Updates in Perioperative Medication Management

LINDEE STRIZICH, MD, MSC

ASSOCIATE PROFESSOR

DEPARTMENTS OF MEDICINE AND
PERIOPERATIVE MEDICINE AND ANESTHESIA

OREGON HEALTH AND SCIENCE UNIVERSITY

Disclosures

- No disclosures

Objectives

- Review the perioperative management guidelines of commonly prescribed medications
- Discuss management strategies based on those guidelines
- Medications to discuss today
  - Aspirin
  - ACEi/ARB's
  - GLP-1's
  - SGLT2i's
  - Marijuana

Case

- A 68 year old man with a history T2DM (last Ha1c 7.2), HTN, HFmrEF (EF 50%), h/o CABG in 2010, PCI with DES x2 in 2021, and another DES placed in 2023. A recent angiogram was performed for evaluation of exertional chest pain with evidence of diffuse CAD and a CTO, and no intervenable lesions were identified. Isosorbide mononitrate was added with significant improvement in his symptoms. Other medications include carvedilol, clopidogrel, furosemide, lisinopril, metformin, and dapagliflozin. He is under consideration for a colon resection for low grade colon cancer. What do you recommend for perioperative management of his CAD?

A. Stop clopidogrel 5 days prior to surgery
B. Stop clopidogrel 5 days prior to surgery and bridge with full dose enoxaparin
C. Stop clopidogrel 5 days prior to surgery and bridge with aspirin
D. Stop clopidogrel 5 days prior to surgery and admit to the hospital to start IV cangrelor

Updates in Aspirin Management

- POISE-2:
  - Post hoc analysis of 470 patients (<5%) who had undergone previous PCI
  - ASA use associated with a significant reduction in death or MI (HR, 0.50; 95% CI, 0.26–0.95; *P* = 0.036) and MI alone (HR, 0.44; 95% CI, 0.22–0.87; *P* = 0.021)
  - Risk of major or life-threatening bleeding was not significantly increased
- 2022 ESC Guidelines
- 2024 AHA/ACC Guidelines

Graham MM, et al Aspirin in Patients With Previous Percutaneous Coronary Intervention Undergoing Noncardiac Surgery. Ann Intern Med. 2018;168:237-44.

1 B-NR

For patients with CAD undergoing elective NCS, management of perioperative antiplatelet therapy and timing of surgery should be determined by a multidisciplinary team with shared decision-making to weigh the risks of bleeding, thrombosis, and consequences of delayed surgery.

2b B-R

In patients with CCD without prior PCI undergoing elective NCS, it may be reasonable to continue aspirin in selected patients when the risk of cardiac events outweighs the risk of bleeding

Perioperative Antiplatelet Management Post PCI

1 B-NR 14 days

Recent coronary artery balloon angioplasty w/o stent placement: delay elective NCS for a minimum of 14 days to minimize perioperative MACE

3: Harm B-NR 30 days

BMS or DES-PCI ≤30 days: elective NCS requiring interruption of ≥1 antiplatelet agents is potentially harmful due to a high risk of stent thrombosis and ischemic complications

2b B-NR 3 months

DES-PCI who require time-sensitive NCS with interruption of ≥1 antiplatelet agents: NCS may be considered ≥3 months after PCI *if* the risk of delaying surgery outweighs the risk of MACE

2a B-NR 6 months

DES-PCI placed for CCD who require elective NCS with interruption of ≥1 antiplatelet agents: reasonable to delay surgery for ≥6 months after PCI to minimize perioperative MACE

1 B-NR 12 months

DES-PCI placed for ACS who require elective NCS with interruption of ≥1 antiplatelet agents: ideally delay surgery ≥12 months to minimize perioperative MACE

1 B-NR

CAD and requiring time-sensitive NCS within 30 days of PCI with BMS or <3 months of PCI with DES: DAPT should be continued unless risks of bleeding outweigh benefit of the prevention of stent thrombosis

2b B-NR

Select patients after PCI with high thrombotic risk, periop bridging with IV antiplatelet therapy may be considered <6 months after DES or <30 days after BMS if NCS cannot be deferred.

