Do We Need to Withhold the New Medications Jardiance (SGLT2 Inhibitors) or Ozempic (GLP-1 Agonists) Before Cardiac Catheterization?

Dr. Morton J. Kern with contributions from Drs. David J. Cohen, St. Francis Hospital, Roslyn, New York; Kirk Garratt, Christiana Medical Center, Newark, Delaware; Spencer King, Atlanta, Georgia; Neal S. Kleiman, Methodist DeBakey Heart and Vascular Center, Houston, Texas; Srihari S. Naidu, Westchester Medical Center, Valhalla, New York; Matthew J. Price, Scripps Clinic, La Jolla, California; Steve Ramee, Ochsner Clinic, New Orleans, Louisiana; Chet Rihal, Mayo Clinic, Rochester, Minnesota; Bonnie Weiner, Worchester, Massachusetts.

New information comes to all of us in the cath lab all the time. A recent experience I had involved new medications. Immediately before one of our scheduled cardioversions in a patient who had been NPO (nothing by mouth) per our usual procedure instructions, an anesthesiologist canceled the case. We were informed from anesthesia that because the patient was on Jardiance (a sodium-glucose cotransporter-2 [SGLT2] inhibitor), gastric content retention was an issue. Doing the procedure without withholding Jardiance for 3 days was against American Society of Anesthesiologists guidelines. I called our anesthesia consultant and said it was the first I have ever heard of this requirement, since we have been working without thinking about Jardiance. Instead of arguing from my ignorance, we rescheduled the cardioversion (which is usually done using propofol) after holding Jardiance for 72 hours.

However, I googled the pharmacologic and clinical actions of Jardiance and the anesthesia guidelines, and could find nothing to support the anesthesiologist's statement. Jardiance is rarely associated with ketoacidosis during general anesthesia but not significant gastric retention, which was more associated with Ozempic, a glucagon-like peptide-1 (GLP-1) receptor agonist. Before calling the anesthesia chief, I wanted to ask my colleagues what they are doing and see whether I missed something.

What About Holding the SGLT2 Inhibitors Versus GLP-1 Agonists?

Matthew J. Price, Scripps Clinic, La Jolla, California: I think the anesthesiologist mixed up the class of medications when referring to gastric retention, as it is not Jardiance (SGLT2 inhibitors), but the GLP-1 agonists (Ozempic, Wegovy) that are the issue in that regard. The anesthesiology group we work with is now asking these drugs to be held for some time before any NPO procedures given the delayed gastric emptying.

Steve Ramee, Ochsner Clinic, New Orleans, Louisiana: My anesthesiologists agree with Matthew Price. "The drugs that have given us [anesthesia docs] issues are the glucagon-like peptides like Mounjaro, Ozempic, and Trulicity. We have been holding the last dose (if given weekly, then holding the previous week; if given daily, then the previous day). Issues with not holding [the meds] are gastroparesis and aspiration."

Srihari S. Naidu, Westchester Medical Center, Valhalla, New York: The anesthesiologists came out with a warning several months ago for both these novel agents as a societal consensus and it is painful but probably reasonable. Here we have agreed to advise patients and hold GLP-1 meds for a week (since they are weekly injections). If the case is urgent, they do a gastric ultrasound to check contents before procedures and proceed if safe. And if the procedure is emergent, they will just proceed and document the risk-benefit ratio.

The SGLT2 inhibitors also need to be stopped for 3-4 days as well, due to the risk of normoglycemic ketoacidosis. We had a case of this and it was serious. The bicarb content was 8 (normal is 20, a low value indicates acidosis) in an acute myocardial infarction patient with normal lactate and high ketones. The patient needed an insulin drip as well to restore acid/base balance.

Because of the ketoacidosis that can often be asymptomatic in the patient taking SGLT-2 meds, especially in the setting of another cardiac illness, we are starting to check lactate more often prior to leaving the lab. We have point-of-care availability of arterial blood gases and serum lactate in the lab. I put that protocol in place for detection of shock, but now it is helpful for early detection of ketoacidosis.

