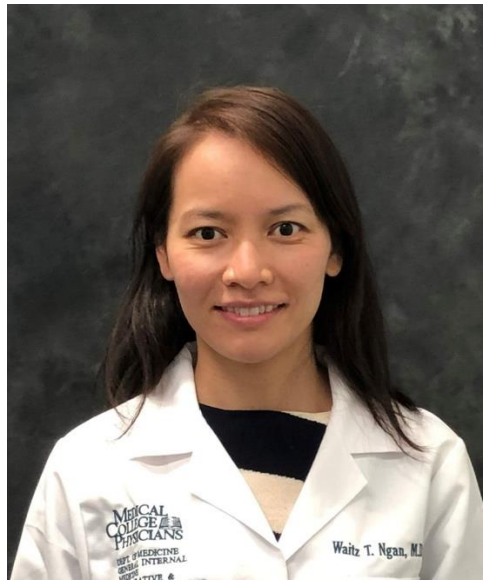


Perioperative Medicine Updates

September 7, 2024

Waitz Ngan MD

Director, Inpatient Medicine Consult Service, Froedtert Hospital

Assistant Professor, Medical College of Wisconsin

Disclosures

- None

Objectives

Review perioperative medicine literature 2023-2024:

- **Identify the predictors of cognitive decline in older adults undergoing surgery**
- **Describe the data on prehabilitation on preoperative and postoperative outcomes**
- **Describe the relationship between postoperative mobilization and postoperative complications**
- **Apply the most recent evidence on perioperative medication management**

Mr. C

65-year-old man with a history of nonobstructive CAD, heart failure with preserved ejection fraction, diabetes, hypertension, obesity, and osteoarthritis, presents for preoperative evaluation prior to right total hip arthroplasty. His medical conditions are well-controlled. No ischemic or HF symptoms. Still able to do > 4METS. Hgb a1c 6.5. He is on the following medications:

- Metoprolol succinate 50mg daily
- Lisinopril 20mg daily
- Furosemide 40mg daily
- Aspirin 81mg daily
- Atorvastatin 80mg daily
- Dapagliflozin 10mg daily
- Metformin 1000mg twice daily
- Semaglutide 0.5mg subcut weekly
- Acetaminophen 500mg as needed

Cardiac evaluation?

Preoperative Cardiac Imaging

APPROPRIATE USE CRITERIA

ACC/AHA/ASE/ASNC/HFSA/ HRS/SCAI/SCCT/SCMR/STS 2024 Appropriate Use Criteria for Multimodality Imaging in Cardiovascular Evaluation of Patients Undergoing Nonemergent, Noncardiac Surgery

A Report of the American College of Cardiology Solution Set Oversight Committee, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons

The American Society of Anesthesiologists affirms the value of this document.

Doherty JU, et al. JACC. August 2024.PMID 39207318

Mr. C has a few questions…

"I heard that anesthesia can cause dementia. Am I going to get dementia?"

Cognitive Trajectory After Surgery

Cognitive trajectory after surgery

Anaesthesia 2024 doi:10.1111/anae.16365

Original Article

Prevalence of neurocognitive disorders 5 years after elective orthopaedic surgery

Kelly J. Atkins,[1,2] **Brendan Silbert,**[2,3] **David A. Scott**[2,3] and **Lis A. Evered**[1,2]

1 Department of Anesthesiology, Weill Cornell Medicine, New York, NY, USA
2 Department of Critical Care, Melbourne Medical School, University of Melbourne, Melbourne, VIC, Australia
3 Department of Anaesthesia and Acute Pain Medicine, St Vincent's Hospital Melbourne, Melbourne, VIC, Australia

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Objective: To report the prevalence of mild cognitive impairment and dementia and identify pre-operative factors associated with neurocognitive disorders 5 years after elective orthopedic surgery

Methods:

- The Anethesia Cognitive Evaluation (ACE) study
  - Prospective, longitudinal study, in 3 hospitals in Melbourne, Australia
- Age >60
- Excluded: pre-existing neurovascular disease; clinically relevant cognitive impairment (MMSE<26); non-English speakers; blindness; deafness; medical comorbidities likely to lead to complications and loss to follow-up

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Methods:

- Assessments pre-operatively or at baseline, at 7 days, 3 months, 12 months, and 5 years – cognitive tests, questionnaires on ADL, mood and subjective cognitive change, and frailty.
- National Institute on Aging and the Alzheimer's Association's criteria for mild cognitive impairment and major neurocognitive disorder were used.
- Primary outcome: prevalence of neurocognitive disorder
- Secondary outcome: predictors of cognitive status at 5-year follow-up

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Results:

- 197 study patients; Mean age at follow-up 75; 66% women
- Mean time to follow-up 60 months
- 21 control patients eligible and had not undergone surgery at 5 years
  - Control group used for secondary outcome only
  - “Primary outcomes (e.g. neurocognitive disorder) were not calculated for the control group as these would be self-referential and, consequently, of little meaning”

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Results:

Primary outcome: Prevalence of neurocognitive disorder

	Pre-operative	5 years post-operative
Mild	61 (30%)	88 (45%)
Major	14 (7%)	33 (**17%**)
Total	75 (38%)	121 (**61%**)

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Results:

Secondary outcome: Predictors of 5-year follow-up cognitive status:

- **Age** (OR 1.07, CI 1.01-1.13, p = 0.02)
- **Baseline neurocognitive disorder** (OR 2.1, CI 1.03-4.08, p = 0.04)

- Frailty, sex, estimated IQ, and mood are not significant predictors

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

Conclusion:

- Prevalence of major neurocognitive disorder (i.e. dementia) after 5 years was 17% -- higher than the population prevalence in Australia of 6.8% in aged 75-84. Prevalence of all NCD was 61%.

Limitations: baseline cognitive differences between groups; small control group; post-operative delirium not assessed; baseline frailty assessment was retrospective; new cardiovascular comorbidities at 5 years not assessed; relationship status and social participation not assessed; generalizability

Clinical impact:

- **Surgery and anesthesia may contribute to the trajectory of cognitive decline in at-risk older adults, including those with pre-operative cognitive impairment.** Mechanism is unclear, requires further research
- Cognitive screening should be part of pre-operative assessments of older adults to inform subsequent care

Atkins JK, et al. Anaesthesia. July 2024. PMID 38985478

Cognitive trajectory after surgery

JAMA Internal Medicine | Original Investigation

Six-Year Cognitive Trajectory in Older Adults Following Major Surgery and Delirium

Zachary J. Kunicki, PhD, MS, MPH; Long H. Ngo, PhD; Edward R. Marcantonio, MD, SM; Douglas Tommet, MS; Yi Feng, MA; Tamara G. Fong, MD, PhD; Eva M. Schmitt, PhD; Thomas G. Travison, PhD; Richard N. Jones, ScD; Sharon K. Inouye, MD, MPH

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

Cognitive trajectory after surgery

Objective:

- To examine patterns and pace of cognitive decline in older adults up to 72 months after experiencing postoperative delirium

Rationale:

- Delirium is the most frequent postop complication in older adults
- Associated with higher risk for long-term cognitive decline and dementia
- A better understanding of the association between delirium and cognitive decline is needed

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

Cognitive trajectory after surgery

Methods:

