GLP-1 Receptor Agonists Used for Medically-Supervised Weight Loss:
Considerations for the Arthroplasty Surgeon

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Arthroplasty for the Modern Surgeon
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Disclosures

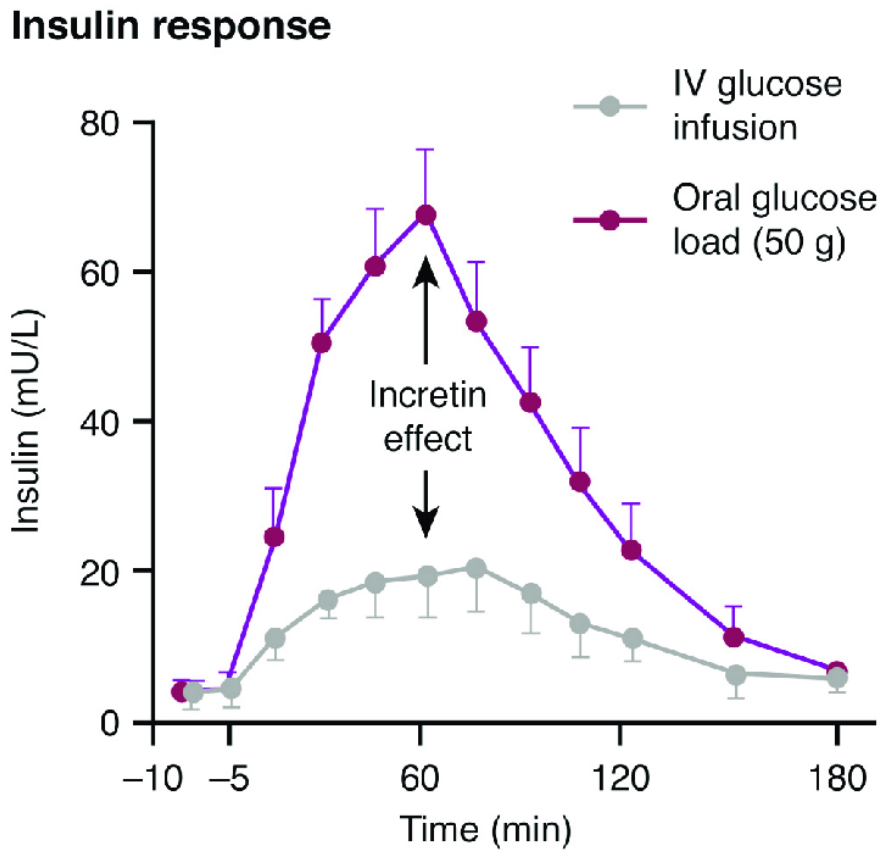
- **Consulting:**
  - Corin
  - Intellijoint
  - Zimmer-Biomet
  - DJO/Enovis
- **Development:**
  - Zimmer-Biomet
  - DJO/Enovis
- **Stock ownership:**
  - Intellijoint
- **Research support:**
  - OREF
  - Intellijoint
  - Corin
  - Zimmer-Biomet
- **Committee membership:**
  - AAHKS
  - AAOS
  - WOA

Goals of talk:

1. How do GLP-1 receptor agonists work?
2. Why should I care about this class of medications?
3. Considerations for the arthroplasty surgeon.