1 B-NR

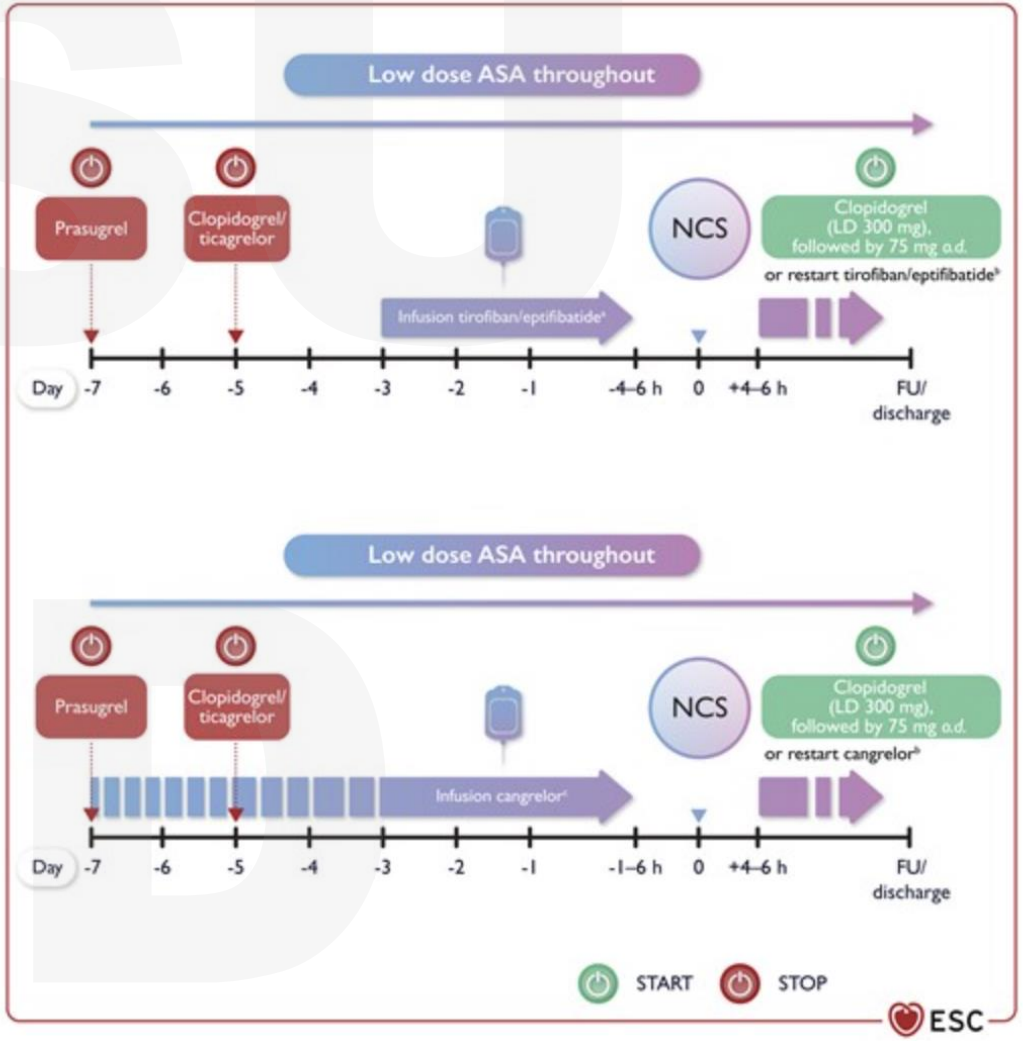
Patients with prior PCI in whom OAC monotherapy must be discontinued before NCS, ASA should be substituted until OAC can be safely reinitiated

Thompson A, et al Peer Review Committee Members. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024 Nov 5;150(19):e351-e442.