- Successful Aging after Elective Surgery (SAGE) cohort
  - Prospective observation cohort study, 2 centers in Boston, MA
- 560, Age 70+, English speaking, elective surgery with LOS 3+
- 119 nonsurgical comparison group
- Baseline assessment within 30 days of surgery
- Daily delirium screening while hospitalized
  - Brief cognitive testing
  - Abbreviated delirium symptom interview
  - Interviews with family members and nurses
  - Delirium rated using CAM method

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

Cognitive trajectory after surgery

Methods:

- Post-discharge follow-up assessments at 1, 2, 6, 12, 18, 24, 30, 36, 48, 60, and 72 months
- Cognitive performance using battery of 11 neuropsych tests
- **Composite General Cognitive Performance (GCP) score** created
- Proxy-rated Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) to estimate decline from preexisting levels of cognitive functioning by family members compared with 10 years prior

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

Cognitive trajectory after surgery

Methods:

- Primary outcome:
  - Longitudinal cognitive change on GCP
- Additional Study Variables:
  - Age
  - Sex
  - Race
  - Ethnicity
  - Geriatric depression scale score
  - Surgery type
  - Charlson comorbidity index
  - Impairments in IADLs

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

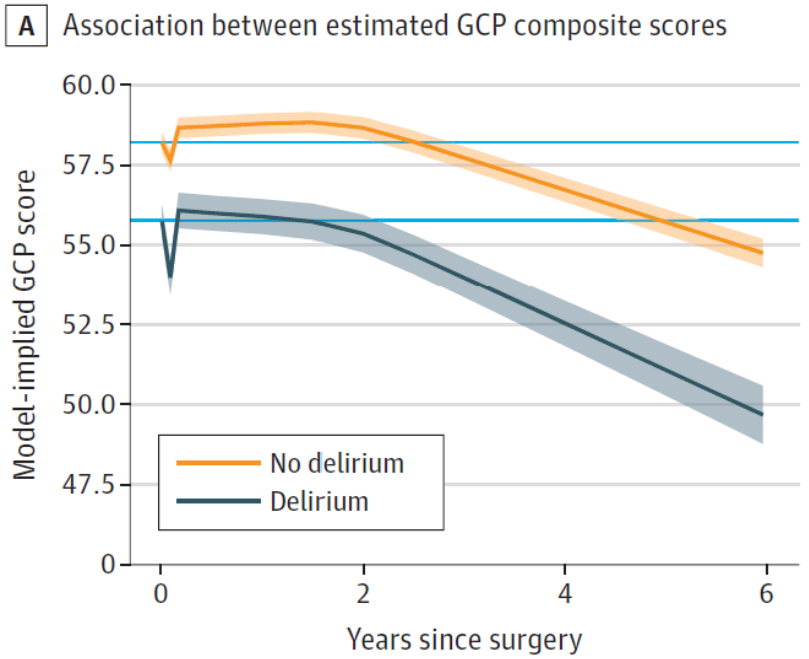
Cognitive trajectory after surgery

Results

Table 3. Adjusted Mean GCP Composite Scores Over Time by Delirium Status

Assessment/point	Mean (SE)[a] Delirium (n = 134)	No delirium (n = 426)	Difference in adjusted scores
Baseline	57.60 (0.26)	57.60 (0.26)	NA
Month 1	55.85 (0.39)	57.06 (0.29)	−1.21 (0.34)
Month 2	57.97 (0.42)	58.07 (0.28)	−0.11 (0.39)
Month 6	57.90 (0.40)	58.12 (0.28)	−0.22 (0.35)
Month 12	57.81 (0.38)	58.19 (0.28)	−0.38 (0.32)
Month 18	57.68 (0.39)	58.22 (0.29)	−0.54 (0.33)
Month 24	57.33 (0.41)	58.05 (0.30)	−0.72 (0.36)
Month 30	56.70 (0.44)	57.61 (0.30)	−0.91 (0.39)
Month 36	56.00 (0.47)	57.11 (0.31)	−1.10 (0.42)
Month 48	54.61 (0.55)	56.10 (0.33)	−1.49 (0.52)
Month 60	53.21 (0.66)	55.09 (0.37)	−1.87 (0.65)
Month 72	51.82 (0.78)	54.08 (0.41)	−2.26 (0.78)
Change from baseline			
Month 1	−1.75 (0.30)	−0.54 (0.15)	
Month 2	0.36 (0.35)	0.47 (0.14)	
Month 6	0.30 (0.32)	0.51 (0.13)	
Month 12	0.21 (0.29)	0.59 (0.13)	
Month 18	0.08 (0.29)	0.62 (0.14)	
Month 24	−0.28 (0.32)	0.44 (0.16)	NA
Month 30	−0.90 (0.34)	0.01 (0.17)	
Month 36	−1.60 (0.38)	−0.50 (0.17)	
Month 48	−2.99 (0.48)	−1.51 (0.21)	
Month 60	−4.39 (0.60)	−2.52 (0.25)	
Month 72	−5.79 (0.72)	−3.53 (0.31)	

Figure. General Cognitive Performance (GCP) Trajectory by Delirium Status



Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

Cognitive trajectory after surgery

Conclusion: Delirium was associated with a 40% acceleration in cognitive decline out to 72 months following elective surgery.

Limitations:
- causal relationship cannot be inferred
- preoperative cognitive trajectory unknown
- subjects highly educated and predominantly White
- CSF biomarkers not available
- confounding illnesses or medications not accounted for

Clinical Impact: Patients with heightened brain vulnerability are more likely to progress to long-term cognitive decline and potentially dementia after a noxious insult such as major surgery and anesthesia.

<u>Delirium prevention is potentially important for older adults undergoing elective surgery</u>

Kunicki ZJ et al. JAMA Intern Med. March 2023. PMID 36939716

"I am nervous. Is there anything I can do to do well and recover well?"

Prehabilitation

Prehabilitation

JAMA Network Open

Original Investigation | Orthopedics

Prehabilitation for Patients Undergoing Orthopedic Surgery
A Systematic Review and Meta-analysis

Anuj Punnoose, MSc; Leica S. Claydon-Mueller, PhD; Ori Weiss, MD; Jufen Zhang, PhD; Alison Rushton, EdD; Vikas Khanduja, PhD

Punnoose A, et al. JAMA Netw Open. April 2023.
PMID 37052919

Prehabilitation

Rationale:

- Prior systematic reviews investigating the benefits of prehabilitation have reported varying conclusions and were limited by heterogeneity

Objective:

- Is prehabilitation associated with improved preoperative and postoperative outcomes in patients undergoing orthopedic surgery?