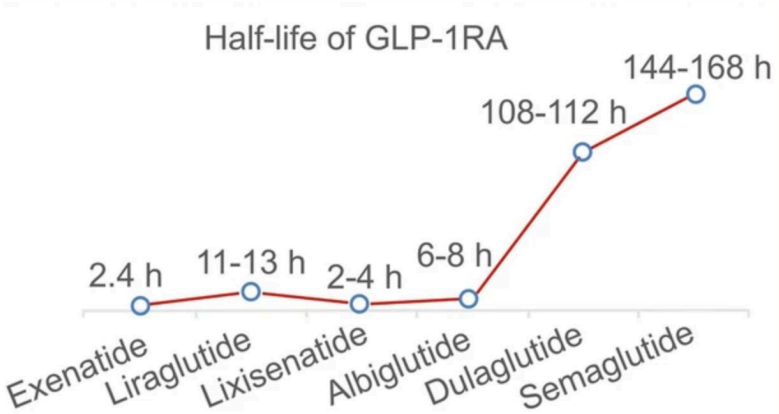
Background

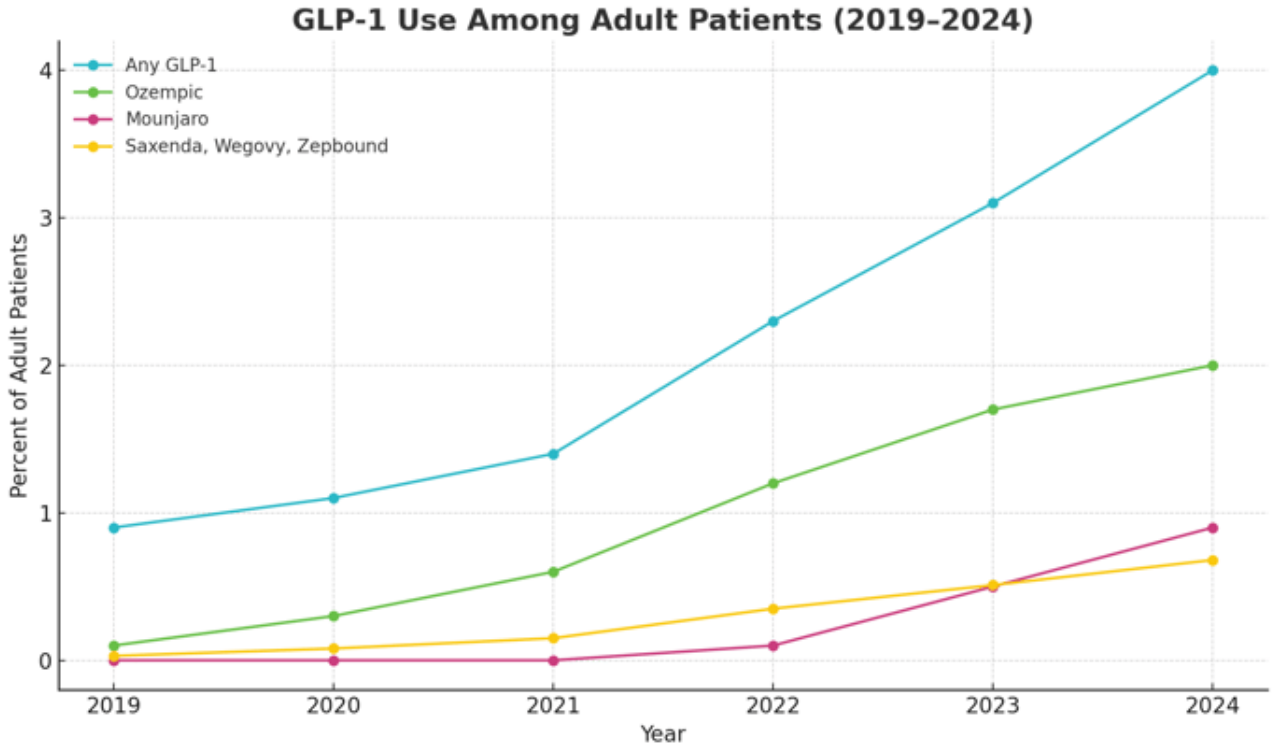
- "Incretin effect" – the 2- to 3-fold increase in insulin in response to oral glucose compared to IV glucose
- GLP-1 and GIP are the two most abundant incretin hormones
- Endogenous GLP-1 and GIP have relatively short half-lives
- Exendin-4 in the venom of the Gila monster lizard has similar structure as GLP-1 but far more stable.



