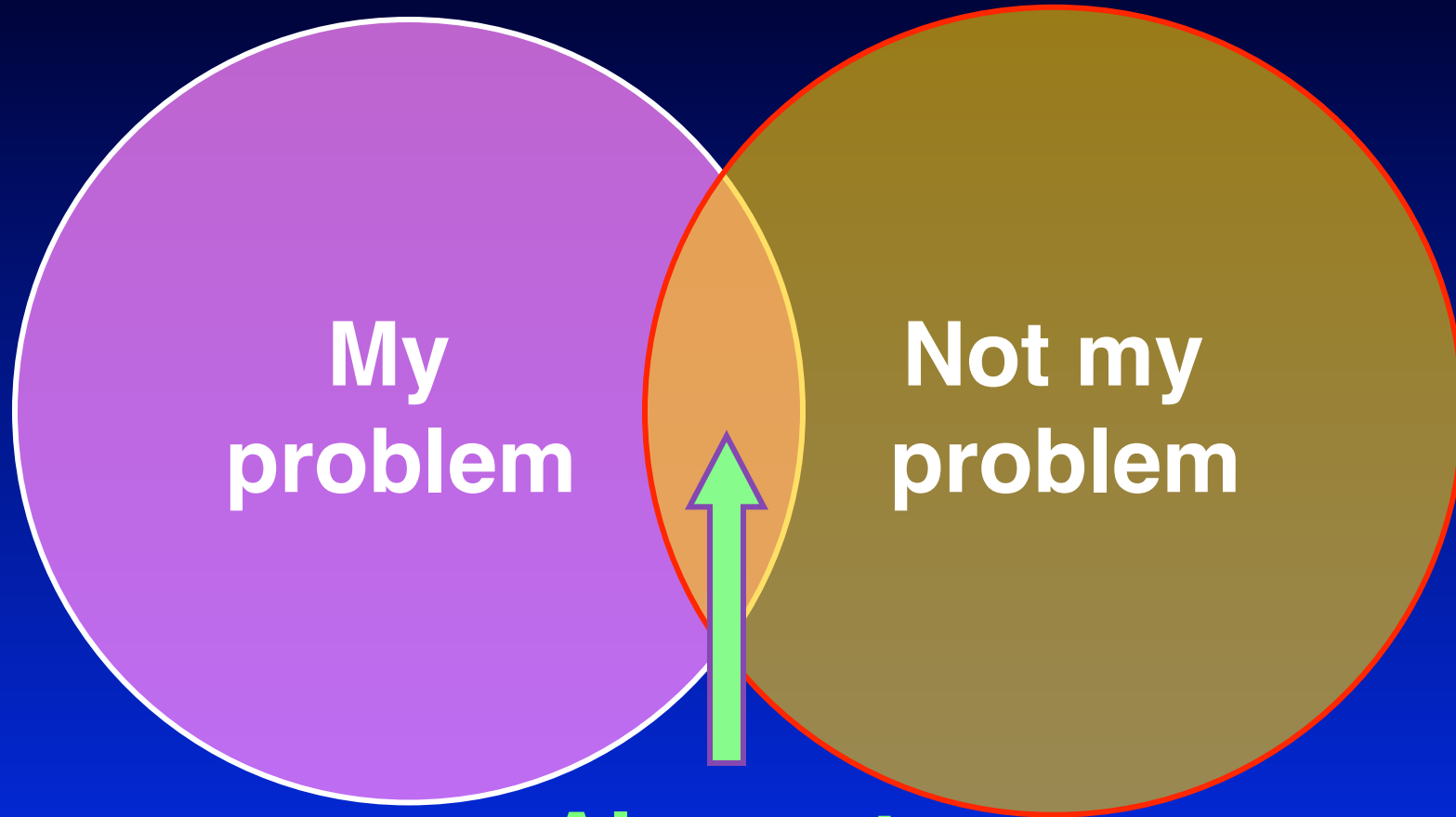
Postoperative Atrial Fibrillation

70-y.o. woman with hypertension undergoes knee replacement. On POD #1, she develops new atrial fibrillation. She is started on metoprolol and converts spontaneously to sinus rhythm the next day. A recent TTE shows normal LV function with mild LAE. Her CHA₂DS₂VASc = 3.

Would you recommend long-term anticoagulation?