Punnoose A, et al. JAMA Netw Open. April 2023. PMID 37052919

Prehabilitation

Methods:

- Meta-analysis – Randomized clinical trials (RCT) comparing prehabilitation with standard care for any orthopedic surgery
- Age >18, Jan 2000 through June 2022, English language
- Primary outcomes: pain, muscle strength, function, health-related quality of life (HRQOL), disease- and/or joint-specific outcomes
- Secondary outcomes: anxiety and depression, range of motion, measures of functional performance, and health economic measures

Punnoose A, et al. JAMA Netw Open. April 2023. PMID 37052919

Prehabilitation

Results:

- 48 trials, 3570 patients, 61.5% female, mean age 64.1
  - 28 TKA
  - 7 THA
  - 6 THA & TKA
  - 5 lumbar surgery
- 39 used variety of exercises
  - 10 combined with preop education, 2 with acupuncture, 3 with muscular electrical stimulation
- 39 implemented prehab for at least 4 weeks, 37 had 2 prehab sessions/week.
- Adherence reported in 21 trials (44%)

Punnoose A, et al. JAMA Netw Open. April 2023. PMID 37052919

Prehabilitation

Primary outcomes:

- Improvements in some *preoperative* outcomes for patient undergoing all orthopedic surgical procedures.
  - **Moderate certainty evidence for function, knee flexor strength, 6-minute walk test performance for TKA, abduction strength for THA, and HRQOL for THA and lumbar surgery.**
  - **High-certainty evidence for lumbar surgery and back pain**
- Quality of evidence was inconsistent *postoperatively*
  - **Moderate-certainty evidence favoring prehabilitation for function at 6 weeks in TKA and at 6 months in lumbar surgery**
  - Significant differences in other outcome measures (pain, range of motion, function) but quality of evidence is low to very low

Punnoose A, et al. JAMA Netw Open. April 2023. PMID 37052919

Table. Summary of Evidence Favoring Prehabilitation

Outcome assessment point	Certainty of evidence	Procedure	Statistically significant outcomes favoring prehabilitation
Preoperative	High	Lumbar surgery	Back pain
	Moderate	TKR	Function
			Knee flexor strength
			6MWT
		THR	HRQOL
			Hip Abductor strength
		Lumbar surgery	HRQOL
	Low	TKR	Pain
			Knee extensor strength
			Knee flexion ROM
			TUG
			Stair test
		THR	Pain
			Function
			HRQOL
		Lumbar surgery	Function
6 wk Postoperative	Moderate	TKR	Function
	Low	TKR	Function
			HRQOL
			Knee flexor ROM
			Knee flexor strength
			Knee extensor strength
			TUG
3 mo Postoperative	Low	TKR	Function
			HRQOL
			Stair test
		THR	Function
		Lumbar surgery	Back pain
6 mo Postoperative	Moderate	Lumbar surgery	Function
12 mo Postoperative	Low	THR	Function

Prehabilitation

Conclusion:

- Prehabilitation was associated with moderate improvement in several preoperative outcomes but evidence was inconsistent and quality of evidence was low to very low for postoperative outcomes
- Minimum duration of 4-6 weeks and 2 sessions per week may be recommended for patients undergoing orthopedic surgery.

Limitations:

- Most surgeries are joint replacements and lumbar surgeries, may not be applicable to other surgeries
- No day cases
- Moderate-to-high risk of bias and heterogeneity → certainty of evidence reduced to low to very low
- Need RCTs with low risk of bias

Punnoose A, et al. JAMA Netw Open. April 2023. PMID 37052919

Postoperative Mobilization

Postoperative Mobilization

JAMA Surgery | Original Investigation

Association Between Mobilization and Composite Postoperative Complications Following Major Elective Surgery

Alparslan Turan, MD; Ashish K. Khanna, MD, MS; Jack Brooker, MD; Amit K. Saha, PhD; Clancy J. Clark, MD; Anusha Samant, BS; Elif Ozcimen, MD; Xuan Pu, MS; Kurt Ruetzler, MD; Daniel I. Sessler, MD

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Postoperative Mobilization

Rationale:

- Enhanced Recovery After Surgery (ERAS) protocols are perioperative pathways designed to promote recovery, expedite healing, and reduce postoperative complications. Prompt postsurgical mobilization is an important component of ERAS but there is little evidence it improves postoperative outcomes. Current recommendations are largely based on expert opinion.

Objective:

- What is the association between postoperative mobilization and a composite of postoperative outcomes, cumulative postoperative pain, and 30-day readmission risk in patients after major elective surgery?

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Postoperative Mobilization

Methods:

- Retrospective observational study, single quaternary US referral center
- Elective surgery lasting at least 2 hours, stayed overnight, had at least 12 hours of position and activity monitoring via wearable accelerometers during the initial 48 postoperative hours

Primary outcome: postoperative composite of myocardial injury, ileus, stroke, VTE, pulmonary complications, all-cause in-hospital mortality

Secondary outcome: postoperative pain, 30-day readmission risk, and LOS

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Postoperative Mobilization

Results:

- 8653 patients, mean age 57.6, 52.4% female
- 633 (7.3%) experienced postoperative composite outcome, pulmonary complications were most common
- Median amount of mobilization was 3.9 minutes per hour
- ***Each 4-minute-per-hour increase in mobilization associated with 25% reduction in composite complications***

Table 2. Primary and Secondary Analysis Results, Amount of Mobilization

	No. (%)					
	0-1.6 min/h (n = 2163)	1.6-3.9 min/h (n = 2163)	3.9-7.8 min/h (n = 2163)	7.8-55.3 min/h (n = 2163)	Average relative effect OR (95% CI)[a]	*P* value
Primary analysis						
Composite outcome	249 (12)	161 (7.4)	109 (5)	114 (5.3)	0.75 (0.67 to 0.84)	<.001
Sensitivity analysis[b]						
Composite outcome	249 (12)	161 (7.4)	109 (5)	114 (5.3)	0.75 (0.67 to 0.84)	<.001
Secondary analysis						
TWA pain score, mean (SD)	3.8 (2.1)	3.8 (2.1)	3.7 (2.1)	3.7 (2.2)	0.01 (−0.02 to 0.04)[c]	.43

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Postoperative Mobilization

Results:

Table 3. Association of Mobilization With Collapsed Composite Outcome by Surgery Type

Every 4-min increase in mobilization	No.	Estimated OR (95% CI)	*P* value
Thoracic	342	0.79 (0.72-0.87)	<.001
Cardiac	80	0.83 (0.58-1.20)	.32
Colorectal	1607	0.75 (0.63-0.89)	.001
Orthopedic	2387	0.68 (0.57-0.81)	<.001
Other	4237	0.90 (0.81-1.00)	.06

- ***Each 4-minute increase in mobilization was associated with LOS decrease of 0.12 days (~3 hours)***
- Myocardial injury, ileus, pulmonary complications, and mortality were individually significantly associated with mobilization time
- No association between 30-day readmission and mobilization time
- No association between pain score and mobilization time

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Postoperative Mobilization

Conclusions: Mobilization was associated with fewer postoperative complications and shorter hospital length of stay. ***A 1.5-h increase in mobilization per day – nearly doubling baseline mobilization – to reduce complications by a quarter.*** Substantial nursing and patient effort.