ASA Bridging

- ESC 2022:
  - For patients without an indication for OAC and with previous PCI: patients on ASA should continue low-dose ASA perioperatively unless bleeding risk is very high
  - For patients treated with $P2Y_{12}$ inhibitor monotherapy: consider switching to aspirin perioperatively
  - For patients treated with an $P2Y_{12}$ inhibitor in combination with ASA: consider interrupting the $P2Y_{12}$ inhibitor while continuing ASA perioperatively
  - For all patients with previous coronary intervention and without an indication for OAC: consider continuing ASA perioperatively unless the bleeding risk is very high
- Strategy: 300 mg bolus followed by 81 mg PO QD until safe to resume P2Y12

- IV Bridging – BRIDGE and MONET-BRIDGE trials
  - In patients who are within 1 to 6 months of PCI and continue to need DAPT, use of intravenous antiplatelet therapy as a bridge for nondeferrable surgery has been inadequately studied



.Halvorsen S, et al, Scientific Document Group. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J. 2022;43:3826-924.

Considerations for urgent/emergent surgery

- Continue aspirin monotherapy if at all possible
- For patients with an indication for DAPT that must be interrupted, surgery should be performed at an institution with 24/7 cath lab availability
- When time-sensitive surgery cannot be postponed and be performed with the recommended DAPT on board, de-escalation or shortening of DAPT is recommended.
  - A switch from the more potent $P2Y_{12}$ inhibitors prasugrel or ticagrelor to clopidogrel,
  - Cessation of aspirin and use of prasugrel or ticagrelor monotherapy
  - Premature discontinuation of the $P2Y_{12}$ inhibitor may be considered with bridging with IV therapy
- For patients receiving APT with excessive or life-threatening peri-operative bleeding, transfusion of platelets is recommended as a bail-out strategy. However, ticagrelor and its active metabolite may also inhibit aggregation of transfused platelets.

In patients with a recent PCI scheduled for NCS, it is recommended that management of antiplatelet therapy is discussed between the surgeon, anaesthesiologist, and cardiologist.	I	C

.Halvorsen S, et al, Scientific Document Group. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J. 2022;43:3826-924.

Case continued

- At your visit with your 68 year old patient you note that his blood pressure is 147/89. Looking back through prior in person visits with other providers you notice that his blood pressure ranges from 140-160/70-90. His medications include: carvedilol, isosorbide mononitrate, lisinopril, furosemide. What do you recommend for antihypertensive management?

A. Continue carvedilol and isosorbide mononitrate, stop lisinopril and furosemide on the morning of the surgery
B. Continue carvedilol, isosorbide mononitrate, and lisinopril, stop furosemide on the morning of surgery
C. Continue lisinopril and isosorbide mononitrate, hold carvedilol and furosemide on the morning of surgery
D. Hold all medications with an antihypertensive effect

ACEi

- PREOP-ACEi – Prospective randomized trial of patients on a stable ACEi/ARB dose for at least 6w prior to surgery, randomized to hold their dose immediately before surgery
  - Fewer episodes of intraop hypotension in those who held their ACEi/ARB but no difference MACE, PACU recovery time, or hospital LOS
- POISE-3 – prespecified subgroup analysis of 7500 patients withvascular disease or risk factors randomized to hypotension-avoidance or hypertension-avoidance perioperative BP strategies
  - no difference in major vascular events (MINS, vascular death, stroke, or cardiac arrest at 30 days) in nearly 72% of patients in both groups were taking an ACEi/ARB at the time of randomization
  - NO excess adverse events in the group randomly assigned to continue their home BP regimen on the morning of surgery
- STOPorNOT – multicenter randomized clinical trial of 2222 patients to understand the impact of RAASi Continuation on Outcome after Major Surgery
  - rates of all-cause mortality and major postoperative complications was 22% in the discontinuation group and 22% in the continuation group (risk ratio, 1.02)