Chet Rihal, Mayo Clinic, Rochester, Minnesota: Would a longer NPO period, for example, skipping the evening meal that day before, help mitigate the issue of delayed gastric emptying with GLP-1 agonists? I agree this is an issue that will only increase as we learn more about the effects of these latest drugs. Point-of-care ultrasound (POCUS) is a nice idea. It's important not to overreact to extremely low frequency events, eg, lactic acidosis with metformin.

Srihari S. Naidu, Westchester Medical Center, Valhalla, New York: The NPO aspect is complicated. Personally, I favor getting rid of NPO for all cath procedures not needing general anesthesia as the glucose present should get rid of the SGLT-2 ketoacidosis risk altogether.

NPO, on the other hand, is most important for the GLP-1 inhibitor and of course, the longer NPO, the better. So yes, making them skip dinner would probably help.

Neal S. Kleiman, Methodist DeBakey Heart and Vascular Center, Houston, Texas: We had this issue arise several months ago. As it turns out, the message on Jardiance and its cousins didn't get disseminated very well or widely, but it has been out there for a while. Apparently, the issue has mainly been in patients undergoing gastrointestinal surgery, but it has largely been extended to all patients getting deep sedation or general anesthesia. Basically, we have just tried to be compliant with the recommendation, although I am sure that if we pushed hard enough, we would be able to get many of these patients anesthetized.

Anesthesia Support More Than Drugs?

Kirk Garratt, Christiana Medical Center, Newark, Delaware: Our anesthesia folks pushed us early on this, but they haven't (yet) cancelled cardioversions that I know of. They were more focused on electrophysiology (EP) and cath cases. I agree with Hari [Naidu], it's painful but reasonable to hold these meds for a few days to reduce risk. Gastric ultrasound should be done on patients on GLP-1 agonists who can't wait.

Frankly, the bigger challenge with anesthesia for us is the lack of anesthesiologists. I hear there's a nationwide shortage, but I can tell you it is a huge problem in the mid-Atlantic. We may have to defer cases due to lack of anesthesia support despite the fact our anesthesia people are working long overtime hours and supervising as many certified registered nurse anesthetists (CRNAs) as possible. We have migrated some EP work and cardioversions to conscious sedation — really unpopular with docs but completely effective. We are used to doing conscious

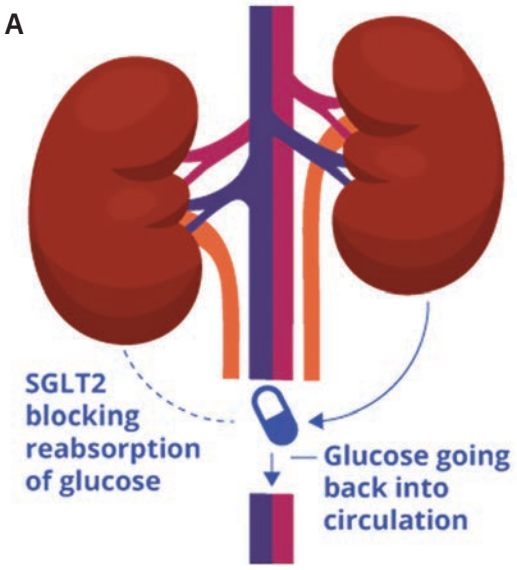

Figure 1A. SGLT-2 blocks resorption of glucose.
Reprinted from Compton K. SGLT2 inhibitors. Last modified September 5, 2023. Accessed January 19, 2024. https://www.drugwatch.com/sglt2-inhibitors/

sedation in the cath lab, but other procedural areas have relied on anesthesia support.

David Cohen, St. Francis Hospital, Roslyn, New York: As you note, Kirk, anesthesiologists are a precious resource for support of cath lab cases. This is part of the reason we need to make strong efforts as a field to move those procedures that can be done safely and effectively with cath-lab level conscious sedation to a non-anesthesiologist supported model. Ultimately, I suspect we can do this for the majority of transcatheter aortic valve replacement (TAVR) procedures and left atrial appendage occlusion (LAAO) at a minimum. Much more challenging right now for procedures like mitral transcatheter edge-to-edge repair (M-TEER) and tricuspid (T)-TEER.