1. No
2. Yes
3. Tough call...I'll ignore it and inform the PCP

Hospitalist Mentality



**Also not
my problem**

Incidence & Risk Factors

- New onset AF requiring treatment occurs after ~ 1% of major **non**-cardiac surgery
- Risk factors: male, white race, pre-existing cardiovascular disease or cardiac risk factors
- More common with thoracic, abdominal, vascular, intra-cranial, and head & neck operations
- Associated with prolonged hospitalization, increased mortality, readmission

Stroke Risk with Postop AF

Does postop AF (POAF) have similar risk for stroke as “regular” non-valvular AF (NVAF)?

California database: 12,874 patients with new POAF

	POAF	No POAF	Adjusted HR
1-yr Stroke Risk	1.47%	0.36%	2.0 [1.7-2.3]

- 1.47% risk is similar to NVAF with CHA₂DS₂VASc between 1-2
- Median CHA₂DS₂VASc in this study = 3. Expected stroke risk in NVAF would be 3.2% (twice higher)

Stroke Risk with Postop AF

Danish registry: 3830 patients with new onset POAF

- Adjusted HR for thromboembolism = 1.9 compared to surgical patients who did not develop POAF
- Matched by CHA₂DS₂VASc score to patients with new onset NVAf:

	POAF	NVAf	Adjusted HR
Thromboembolism (TE) Risk (events per 1000 person-yrs)	32	30	0.95 (NS)
Hazard ratio for TE if anticoagulant prescribed	0.52	0.56	NS

Stroke Risk Conclusions

Long-term stroke risk from POAF underappreciated:

- Patients with POAF have 2-fold (adjusted) risk of stroke compared to surgical patients who do not develop AF
- Stroke risk for POAF may be similar to patients with usual, non-surgical NVAf
- Anticoagulation may have similar benefit in POAF

What to do?

- Take POAF seriously; not unreasonable to offer AC, especially if higher CHA₂DS₂VASc score
- Limited by retrospective data, lack of consensus & guidelines

Perioperative Steroid Coverage

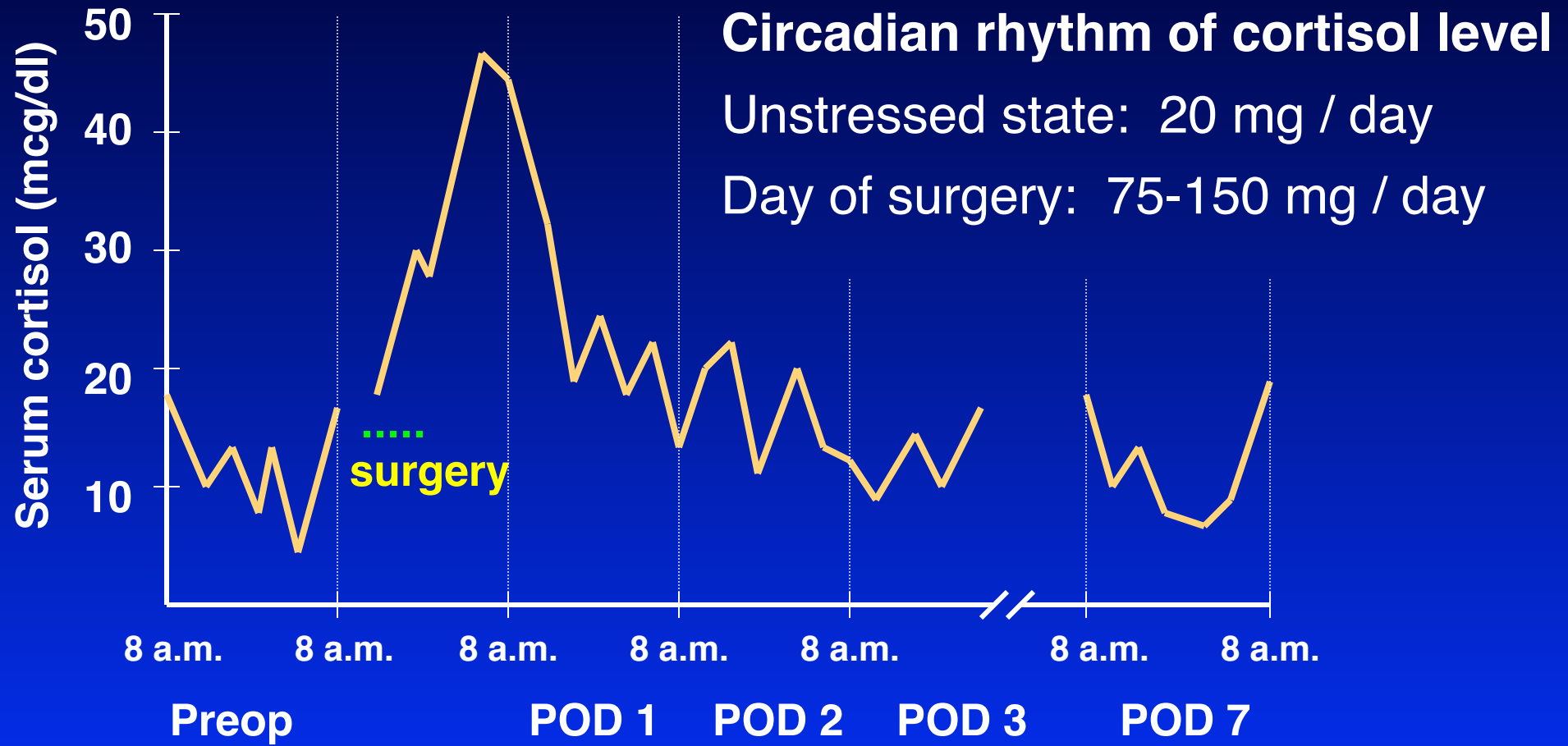
You perform a preoperative medical evaluation on a 60-y.o. woman with rheumatoid arthritis who suffered a peri-prosthetic hip fracture. She takes prednisone 10 mg daily, leflunomide (Arava), and a TNF-inhibitor.