Shiffermiller JF, et al. Prospective Randomized Evaluation of Preoperative Angiotensin-Converting Enzyme Inhibition (PREOP-ACEI). J Hosp Med. 2018 Sep;13(10):661-667.
POISE-3 Trial Investigators and Study Groups. A sub-study of the POISE-3 randomized trial examined effects of a perioperative hypotension-avoidance strategy versus a hypertension-avoidance strategy on the risk of acute kidney injury. Kidney Int. 2025 Jan;107(1):155-168.
Legrand M, Falcone J, Cholley B, et al. Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery: The Stop-or-Not Randomized Clinical Trial. JAMA. 2024;332(12):970–978. doi:10.1001/jama.2024.17123

ACEi/ARBs

Recommendations for Perioperative Renin-Angiotensin-Aldosterone System Inhibitors
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	Recommendations
2b	B-R	1. In select* patients on chronic renin-angiotensin-aldosterone system inhibitors (RAASi) for hypertension undergoing elevated-risk NCS, omission 24 hours before surgery may be beneficial to limit intraoperative hypotension.[1–6]
2a	C-EO	2. In patients on chronic RAASi for HFrEF, perioperative continuation is reasonable.†[1,2]

*Patients with controlled BP and undergoing elevated-risk surgical procedures.
†Modified from the "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure."[7]

Considerations for urgent/emergent surgery

- Do not need to automatically hold ACEi/ARB
- Can use clinical context to drive decision making
  - What is the patient's current BP and hemodynamic stability?
  - What is their current kidney function compared to baseline?

Case (cont.)

- While reconciling medications with your patient he mentions that his PCP recently started a new medication, an injectable medicine that is supposed to help him lose weight and make his blood sugars better. He's had two doses and hasn't noticed much difference yet. His surgery is in 9 days and he is due for next dose in 5 days. He is wondering if he can give himself this medication prior to surgery. Realizing this is most likely an injectable GLP-1, how do you counsel him?

A. Delay his surgery as he should be off this medication for at least 30 days prior to surgery

B. He can give himself his injection as planned

C. He should give himself his next dose early, 2 days from now

D. Skip his next injection and resume after surgery once PO intake is normal

GLP-1s

- Glucagon-like polypeptide-1 (GLP-1) agonists, increasingly used for the management of diabetes, can cause clinically significant gastroparesis and delayed gastric emptying

- Consensus statement from the ASA recommends that weekly formulations of GLP-1 agonists be held >1 week before elective NCS for weekly dosed GLP-1 agonists and the day before for daily dosed GLP-1 agonists to reduce the risk of pulmonary aspiration of gastric contents at the time of surgery