Limitations:

- Retrospective, observational study
- Pandemic interrupted the end of the study
- Confounding factors? Sicker patients ambulate less and are more likely to have postoperative complications? Patients with complications ambulate less. Need RCT

Clinical impact: easily attainable and worth counseling patients preoperatively regarding postoperative mobilization

Turan A, et al. JAMA Surgery. August 2023. PMID 37256591

Medication Management

Perioperative Management of ACE-I and ARB

Discontinuation vs. continuation of renin–angiotensin system inhibition before non-cardiac surgery: the SPACE trial

Gareth L. Ackland [1]*, Akshaykumar Patel[1], Tom E. F. Abbott[1], Salma Begum[1], Priyanthi Dias[1], David R. Crane[1], Sameer Somanath[2], Alexander Middleditch[3], Stuart Cleland[4], Ana Gutierrez del Arroyo[1], David Brealey[5,6,7], and Rupert M. Pearse[1]; on behalf of the Stopping Perioperative ACE-inhibitors or angiotensin-II receptor blockers (SPACE) trial investigators[†]

[1]Translational Medicine and Therapeutics, William Harvey Research Institute, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK; [2]County Durham and Darlington NHS Foundation Trust, Darlington, UK; [3]University Hospitals Bristol NHS Foundation Trust, UK; [4]University Hospitals Plymouth NHS Trust, UK; [5]Bloomsbury Institute of Intensive Care Medicine, University College London, London, UK; [6]UCL Hospitals NHS Foundation Trust, London, UK; and [7]NIHR University College London Hospitals Biomedical Research Centre, London, UK

Received 2 March 2023; revised 7 September 2023; accepted 10 October 2023; online publish-ahead-of-print 3 November 2023

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

Perioperative Management of ACE-I and ARB

Objective:

- Will discontinuation of ACE-I/ARB before non-cardiac surgery reduce myocardial injury and post-op complications?

Methods:

- Multi-center, randomized, open-label trial in the UK
- Age ≥ 60 on ACE-I/ARB, ASA 3+, elective surgery under general anesthesia > 120 min.
- Exclusion: MI within 3 months
- Randomized to stop or continue ACE-I/ARB 24-48h pre-op *depending on drug's duration of action*; restarted POD2 in AM per ESC guidelines
- Blood collected before induction, 24h post-op and 48h post-op

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

Perioperative Management of ACE-I and ARB

- **Primary endpoint**: Myocardial injury (MINS) within 48h of surgery
- **Secondary endpoints**:
  - Highest absolute high sensitivity troponin-T level (hs-TnT) within 48h of surgery
  - Events within 30 days:
    - MI
    - Acute heart failure
    - Stroke
    - Infection
    - Mortality
- **Safety outcomes**
  - Hypotension requiring vasopressor
  - Acute hypertension >180/>100
  - AKI within 30 days
  - Intra-op hypotension or pressor use

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

Results:

- 260 patients – 130 on each arm, 5 centers in UK
- Median age 71
- ~50:50 male:female
- Majority ASA3
- ~2/3 on ACE-I, 1/3 on ARB
- 97% had HTN
- Most prevalent comorbidities included DM, ischemic heart disease, active cancer

Table 1 Baseline characteristics

	Stop[a]	Continue[b]
Sex—no. (%)		
Male	66 (51.2)	68 (51.9)
Female	63 (48.8)	63 (48.1)
Ethnicity (*n*; % black/Afro-Carribean)	6 (5)	4 (3)
Age (years)	72 (67–78)	71 (66–76)
Current smoker—no. (%)	12 (9.4)	10 (7.6)
American Society of Anaesthesiology grade—no. (%)		
III	125 (98.4)	128 (100.0)
IV	2 (1.6)	0 (0.0)
Chronic comorbid disease—no. (%)[c]		
COPD	14 (11.0)	18 (13.7)
Asthma	13 (10.2)	18 (13.7)
Interstitial lung disease or pulmonary fibrosis	0 (0.0)	1 (<1)
Ischaemic heart disease	28 (22.0)	26 (19.8)
Diabetes mellitus	33 (26.0)	41 (31.3)
Heart failure	10 (7.9)	6 (4.6)
Liver cirrhosis	1 (<1)	2 (1.5)
Active cancer	31 (24.4)	32 (24.6)
Stroke or transient ischaemic attack	9 (7.1)	10 (7.6)
Peripheral vascular disease	8 (6.3)	7 (5.3)
Hypertension	124 (97.6)	127 (96.9)
Any treated infections within the previous month	2 (1.6)	4 (3.1)
Planned surgical procedure—no. (%)		
Surgery involving the gut	24 (18.6)	25 (19.1)
All other surgery	105 (81.4)	106 (80.9)
Class of drug routinely taken—no. (%)		
ACE-I	83 (64.3)	79 (60.3)
ARB	46 (35.7)	52 (39.7)

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

Perioperative Management of ACE-I and ARB

Results:

- Preop BP higher when ACEI-I/ARB held
- Primary outcome: ***no significant difference in MINS***
  - 48% if ACE-I/ARB held vs. 41%
- Secondary outcomes:
  - Peak hs-TnT similar between groups
  - MI, stroke, death in < 10 participants
- Adverse events:
  - More frequent hypertensive events if ACE-I/ARB held; no difference in hypotensive events
  - Combination of adverse hypotension and hypertension more common when ACE-I/ARB held and associated with delayed hospital discharge (LOS 6 vs 8 days)

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

Perioperative Management of ACE-I and ARB

Conclusions:

- Discontinuation of ACE-I/ARB did not result in significant reduction in MINS or other complications, but did increase hypertensive events

Limitations:

- *Underpowered*
- Minority under-represented
- Open-label design may have influenced clinical care
- Majority prescribed ACE-I/ARB for HTN; <10% CHF

Further studies needed

Ackland GL, et al. European Heart Journal. November 2023. PMID 37935833

ACP American College of Physicians Leading Internal Medicine, Improving Lives | Wisconsin Chapter

Perioperative Management of ACE-I and ARB

JAMA | Original Investigation

Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery

The Stop-or-Not Randomized Clinical Trial

Matthieu Legrand, MD, PhD; Jérémy Falcone, MD; Bernard Cholley, MD, PhD; Hélène Charbonneau, MD, PhD; Amélie Delaporte, MD; Adrien Lemoine, MD; Matthias Garot, MD; Alexandre Joosten, MD, PhD; Claude Meistelman, MD; Delphine Cheron-Leroy, MD; Jean-Philippe Rives, MD; Bruno Pastene, MD; Antoine Dewitte, MD, PhD; Stéphanie Sigaut, MD, PhD; Marc Danguy des Deserts, MD; Cyrille Truc, MD; Matthieu Boisson, MD, PhD; Sigismond Lasocki, MD, PhD; Philippe Cuvillon, MD, PhD; Ugo Schiff, MD; Samir Jaber, MD, PhD; Morgan Le Guen, MD, PhD; Anaïs Caillard, MD; Stéphane Bar, MD, PhD; Edmundo Pereira de Souza Neto, MD, PhD; Vincent Colas, MD; Florin Dimache, MD; Thibaut Girardot, MD; Elsa Jozefowicz, MD; Simon Viquesnel, MD; Francis Berthier, MD; Eric Vicaut, MD, PhD; Etienne Gayat, MD, PhD; for the Stop-or-Not Trial Group

Legrand M, et al. JAMA. August 2024. PMID 39212270

Perioperative Management of ACE-I and ARB

Objective: to compare the effect of preoperative discontinuation vs continuation of renin-angiotensin system inhibitor (RASI) therapy on all-cause mortality and postoperative complications after major noncardiac surgery

Methods:

- Multi-center, open-label randomized clinical trial at 40 French hospitals
- Age 18+, elective major noncardiac surgery > 2h, hospital stay 3+ days, on ACE-I or ARB for at least 3 months preoperatively
- Continuation: until day of surgery
- Discontinuation: stopped 48h preop
  - Last dose 3 days before surgery

Legrand M, et al. JAMA. August 2024. PMID 39212270

Perioperative Management of ACE-I and ARB

Primary outcome: composite of all-cause mortality and major postoperative complications (major cardiovascular events, sepsis or septic shock, respiratory complications, unplanned ICU admission, AKI, hyperkalemia, surgical reintervention within 28 days)