She is hemodynamically stable & does not appear Cushingoid

What should you about glucocorticoid dosing?

1. Give “stress dose steroids”
2. Just give usually home prednisone
3. Perform ACTH-stimulation test

Adrenal Response to Surgical Stress



Adapted from Lamberts et al. *NEJM*, 1997

Adrenal Crisis: Does it Happen?

Review of published cases of perioperative hypotension or death attributed to adrenal insufficiency in steroid-treated patients:

- Plasma cortisol level measured in only 6 cases
- Only 3 of these cases also fulfilled other criteria for adrenal insufficiency

Do Patients Really Need Stress-dose Steroids?

80 patients on chronic steroids underwent transplant nephrectomy (n= 52) or major arthroplasty (n = 28):

- All received their usual daily prednisone (average dose 10 mg)
- No additional steroid coverage
- **No episodes of unexplained hypotension**

Bromberg et al. *J Am Coll Surg*, 1995

Friedman et al. *J Bone Joint Surg*, 1995

2017 ACR Guideline for Arthroplasty

Guideline from American College of Rheumatology
and American Association of Hip & Knee Surgeons:

Continue the current daily dose of glucocorticoids in adult patients...who are receiving glucocorticoids for their rheumatic condition and undergoing THA or TKA, rather than administering perioperative supra-physiologic glucocorticoid doses (so-called “stress dosing”).

But I Want to Use Stress-dose Steroids

Assume HPA axis suppressed:

- Prednisone \geq 20 mg daily for at least 3 weeks

Assume HPA axis normal:

- Prednisone < 5 mg every morning for any duration
- Prednisone < 10 mg every other day for any duration
- Prednisone at any dose for < 3 weeks

Unknown HPA axis status:

- Everyone else \rightarrow consider ACTH-stimulation test

But I Want to Use Stress-dose Steroids

Moderate Stress:

open chole, hemicolectomy,
major orthopedic surgery

Hydrocortisone 50 mg IV x 1 preop &
25 mg IV q 8 hrs x 3 doses post-op

Severe Stress:

major cardiac surgery,
organ transplantation

Hydrocortisone 100 mg IV x 1 preop &
50 mg IV q 8 hrs post-op;
Taper by 50% per day to baseline

2017 ACR Guideline for Arthroplasty

DMARDS & Biologics in RA patients:

Continue nonbiologic DMARDs (methotrexate, leflunomide, hydroxychloroquine, and/or sulfasalazine) for patients undergoing elective THA or TKA.

Withhold biologic agents prior to surgery and plan the surgery at the end of the dosing cycle for that specific medication. Resume at least 14 days after surgery in absence of wound complications.

ACE-I & ARB: Hold or Continue?