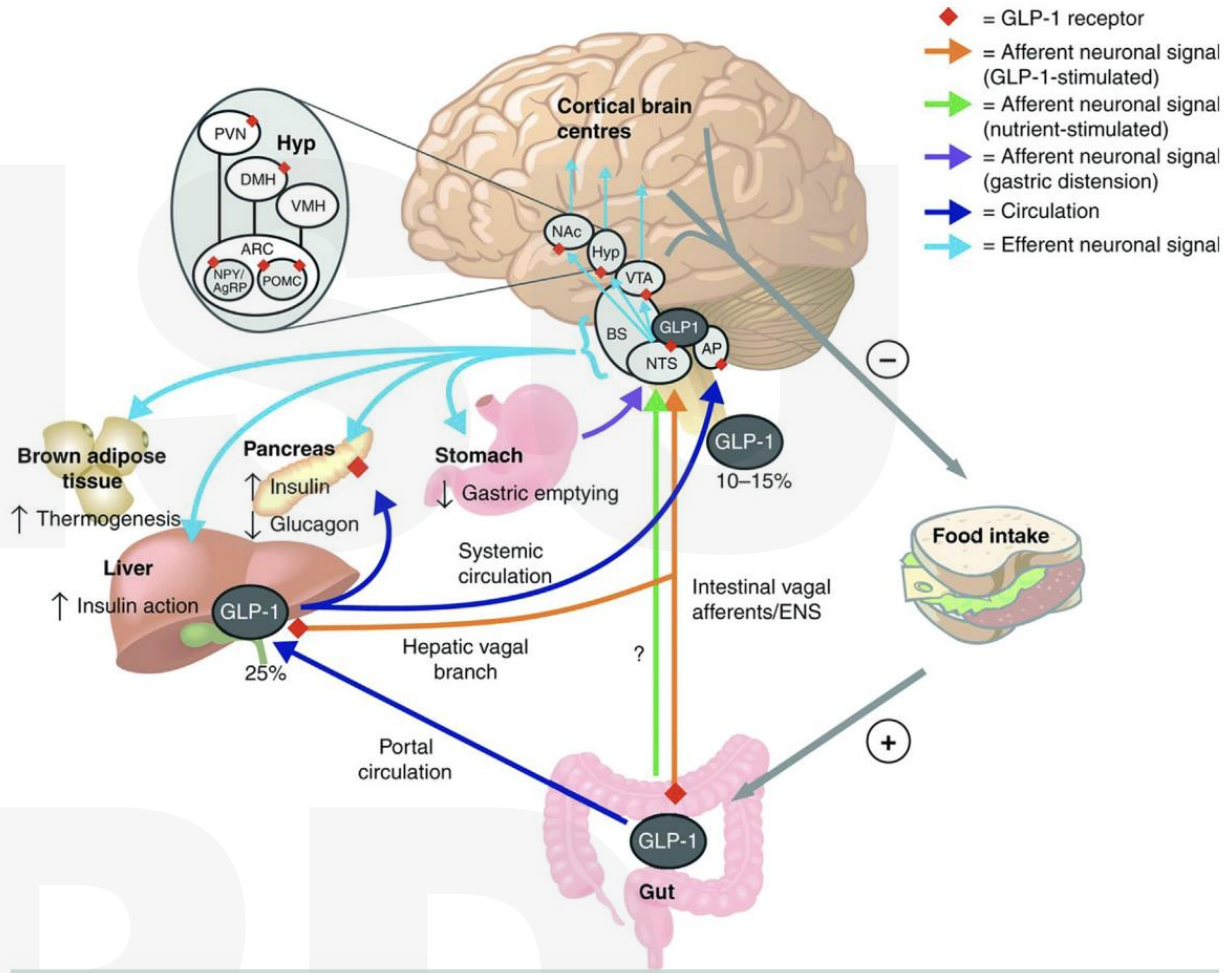


Figure 1 Proposed routes of action of GLP-1 in the central regulation of feeding and glucose metabolism. *Note.* Reprinted with permission from van Bloemendaal et al.[6] doi:10.1530/JOE-13-0414. AgRP = agouti-related peptide; AP = area postrema; ARC = arcuate nucleus; BS = brain stem; DMH = dorsomedial hypothalamus; ENS = enteric nervous system; Hyp = hypothalamus; NAc = nucleus accumbens; NPY = neuropeptide Y; NTS = nucleus tractus

Moiz, Areesha et al., Mechanisms of GLP-1 Receptor Agonist-Induced Weight Loss: A Review of Central and Peripheral Pathways in Appetite and Energy Regulation, The American Journal of Medicine, Volume 138, Issue 6, 934 - 940

American Society of Anesthesiologists Task Force on Preoperative Fasting. Consensus based guidance on preoperative management of patients (adults and children) on glucagon-like peptide-1 (GLP-1) receptor agonists. Accessed January 15, 2024

Considerations for urgent/emergent surgery

Retrospective chart review comparing residual gastric contents of patients on GLP-1s undergoing endoscopy. 1.5% of patients on CLD had residual food vs. 10% on a regular diet prior to endoscopy	Vs.	Cohort study based on claims data of 23,679 patients, ~15% of whom had a GLP-1 Rx filled found no difference in postop respiratory complications (adjusted OR, 1.03; 95% CI, 0.82–1.29; *P* = .80)

- Discuss risks with patient, surgical team, and make sure anesthesia team is aware of GLP1 use
- Most surgical centers have specific "full stomach" protocols in place to mitigate risk of regurgitation and aspiration during intubation
  - gastric ultrasound
  - Head-of-bed elevated or “ramped” intubation,
  - Decreased use of bag-valve-mask for oxygenation due to the risk of gastric insufflation

Ghazanfar H, et al. Is it necessary to stop glucagon-like peptide-1 receptor agonists prior to endoscopic procedure? A retrospective study. World J Gastroenterol. 2024 Jul 14;30(26):3221-3228.
Dixit AA, et al. Preoperative GLP-1 Receptor Agonist Use and Risk of Postoperative Respiratory Complications. JAMA. 2024;331(19):1672–1673.