Secondary outcomes:

- Intraoperative hypotension (MAP<60)
- All-cause mortality
- AKI
- Postop organ failure
- LOS

Legrand M, et al. JAMA. August 2024. PMID 39212270

Results

Baseline Demographic

Table 1. Baseline Demographic and Perioperative Characteristics

	Discontinue use of RASIs (n = 1115)	Continue use of RASIs (n = 1107)
Age, median (IQR), y	68 (61-73)	68 (61-73)
Sex, No. (%)		
Male	730 (65)	721 (65)
Female	385 (35)	386 (35)
Body mass index, median (IQR)[a]	28 (25-32)	28 (25-32)
Coexisting medical condition, No. (%)		
Hypertension	1096 (98)	1083 (98)
Coronary artery disease	179 (16)	183 (17)
Peripheral artery disease	158 (14)	172 (16)
Obstructive sleep apnea	156 (14)	134 (12)
Chronic obstructive pulmonary disease	112 (10)	114 (10)
Chronic kidney disease	102 (9)	96 (9)
Diabetes	89 (8)	87 (8)
History of stroke	74 (7)	67 (6)
Heart failure	72 (6)	69 (6)
Currently smoke	153 (14)	179 (16)
Long-term medication use, No. (%)		
Angiotensin receptor blockers	595 (54)	594 (54)
Statins	515 (46)	473 (43)
Angiotensin-converting enzyme inhibitors	513 (46)	509 (46)
Aspirin	393 (35)	374 (34)
Calcium channel blockers	349 (31)	364 (33)
Diuretics	348 (31)	362 (33)
β-Blockers	334 (30)	354 (32)
Preoperative levels, median (IQR)		
Hemoglobin, g/dL	13.5 (12.5-14.6)	13.6 (12.5-14.6)
Creatinine, mg/dL	0.9 (0.7-1.1)	0.9 (0.7-1.1)
Preoperative hemodynamic parameters, median (IQR)		
Systolic blood pressure, mm Hg	134 (124-146)	131 (121-143)
Diastolic blood pressure, mm Hg	95 (87-103)	93 (85-101)
Ejection fraction, %	57 (49-64)	55 (45-62)
Intraoperative care, No. (%)		
Invasive blood pressure monitoring	329 (30)	334 (30)
Cardiac output or stroke volume monitoring	152 (14)	136 (12)
Central venous pressure monitoring	139 (12)	145 (13)
Neuraxial block	128 (11)	135 (12)
Type of surgery, No. (%)		
Abdominal	376 (34)	364 (33)
Thoracic	177 (16)	192 (17)
Vascular	127 (11)	131 (12)
Urological	112 (10)	106 (10)
Orthopedic	96 (9)	96 (9)
Pelvic	65 (6)	71 (6)
Neurosurgical	53 (5)	52 (5)
Liver	45 (4)	44 (4)
Other[b]	64 (6)	51 (5)
Duration of surgery, median (IQR), min	182 (130-270)	187 (126-270)

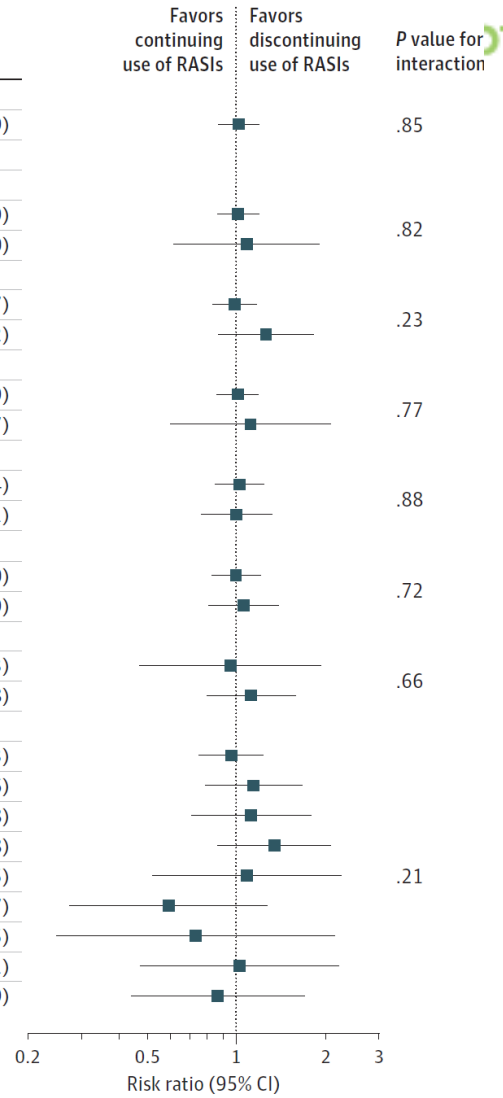
Legrand M, et al. JAMA. August 2024.
PMID 39212270

Results

Primary outcome

Figure 2. Primary Outcome for All Patients and by Individual Patient Subgroups

	Discontinued use of RASIs		Continued use of RASIs			
	No. of events	No. of patients	No. of events	No. of patients	Risk ratio (95% CI)	*P* value for interaction
Primary outcome						
All patients	245	1115	247	1107	1.02 (0.87-1.19)	.85
Patient subgroups						
Age group, y						
≤80	225	1026	230	1037	1.01 (0.86-1.19)	.82
>80	20	89	17	70	1.08 (0.61-1.90)	
History of chronic kidney disease						
No	212	1013	208	1011	0.98 (0.83-1.17)	.23
Yes	33	102	39	96	1.26 (0.87-1.82)	
History of heart failure						
No	230	1043	231	1038	1.01 (0.86-1.19)	.77
Yes	15	72	16	69	1.11 (0.60-2.07)	
Diuretic use						
No	167	767	166	745	1.02 (0.85-1.24)	.88
Yes	78	348	81	362	1.00 (0.76-1.31)	
β-Blocker use						
No	170	781	163	753	0.99 (0.82-1.20)	.72
Yes	75	334	84	354	1.06 (0.80-1.39)	
Elevated level of natriuretic peptide						
No	13	80	13	84	0.95 (0.47-1.93)	.66
Yes	42	143	47	143	1.12 (0.79-1.58)	
Type of surgery						
Abdominal	96	376	89	364	0.96 (0.75-1.23)	
Thoracic	38	177	47	192	1.14 (0.78-1.66)	
Vascular	26	127	30	131	1.12 (0.70-1.78)	
Urological	26	112	33	106	1.34 (0.86-2.08)	
Orthopedic	12	96	13	96	1.08 (0.52-2.25)	.21
Pelvic	14	65	9	71	0.59 (0.27-1.27)	
Neurosurgical	7	53	5	52	0.73 (0.25-2.15)	
Liver	8	45	8	44	1.02 (0.47-2.21)	
Other	16	64	11	51	0.86 (0.44-1.69)	



The primary outcome was a composite of all-cause mortality and major postoperative complications (including major cardiovascular events, sepsis or septic shock, respiratory complications, unplanned intensive care unit admission or readmission, acute kidney injury, hyperkalemia, and need for surgical reintervention) within 28 days after surgery.