Background:

- ACE-inhibitors & angiotensin receptor blockers (ACEI/ARBs) associated with hypotension and need for vasopressors during surgery
- Individual studies mostly retrospective and too small to show effect on clinical outcomes
- Guidelines vary on whether to hold or continue ACEI/ARBs on day of surgery

USA: Continue

Canada: Hold

Europe: Continue
for CHF, not HTN

New Studies on Periop ACEI/ARB

Randomized trial:

- 291 elective noncardiac, nonvascular operations on patients taking ACEI chronically
- Final preop dose either given or held
- Excluded patients with decompensated HF, EF < 40%, ESRD, or SBP < 90 or > 160

	Given	Held	NNH
Intraop SBP <80 + pressor	64%	45%	6
Postop SBP < 90	11%	22%	9
Postop SBP > 180	12%	24%	9

New Studies on Periop ACEI/ARB

Large cohort trial:

- 4802 noncardiac operations on patients taking ACEI/ARB
- Examined association between giving ACEI/ARB and hypotension & composite endpoint of death, stroke, MINS

	Adjusted Risk if ACEI/ARB Held
Intraop hypotension requiring intervention	0.80 (0.73-0.88)
Death, Stroke, MINS	0.82 (0.70-0.96)

ACE-I & ARB: Hold or Continue?

Conclusions:

- Trade off between hypotension (especially intraoperative) and postoperative hypertension
- Difficult to demonstrate effect on hard endpoints
- **Personal & UCSF practice:** Hold on morning of surgery; restart when BP and renal function stable

Perioperative DOAC Management

You admit a 75-year-old woman for suspected acute cholangitis. She has atrial fibrillation and took her last dose of apixaban last night. Creatinine is normal. She is stable, but GI wants to perform ERCP as soon as possible.

When should she have the procedure?


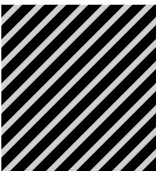
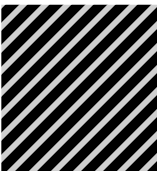

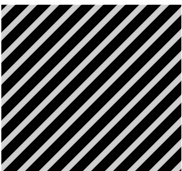




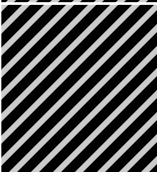




1. Today
2. Tomorrow (hold apixaban 1 day)
3. Day after tomorrow (hold 2 days)
4. When DOAC level is undetectable

How to PAUSE a DOAC


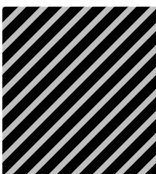
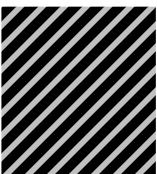
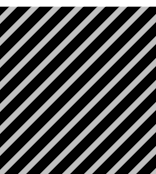
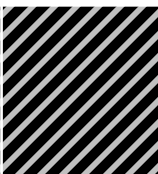

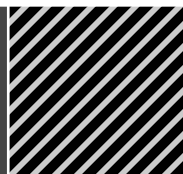





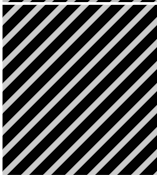
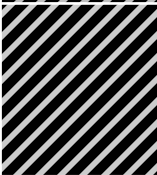




Perioperative Anticoagulation Use for Surgery Evaluation

- International study of 3007 elective surgery patients taking **apixaban, rivaroxaban or dabigatran** for atrial fibrillation
- Interrupted & resumed DOAC using standardized protocol
- Considered surgical bleeding risk and (for dabigatran) CrCl
- No bridging was permitted
- Drug level and coagulation times checked but not used for clinical decision-making

Dabigatran (CrCl \geq 50), Apixaban, Rivaroxaban:

	Day -3	Day -2	Day -1	OR	Day +1	Day +2	Day +3
High Bleed Risk							
Low Bleed Risk							

Dabigatran with CrCl < 50:

	Day -5	Day -4	Day -3	Day -2	Day -1	OR	Day +1	Day +2	Day +3
High Bleed Risk									
Low Bleed Risk									

PAUSE Trial Results

- Average CHADS2 = 2.1 (CHA₂DS₂VASc = 3.4)
- Patients having high bleeding risk surgery = 33%

	Dabigatran	Apixaban	Rivaroxaban
Major Bleeding	0.9%	1.35%	1.85%
Arterial Thrombo-embolism	0.6%	0.16%	0.37%

Take Home Points

1. Silent myocardial injury predicts mortality – unfortunately effective management remains uncertain
2. Take postoperative atrial fibrillation seriously and consider offering anticoagulation
3. Stress-dose steroids probably treats the provider more than the patient – consider just giving usual daily steroid dose
4. A standardized protocol for PAUSE-ing DOACs leads to low risk of thromboembolism and bleeding
5. Hold ACE-I and ARB on morning of surgery by default

Thank You

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