Case (cont)

- What do you recommend regarding your patient's empagliflozin?
  A. Stop 3 full days prior to his surgery
  B. Hold on the morning of surgery
  C. Discontinue now (9 days before surgery)
  D. Have him cut his dose in half prior to surgery

Euglycemic Diabetic Ketoacidosis

- Euglycemia (blood glucose less than 250 mg/dL) with high anion gap metabolic acidosis (pH < 7.3), and hyperketonemia or hyperketonuria

- Symptoms = malaise, dyspnea, nausea, or vomiting

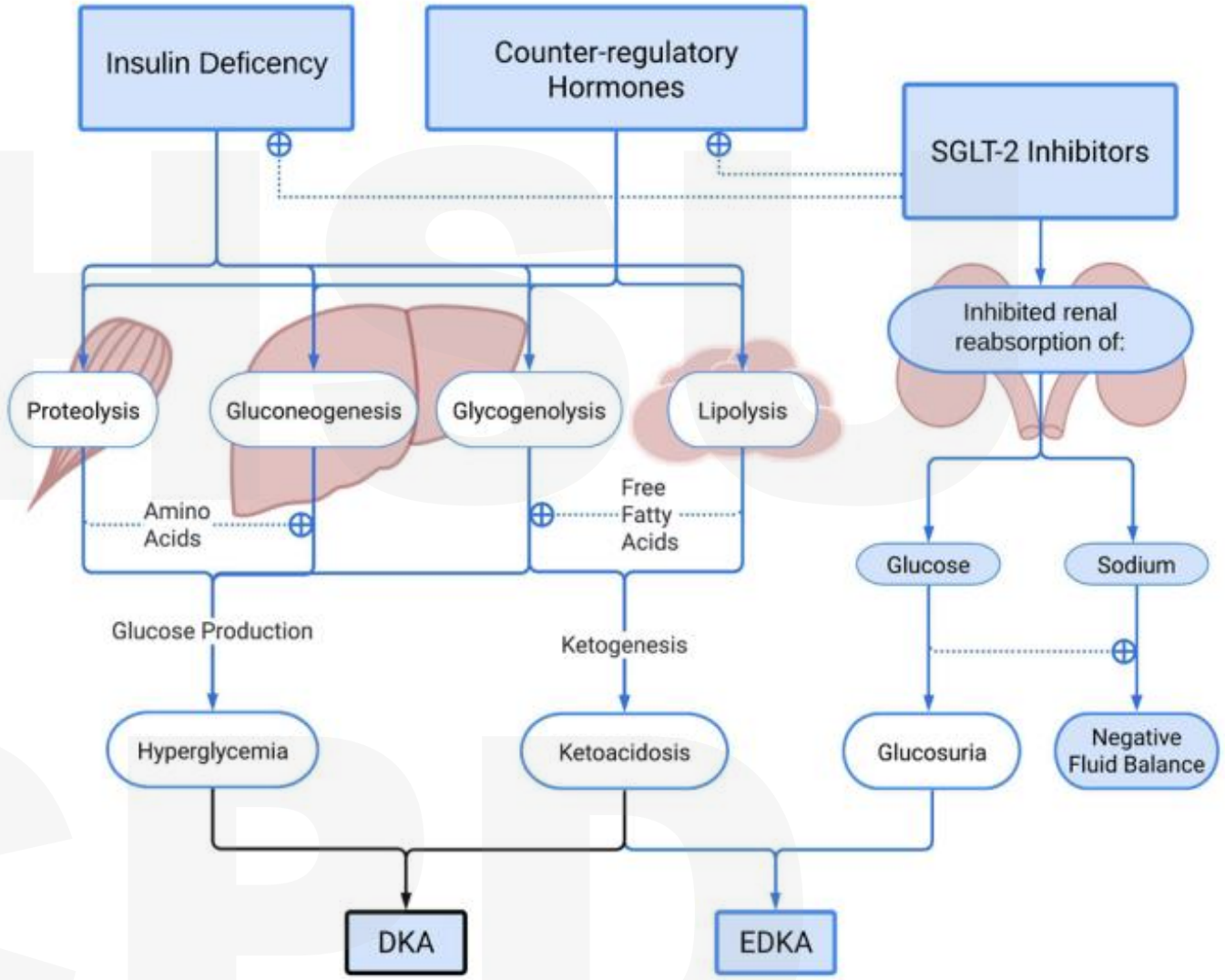


Figure 1 Pathophysiological mechanisms leading to EDKA. EDKA, euglycemic diabetic ketoacidosis; DKA, diabetic ketoacidosis; SGLT-2, sodium-glucose transporter type 2.

Chow E, Clement S, Garg R. Euglycemic diabetic ketoacidosis in the era of SGLT-2 inhibitors. *BMJ Open Diabetes Research & Care*. 2023;11:e003666.

SGLT2s

Recommendations for Heart Failure
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	Recommendations
1	C-LD	1. In patients with HF undergoing elective NCS, sodium-glucose cotransporter-2 inhibitors (SGLT2i) should be withheld for 3 to 4 days* before surgery when feasible to reduce the risk of perioperative metabolic acidosis.[1–3]
2a	C-LD	2. In patients with compensated HF undergoing NCS, it is reasonable to continue GDMT (excluding SGLT2i) in the perioperative period, unless contraindicated, to reduce the risk of worsening HF.[4–8]

*Canagliflozin, dapagliflozin, and empagliflozin should be stopped ≥3 days and ertugliflozin ≥4 days before scheduled surgery.[3]

Considerations for urgent/emergent surgery