Legrand M, et al. JAMA. August 2024. PMID 39212270

Primary and Secondary Outcomes

Table 2. Primary and Secondary Outcomes

	No. (%)[a]				
	Discontinue use of RASIs (n = 1115)	Continue use of RASIs (n = 1107)	Between-group difference (95% CI), %[a]	Unadjusted risk ratio (95% CI)[b]	Adjusted odds ratio (95% CI)[a,c]
Primary outcome[d]					
All patients	245 (22)	247 (22)	0 (−3 to 4)	1.02 (0.83 to 1.25)	1.01 (0.82 to 1.24)
Components of the primary outcome					
All-cause mortality	11 (1)	12 (1)	0 (−1 to 1)	1.10 (0.49 to 2.48)	1.12 (0.48 to 2.58)
Type of postoperative event					
Cardiovascular[e]	52 (5)	52 (5)	0 (−2 to 2)	1.01 (0.69 to 1.47)	1.01 (0.68 to 1.50)
Sepsis	20 (2)	18 (2)	0 (−1 to 1)	0.91 (0.48 to 1.70)	0.91 (0.47 to 1.74)
Respiratory complication[f]	36 (3)	33 (3)	0 (−2 to 1)	0.92 (0.58 to 1.47)	0.94 (0.58 to 1.52)
Acute kidney injury	121 (11)	122 (11)	0 (−2 to 3)	1.02 (0.80 to 1.29)	0.98 (0.74 to 1.29)
Hyperkalemia	21 (2)	27 (2)	1 (−1 to 2)	1.30 (0.74 to 2.28)	1.34 (0.73 to 2.46)
Unplanned admission to intensive care unit	52 (5)	50 (5)	0 (−2 to 2)	0.97 (0.66 to 1.42)	0.94 (0.62 to 1.41)
Reoperation or radiological intervention	86 (8)	95 (9)	1 (−1 to 3)	1.11 (0.84 to 1.47)	1.11 (0.81 to 1.51)
Secondary outcomes					
Episodes of hypotension (required treatment with vasopressors)	417 (41)	544 (54)	13 (9 to 17)	1.31 (1.19 to 1.44)	1.78 (1.47 to 2.16)
Duration of hypotension, median (IQR), min	6 (4 to 12)	9 (5 to 16)	MD, 3.7 (1.4 to 6.0)		AMD, 3.45 (1.11 to 5.78)
Sequential Organ Failure Assessment score at 7 d, median (IQR)[g,h]	3 (1 to 5)	2 (1 to 7)	MD, −0.24 (−1.90 to 1.41)		AMD, −0.01 (−1.73 to 1.71)
Length of hospital stay, median (IQR), d	6 (3 to 8)	5 (3 to 9)	MD, −0.23 (−0.78 to 0.32)		AMD, −0.21 (−0.77 to 0.35)
Length of intensive care unit stay, median (IQR), d[g]	6 (3 to 9)	6 (3 to 10)	MD, 1.07 (−1.63 to 3.78)		AMD, 0.79 (−2.23 to 3.81)
Hospital-free days at day 28 (IQR), d	22 (20 to 25)	23 (19 to 25)	MD, 0.22 (−0.33 to 0.76)		AMD, 0.20 (−0.36 to 0.75)

Abbreviations: AMD, adjusted mean difference; MD, mean difference; RASIs, renin-angiotensin system inhibitors.

[a] Unless otherwise indicated.

[b] The 95% CIs were not adjusted for multiplicity.

[c] Adjusted for age, sex, diabetes status, heart failure status, preoperative serum creatinine level, and preoperative hemoglobin level.

[d] The primary outcome was a composite of all-cause mortality and major postoperative complications (including major cardiovascular events, sepsis or septic shock, respiratory complications, unplanned intensive care unit admission or readmission, acute kidney injury, hyperkalemia, and need for surgical reintervention) within 28 days after surgery.

[e] Included acute myocardial infarction, arterial or venous thrombosis, stroke, acute pulmonary edema, cardiogenic shock, acute severe hypertension crisis, de novo cardiac arrhythmia requiring therapeutic intervention (eTable 1 in Supplement 2).

[f] Patient needed reintubation or noninvasive ventilation for respiratory failure.

[g] Among patients with an unplanned admission to the intensive care unit.

[h] The score range is 0 to 4 points; a higher score indicates a worse predicted outcome.

Legrand M, et al. JAMA. August 2024.
PMID 39212270

Perioperative Management of ACE-I and ARB

- **Conclusions:** a continuation strategy of RASIs before major noncardiac surgery was not associated with a higher rate of postop complications than a discontinuation strategy
- **Limitations:**
  - Open-label, patients and anesthesiologists were not blinded
  - Included range of surgeries, may be underpowered to detect differences in rarer primary outcome components
  - Limited number of CHF patients, limits application of this study for this group
  - Single country (France)
- **Clinical impact:** potential change in practice and guidelines

Legrand M, et al. JAMA. August 2024. PMID 39212270

GLP-1 Receptor Agonists

Perioperative Management of GLP1 Agonists

JAMA Surgery | Original Investigation

Glucagon-Like Peptide-1 Receptor Agonist Use and Residual Gastric Content Before Anesthesia

Sudipta Sen, MD; Paul P. Potnuru, MD; Nadia Hernandez, MD; Christina Goehl, MD; Caroline Praestholm, MS; Srikanth Sridhar, MD; Omonele O. Nwokolo, MD

Sen S, et al. JAMA Surgery. June 2024. PMID: 38446466

Perioperative Management of GLP-1 RA

Objectives: To assess the association between GLP-1 RA use and prevalence of increased residual gastric content (RGC) in fasted patients undergoing elective procedures under anesthesia using gastric ultrasonography (GUS)

Methods:

- Cross-sectional study of prospectively enrolled patients at a tertiary university-affiliated hospital
- Age 18+, ASA I-IV, elective procedures under anesthesia, standard preanesthesia fasting protocol
  - 2h clears, 6h light meal, and 8h full, heavy meal
- Exclusions: patients with large hiatal hernia or h/o gastric surgery, pregnancy, trauma within 1 month, inability to lie in right lateral decubitus position
- Exposure: once-weekly GLP-1 RA
  - Semaglutide, dulaglutide, tirzepatide – half-lives 7, 5, and 5 days, respectively

Sen S, et al. JAMA Surgery. June 2024. PMID: 38446466

Perioperative Management of GLP-1 RA

Primary outcome:

- Increased RGC
  - Presence of solids, thick liquids, or more than 1.5mL/kg clear liquids on GUS

Secondary outcome:

- Association between increase RGC and days since the last dose of GLP-1 RA

Sen S, et al. JAMA Surgery. June 2024. PMID: 38446466

Perioperative Management of GLP-1 RA

Results:

- 124 patients, 60% female
- 50% receiving once-weekly GLP-1 RA, 50% control
- GLP-1 RA group: older, higher ASA class, longer time since last oral intake, *more diabetes, GERD, and opioid use*
- **GLP-1 RA use associated with 30.5% higher prevalence of increased RGC, after adjusting for confounders**
- **Prevalence of increased RGC was elevated even after 7-day hold**
- Insignificant trend of decreasing prevalence of increased RGC with each additional day of drug discontinuation

Sen S, et al. JAMA Surgery. June 2024. PMID: 38446466

Perioperative Management of GLP-1 RA

Conclusions:

- Once-weekly GLP-1 RA was associated with a significantly higher prevalence of increased RGC on preprocedural GUS
- Holding GLP-1 RA up to 7 days did not decrease prevalence of increased RGC back to baseline prevalence

Limitations:

- Primary outcome used is only a surrogate for aspiration risk
  - Exact gastric volume at which aspiration risk is meaningfully increased is unclear
- Did not directly assess aspiration events, which are rare
- Observational study, unknown bias from unmeasured confounders
- Results of secondary analyses are potentially underpowered
- Convenience sampling could introduce selection bias
- **No mention of how long patients had been on GLP-1 RA prior to study initiation**

Sen S, et al. JAMA Surgery. June 2024. PMID: 38446466

ACP American College of Physicians Leading Internal Medicine, Improving Lives | Wisconsin Chapter

Perioperative Management of GLP-1 Agonists

Quantified Metrics of Gastric Emptying Delay by Glucagon-Like Peptide-1 Agonists: A Systematic Review and Meta-Analysis With Insights for Periprocedural Management

Brent Hiramoto, MD, MPH[1,2,*], Thomas R. McCarty, MD, MPH[3,4,5,*], Nayna A. Lodhia, MD[1,2], Andrew Jenkins, MD[1,2], Ahmed Elnaiem, MD[2,6], Mayssan Muftah, MD, MPH[1,2], Ryan Flanagan, MD, MPH[1,2] and Walter W. Chan, MD, MPH[1,2]

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Objectives: To quantify the duration of gastric emptying delay associated with glucagon-like peptide-1 (GLP-1) receptor agonists (GLP-1 RA) therapies.

Methods:

- Systematic review and meta-analysis of studies in 2003-2023
- Protocolized search to identify studies on GLP-1 RA that quantified gastric emptying measures by scintigraphic measurement, stable isotope breath testing, acetaminophen-based absorption test (AAT), wireless motility capsule
- GLP-1 RA included both short- and long-acting formulations – liraglutide, lixisenatide, semaglutide, albiglutide, dulaglutide, tirzepatide.
- Exclusion: IV GLP-1 RA, age < 18, lack of quantitative reporting of gastric emptying, lack of comparator arm

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Primary aim:

- To quantify duration of gastric emptying delay associated with GLP-1 RA

Secondary aims:

- Compare short-acting with long-acting GLP-1 RA on gastric emptying delay
- Whether estimates differed based on duration of therapy and diagnostic modality of gastric emptying assessment

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Results:

- 36 studies, 1574 patients
- Gastric emptying assessment modalities:
  - 7 scintigraphy; 19 AAT; 5 stable isotope breath testing; 3 EGD; 2 wireless motility capsule
- Majority done in the US (19) and Europe (12), remainder in Asia (2), Australia (2), and Canada (1)
- Primary indication for GLP-1 RA was diabetes (67% of studies) and overweight or obesity (17%)

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Primary outcome: Quantified gastric emptying by scintigraphy

Time required for 50% of ingested gastric contents to empty ($T_{1/2}$)

- 5 RCTs or randomized crossover trials
- 247 patients, mean age 44, BMI 33, 82% female
- Pooled $T_{1/2}$ was 138.4 mins for GLP-1 RA vs. 95.0 mins for placebo
- ***Pooled mean difference of 36.0 mins***
- No association between formulation and $T_{1/2}$; ***no difference between short- vs. long-acting formulations, no correlation between duration of trial on gastric emptying***
- Greater delay in gastric emptying for patients BMI ≥30kg/m^2

Gastric retention at 4 hours:

- 2 studies: substantial variations in outcome measures
- 1 RCT on weekly semaglutide noted 4-hour gastric retention 37% after 13 weeks of GLP-1 RA vs. 7% before.

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Secondary outcome: Gastric emptying measures by AAT

- Time elapsed until peak level of acetaminophen concentration (T_{max})
- 18 RCT or randomized crossover trials, 1 prospective interventional trial
- 6 measured T_{max}, 284 patients, mean age 45.5, BMI 29.9, 36.6% female
  - ***No significant difference in gastric emptying***
    - Pooled mean difference T_{max} of 1.6 mins
  - No association between GLP-1 RA formulations and T_{max}; ***no difference between short- vs. long-acting formulations, no effect on rate of emptying by trial duration or BMI***
- 8 included gastric emptying estimates at 4 or 5 hours on AAT
  - no difference between GLP-1 RA vs. placebo

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Secondary outcome:

Stable isotope breath testing

- 5 studies, heterogeneity limited ability to perform meta-analysis
- Gastric emptying outcomes were mixed

Wireless motility capsule:

- 2 studies: prospective crossover study, 14 patients; RCT, 39 patients.
- Both used liraglutide, trial duration 3+ weeks
- No difference in gastric transit time

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Conclusion:

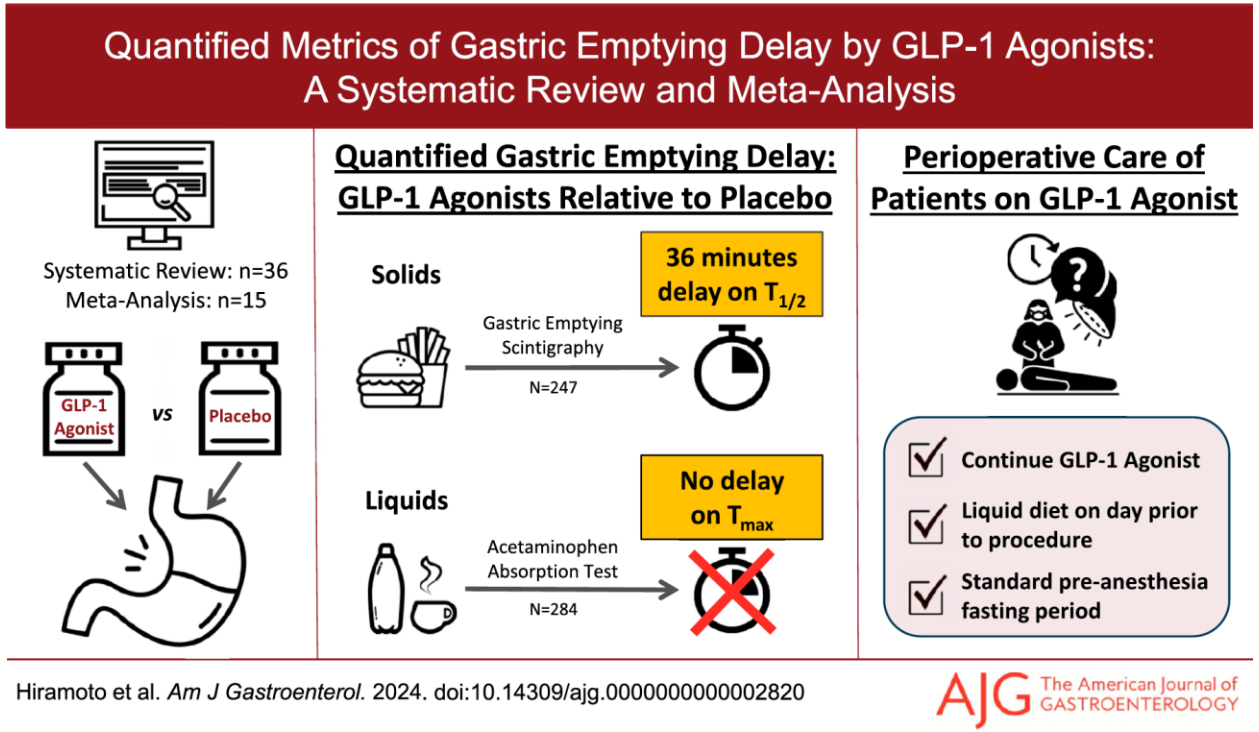
- GLP-1 RA was associated with a mild gastric emptying delay (~36 minutes per $T_{1/2}$) on solid-phase scintigraphy, and no differences in liquid emptying
- No evidence of tachyphylaxis by duration of use or long- vs. short-acting formulation
- More studies quantifying gastric retention on scintigraphy at 4 hours are needed.
- **Proposal: continue GLP-1 RA, liquid diet day prior to procedure, and standard preanesthesia fasting periods**

Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

Perioperative Management of GLP-1 RA

Limitations:

- Small number of studies for certain diagnostic modalities
- Unable to stratify meta-analysis by GLP-1 RA indication (diabetes vs. obesity)
- Few studies employed the optimal scintigraphy test per current guidelines
- AAT is a surrogate measure of gastric emptying that also depends on intestinal absorption



Hiramoto B, et al. Am J Gastroenterol. June 2024. PMID: 38634551

ACP Wisconsin Chapter

Perioperative Management of SGLT-2 Inhibitors

Dose-dependent relationship between SGLT2 inhibitor hold time and risk for postoperative anion gap acidosis: a single-centre retrospective analysis

Benjamin Steinhorn* and Jeanine Wiener-Kronish

Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, USA

Steinhorn B, et al. Br J Anaesth. October 2023. PMID 37541949

Perioperative Management of SGLT-2 Inhibitors

Rationale: Sodium-glucose transporter-2 (SGLT-2) inhibitors are increasingly prescribed for diabetes, CKD, and CHF

Objective: To identify risk factors that predispose surgical patients taking SGLT-2 inhibitors to post-procedural euglycemic diabetic ketoacidosis

Methods:

- Single-center, retrospective analysis in Boston
- All *operating room* procedures in 5/2016-6/2022; non-OR excluded
- 463 patients with SGLT-2 inhibitor on home med list at the time of surgery; 70% male
- 76% with diabetes; non-diabetic patients included

Steinhorn B, et al. Br J Anaesth. October 2023. PMID 37541949

Results

Baseline characteristics

Table 1 Baseline patient, procedural, and laboratory characteristics. ASA, American Society of Anesthesiologists; eGFR, estimated glomerular filtration rate; HbA1c, haemoglobin A1c; IQR, inter-quartile range; SD, standard deviation; SGLT2, sodium-glucose transporter-2.

	n (%)
Sex	
Male	325 (70)
Female	138 (30)
Race	
White	353 (76)
Black or African-American	30 (6)
Asian	26 (6)
American Indian/Alaska Native	1 (<1)
Unknown	53 (11)
SGLT2 inhibitor	
Empagliflozin	399 (86)
Dapagliflozin	64 (14)
Comorbidities	
Diabetes mellitus	354 (76)
Insulin use	256 (55)
Heart failure	169 (37)
Chronic kidney disease	103 (22)
Procedure class	
Elective/non-urgent	421 (91)
Emergent/urgent	42 (9)
Patient class	
Inpatient	135 (29)
Outpatient	328 (71)
ASA physical status	
2	6 (12)
3	46 (51)
4	31 (25)
5	4 (<1)
Unspecified	75 (16)
Surgical service	
Cardiac surgery	130 (28)
General surgery	48 (10)
Vascular surgery	45 (10)
Orthopaedic surgery	44 (10)
Neurosurgery	42 (9)
Interventional cardiology	18 (4)
Urology	11 (2)
Thoracic surgery	10 (2)
Other	115 (25)

Steinhorn B, et al. Br J Anaesth. October 2023. PMID 37541949

Perioperative Management of SGLT-2 Inhibitors

Results:

- Strong inverse association between hold time and postop anion gap
  - -0.43 change in anion gap per day held
  - Effect significantly magnified in patients undergoing emergency surgery
  - Independent of preop anion gap, albumin, lactate, eGFR
- No interaction with insulin use at baseline or cardiac surgery

Table 2 Multivariable regression model for postoperative anion gap. Study variables were SGLT2 inhibitor hold time in days and interactions between hold time, emergency surgery, insulin use, and cardiac surgery. Bolded values indicate $P<0.0125$ ($P<0.05$ with Bonferroni correction) for the four study variables.

Parameter	Coefficient (95% CI)	P-value
Preoperative anion gap (mM)	0.40 (0.27–0.52)	<0.001
eGFR (ml min^{-1} 1.73^{-1} m^{-2})	−0.02 (−0.03 to 0.00)	0.01
Albumin (g dl^{-1})	0.51 (−0.03 to 1.06)	0.06
Lactate (mM)	0.60 (0.46–0.75)	<0.001
SGLT2 inhibitor hold time (days)	−0.43 (−0.76 to −0.11)	**0.01**
Interactions		
Hold time × emergency surgery (days)	1.06 (0.27–1.09)	**0.009**
Hold time × cardiac surgery (days)	0.13 (−0.44 to 0.20)	0.44
Hold time × insulin use (days)	−0.16 (−0.54 to 0.22)	0.42

CI, confidence interval; eGFR, estimated glomerular filtration rate; SGLT2, sodium-glucose transporter-2.

Steinhorn B, et al. Br J Anaesth. October 2023. PMID 37541949

Perioperative Management of SGLT-2 Inhibitors

Conclusion: First evidence that AG acidosis developed in all patients who do not hold SGLT-2 inhibitors rather than a binary relationship in an "idiosyncratic few"

Limitations:

- AG as surrogate for ketoacidosis
- Non-OR anesthesia patients excluded
- Limited generalizability – small sample size at a single institution
- Mean hold time 1.5 days – recommended 3-4 day hold
- Retrospective

Clinical impact: If SGLT-2 inhibitor is not held preop, postop AG and ketone monitoring can help detect significant eDKA and prevent significant metabolic complications, especially in the setting of emergency surgeries.

Steinhorn B, et al. Br J Anaesth. October 2023. PMID 37541949

Take-Home Points

1. Watch out for the 2024 ACC/AHA Guidelines on Perioperative Cardiovascular Evaluation coming out really soon
2. Age, baseline cognitive impairment, and postoperative delirium predict long-term cognitive trajectory following surgery; postop delirium is associated with a faster pace of decline
3. We need more RCTs to study the impact of prehabilitation on postoperative outcomes
4. An increase in postoperative mobilization may reduce complications and reduce LOS
5. It does not seem to matter whether ACEI/ARB is continued preoperatively, at least if the indication is for hypertension
6. We need more data on GLP-1 RA. Holding 1 dose of weekly GLP-1RA does not seem to be enough, and if we continue it, we should consider liquid diet the day prior along with standard preanesthesia precautions.
7. If SGLT-2 inhibitor is not held preoperatively, postop anion gap and ketone monitoring can help detect significant eDKA and prevent complications, especially in the setting of emergency surgeries

ACP American College of Physicians Leading Internal Medicine, Improving Lives | Wisconsin Chapter

Thank you

References