Spencer King, Atlanta, Georgia: Who really needs to be NPO and is it overused? In the old days when "we walked to school 2 miles in the snow uphill both ways", we also never used anesthesia for percutaneous coronary intervention or cardioversion. OK, so we were Neanderthals, but the idea of waiting a week to do a cardioversion also sounds primitive. Anesthesia feels good but is very expensive and often not convenient. When is conscious sedation enough?

Bonnie Weiner, Worchester, Massachusetts: Spencer, I am a Neanderthal as well. Retrograde amnesia from sedation was perfectly fine for cardioversions. I think we need to be careful about gastroparesis and the risk of aspiration as gastric motility is slowed as the major mechanism of action for the newer drugs. That

LETTER TO THE CLINICAL EDITOR

Hi Mort!
Enjoyed the article in *CLD*'s December 2023 issue on radial access.[1] One thought on the right heart cath from the arm: if difficulty is encountered in advancing the catheter through the venous system — particularly if the cephalic vein were entered and not the brachial — a standard BMW can be advanced easily into the right atrium, and the catheter advanced over the wire. Additionally, John Coppola gave me a hint many years ago on advancement of the catheter, and that is to inject about a half cc of saline per second thru the distal port while advancing the catheter through the arm. This opens up the vein a bit more, and usually facilitates passage a bit more easily.
Another trick I found helpful is to inject saline through the distal tip if you are in the right atrium and can't advance into the right ventricle. Gently injecting some saline tends to straighten out the tip just like the tip of a hose straightens out when the water is turned on. I always try to do this gently though because I'm concerned that a forceful injection could potentially perforate the atrial wall.
Credit here should go to Dr. John Coppola from St Vincent's Hospital and Medical Center and NYU in NYC who told me about these techniques initially.
Thanks for all the great work you're doing for us in interventional cardiology!

— Peter L. Duffy, MD, MMM, FSCAI

Peter,
Thanks for your note. I've adopted both the guidewire to cross a perpendicular T junction at the lateral brachial vein to subclavian vein junction and a 'fluid guide wire' by injecting saline as the catheter moves up the vein. This method also permits me to see immediately when the fellow has gotten stuck in the vein for some reason.

— Morton J. Kern, MD, MSCAI

Reference
1. Kern MJ, Seto AH, et al. Upsizing a radial sheath? Methods and cautionary notes. *Cath Lab Digest.* 2023 Dec; 31(12): 6-8. https://www.hmpgloballearningnetwork.com/site/cathlab/clinical-editors-corner/upsizing-radial-sheath-methods-and-cautionary-notes