- Multicenter, propensity-matched, retrospective case-control study from the Veterans Affairs Health Care System (VAHCS) National Registry performed from January 1, 2014, to December 31, 2022
  - 7439 patients were identified as SGLT2i users and compared with 33 489 control patients.
  - SGLT2i use was associated with
    - an increased risk of eKA (odds ratio [OR], 1.11; 95% CI, 1.05-1.17)
    - reduced risks of perioperative AKI (OR, 0.69; 95% CI, 0.62-0.78)
    - Reduced risk of 30-day mortality (OR, 0.70; 95% CI, 0.55-0.88)
- Cohort study of 34, 671 patients with type 2 diabetes who underwent an emergency surgery and therefore were unlikely to withhold their SGLT2i medication per current guidance, preoperative use of SGLT2i medication was not associated with postoperative diabetic ketoacidosis.
- Consider testing for ketoacidosis post operatively, particularly if prolonged NPO

Tallarico RT, Jing B, Lu K, et al. Postoperative Outcomes Among Sodium-Glucose Cotransporter 2 Inhibitor Users. JAMA Surg. 2025;160(6):681–689.
Dixit AA, Bateman BT, Hawn MT, Odden MC, Sun EC. Preoperative SGLT2 Inhibitor Use and Postoperative Diabetic Ketoacidosis. JAMA Surg. 2025;160(4):423–430.

Case (cont)

- As you are concluding your visit your patient mentions that he forgot to tell you that he uses marijuana 2-3 times a day to manage his chronic lower back pain. He is hoping he can continue to do this before surgery because he is not sleeping well due to anxiety and is worried his back pain will make sleeping even more difficult. What do you tell him about using marijuana before surgery?