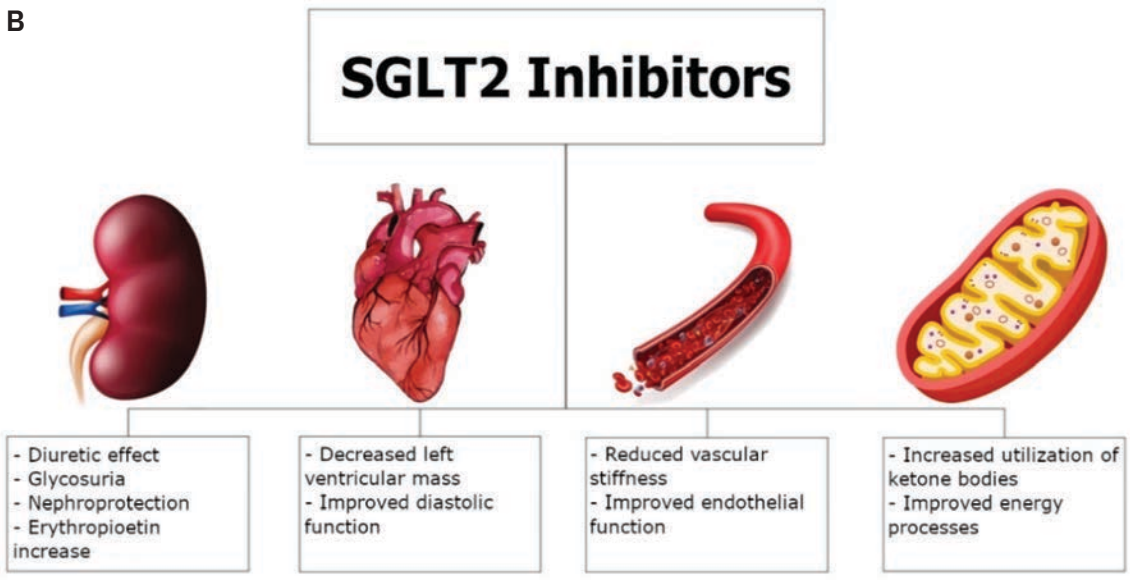

Figure 1B. Pleiotropic mechanism of action of SGLT2 inhibitors. Renal effects include diuretic response, glycosuria nephroprotection, erythropoietin increase. Cardiac effects include decreased left ventricular mass and improved diastolic function, coronary artery disease impact includes reduced vascular stiffness and improved endothelial function, and cellular impact includes increased utilization of ketone bodies and improved energy processes.

Reprinted from Kurczyński D, Hudzik B, Jagosz M, et al. Sodium-glucose cotransporter-2 inhibitors-from the treatment of diabetes to therapy of chronic heart failure. Journal of Cardiovascular Development and Disease. 2022; 9(7): 225. https://doi.org/10.3390/jcdd9070225

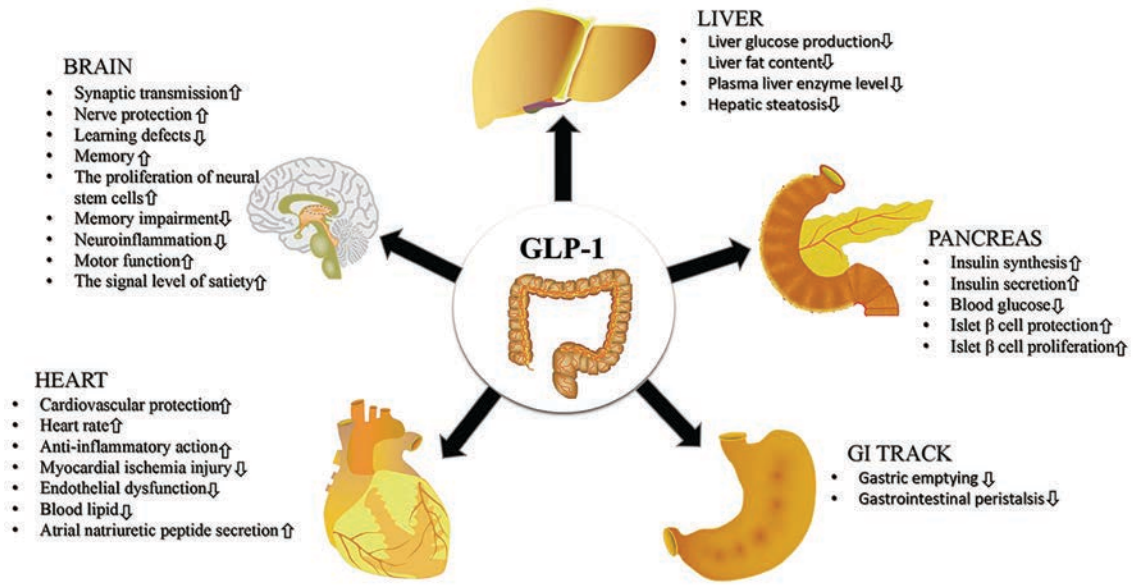

Figure 2. The effects of GLP-1 receptor agonists on multiple human organs. GLP-1 receptor agonists exert a positive therapeutic effect on human brain, pancreas, heart, gastrointestinal tract, and liver.

Reprinted from Zhao X, Wang M, Wen Z, Lu Z, Cui L, Fu C, Xue H, Liu Y, Zhang Y. GLP-1 receptor agonists: beyond their pancreatic effects. Front Endocrinol (Lausanne). 2021 Aug 23; 12: 721135. doi:10.3389/fendo.2021.721135

won't be avoided by conscious sedation and could possibly be a higher risk under those circumstances. At the moment, these patients may be the exception, but will probably not be in the future.