A. Okay to continue using just as he is prior to surgery

B. Don't use marijuana on the morning of surgery

C. Stop for at least a week before surgery

D. Don't use for 48 hours before surgery

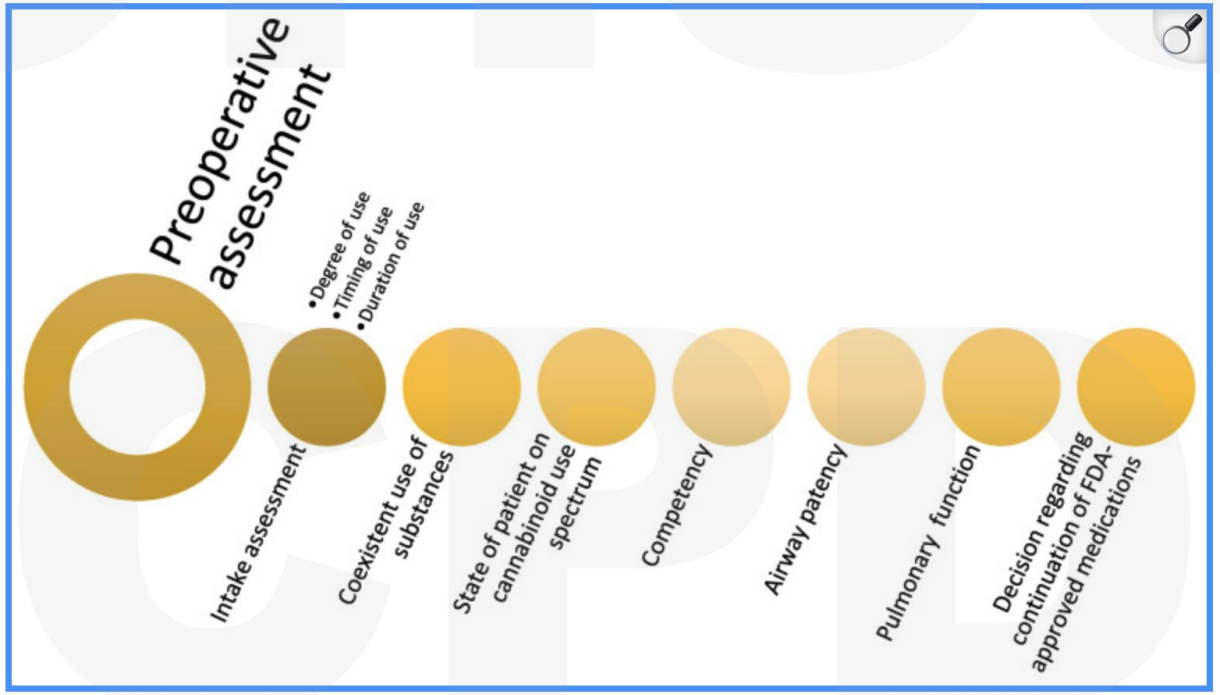
Marijuana

- Cannabinoids compete for CYP3A4 and CYP2C9 enzymes, resulting in a possible decrease in the metabolism of other substrates
- Interact with the GABAergic system, which is critical for the activity of many anesthetic agents
- A prospective trial on a small group of patients determined that the required dose of propofol to facilitate laryngeal mask insertion was higher in patients consuming cannabis
- Currently robust data on the effect of marijuana product usage on anesthetic outcomes is lacking but anecdotal evidence suggests significant impacts, particularly for patients with daily chronic use
- Additional evidence suggests that chronic and possibly even occasional marijuana use increases the risk of perioperative MACE

Laudanski K, Wain J. Considerations for Cannabinoids in Perioperative Care by Anesthesiologists. J Clin Med. 2022 Jan 22;11(3):558.

Considerations for Urgent/Emergent Surgery

Figure 2.



Preoperative consideration in anesthesia in an individual with cannabinoid intake.

Laudanski K, Wain J. Considerations for Cannabinoids in Perioperative Care by Anesthesiologists. J Clin Med. 2022 Jan 22;11(3):558.

Questions?

Kimberly Boyles/Shutterstock