Kirk Garratt, Christiana Medical Center, Newark, Delaware: Good call-out, Bonnie. We should probably hold GLP-1 agonists and SGLT2 inhibitors for scheduled elective procedures whether folks are getting conscious sedation or higher-level anesthesia.

Medications to Hold or Adjust Before Cardiac Cath

The are several common types of medications that may need adjustment before cardiac catheterization. These include anticoagulants (warfarin, heparin, enoxaparin, or direct oral anticoagulants [DOACs, eg, apixaban (Eliquis), dabigatran (Pradaxa), and rivaroxaban (Xarelto)] which may need to be adjusted or stopped to reduce the risk of bleeding during or after the procedure. [MK: for warfarin-like drugs, INR is used to understand bleeding risk. Many labs have an upper limit of INR, above which the case may be postponed until the drug effect has worn off. The standard international normalized ratio (INR) limit for femoral cath was around 1.8u, but for radial procedures, many operators are comfortable with an INR near 2.5u].

Antiplatelet agents, like aspirin, clopidogrel, ticagrelor, or prasugrel are usually not withheld for routine cath but may be withheld in anticipation of a surgery to follow.

Diabetic medications, insulin, or oral hypoglycemic agents (eg, metformin) traditionally have been held before procedures but dietary intake needs to be modified accordingly to prevent hyperglycemia.

Cardiac medications are generally not withheld before cath. These include nitroglycerin or other nitrates, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs), and may be adjusted rather than withheld.

SGLT2 Inhibitors and GLP-1 Agonists

Sodium-glucose cotransporter-2 (SGLT2) inhibitors are a class of medications commonly used to treat type 2 diabetes by blocking renal resorption of glucose. Examples include empagliflozin, canagliflozin, and dapagliflozin. Temporarily discontinuing SGLT2 inhibitors before elective surgeries or procedures is reasonable due to concerns about the risk of euglycemic diabetic ketoacidosis (DKA). The mechanisms of action include renal effects (diuretic response, glycosuria nephroprotection, erythropoietin increase), cardiac effects (decreased left ventricular mass, and improved diastolic function), coronary artery disease impact (reduced vascular stiffness, improved endothelial function), and intracellular impacts (increased utilization of ketone bodies and improved energy processes) (Figure 1).

The glucagon-like-peptide (GLP-1) agonists are associated with adverse gastrointestinal effects such as nausea, vomiting, and delayed gastric emptying, associated with long-term use. The mechanism of action is related to rapid tachyphylaxis at the level of vagal nerve activation. It is thought that delayed gastric emptying from GLP-1 agonists can increase the risk of regurgitation and pulmonary aspiration during general anesthesia and deep sedation. The presence of adverse gastrointestinal symptoms (nausea, vomiting, dyspepsia, abdominal distension) in patients taking GLP-1 agonists is predictive of increased residual gastric contents (Figure 2).

The Bottom Line

New information, methods, and drugs mandate an upgrade of our procedure organization, pre and post medical regimens, and oblige us to attend to any concerns that impact the safety of our procedure. While the SGLT2 inhibitors and GLP-1 agonists were new to me in terms of their potential impact on our procedures, we will likely hold these medications before elective invasive and interventional cardiac procedures. I hope this information will be helpful in your lab as well. ■

References

1. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists task force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. *Anesthesiology*. 2017 Mar; 126(3):376-393. doi:10.1097/ALN.0000000000001452
2. Joshi GP, Abdelmalak BB, Weigel WA, et al. 2023 American Society of Anesthesiologists practice guidelines for preoperative fasting: clear liquids containing carbohydrates with or without protein, chewing gum, and pediatric fasting durations: a modular update of the 2017 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting. *Anesthesiology*. 2023; 138: 132-151. doi:10.1097/ALN.0000000000004381

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Disclosures: Dr. Morton Kern reports he is a consultant for Abiomed, Abbott Vascular, Philips Volcano, ACIST Medical, and Opsens Inc.

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