Background

- Synthetic GLP-1 receptor agonists with increased half-lives lead to broad adoption:
- Liraglutide (Victoza/Saxenda)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic/Wegovy)



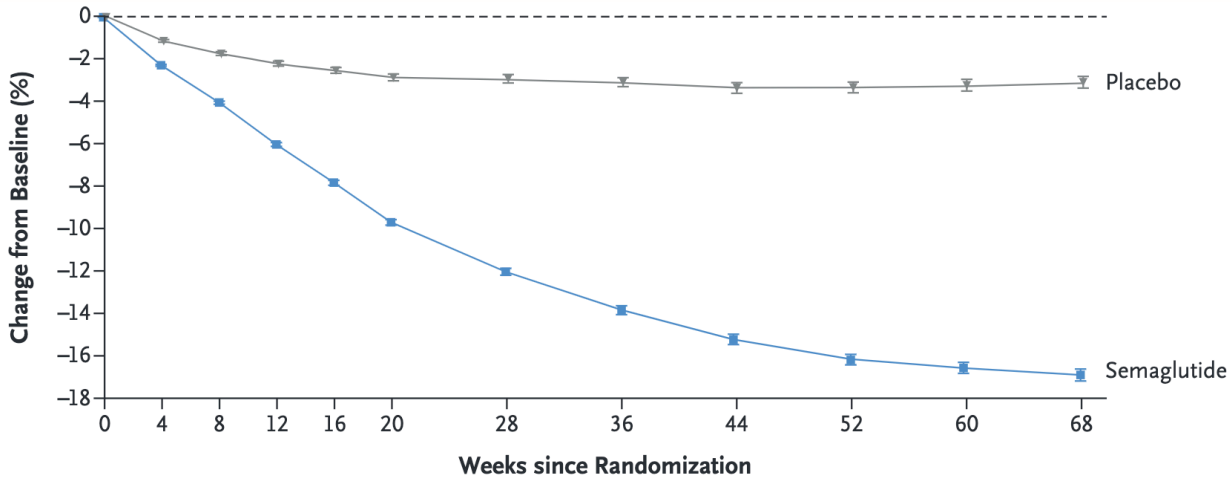


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 18, 2021 VOL. 384 NO. 11

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*



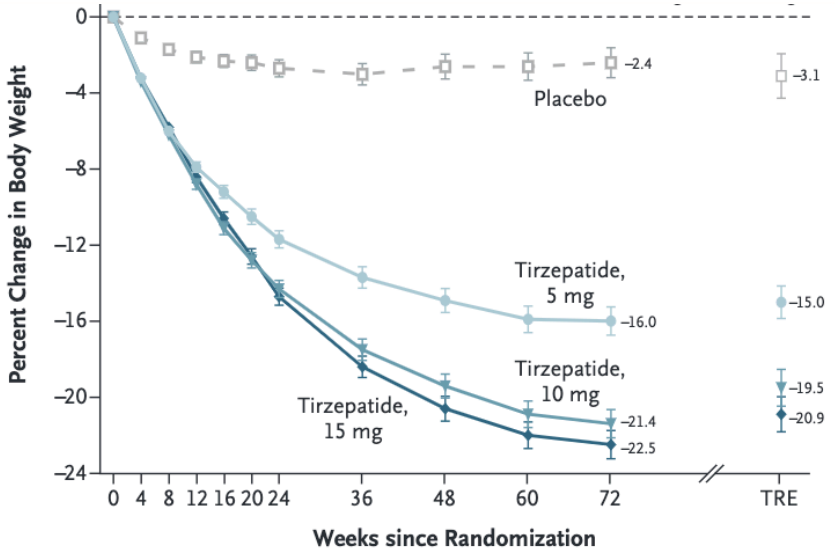
- Semaglutide (Ozempic/Wegovy)
  - **15.8% weight loss**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 21, 2022 VOL. 387 NO. 3

Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators*



- Tirzepatide (Mounjaro/Zepbound)
  - **20.9% weight loss**

Mechanisms of Action

- Increase insulin secretion and production
- Delay gastric emptying leading to early satiety while preventing over-eating
- Acts on central nervous system to decrease hunger and further promote satiety

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Glucagon-Like Peptide Receptor-1 Agonists Used for Medically-Supervised Weight Loss in Patients With Hip and Knee Osteoarthritis: Critical Considerations for the Arthroplasty Surgeon

Nathanael D. Heckmann, MD[a,*], Ryan Palmer, BS[a], Cory K. Mayfield, MD[a], Gligor Gucev, MD[b], Jay R. Lieberman, MD[a], Kurt Hong, MD, PhD[c]

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[b] Department of Anesthesiology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA
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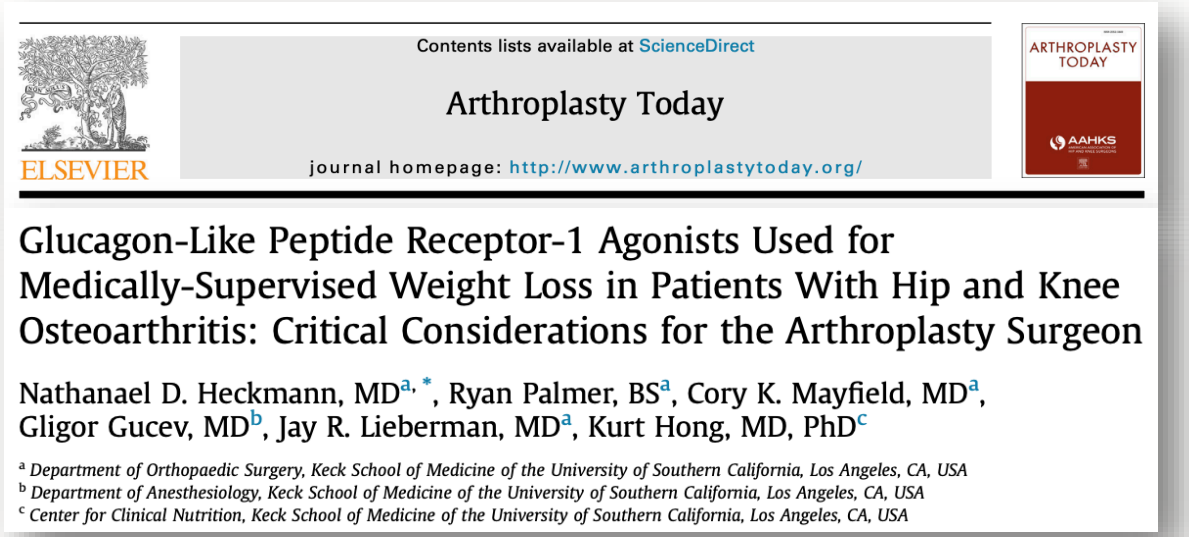
Organ system	Function	GLP-1	GIP	Glucagon
Pancreas	Insulin secretion	↑↑ [54,55]	↑↑ [56]	↑↑ [57]
	Insulin biosynthesis	↑↑ [58-61]	↑↑ [62]	Unknown
	β-Cell proliferation	↑↑ [58-61]	↑↑ [62]	↑/↔ [63]
	β-Cell apoptosis	↓↓ [54,55]	↓↓ [62]	Unknown
Stomach	Gastric emptying	↓↓ [64,65]	↓/↔ [66]	↓↓ [67]
	Gastric acid secretion	↓↓ [68]	↓/↔ [66,69]	↓↓ [70]
Liver (indirect effects)	Glucose production	↓ [62]	↓/↔ [62,71]	↑↑ [62]
Brain	Satiety	↑↑ [72-75]	↑/↔ [76]	↑↑ [77]
	Hunger	↓↓ [78-82]	↓/↔ [83]	↓ [84,85]
Adipose	Lipogenesis	↑ [86]	↑↑ [87,88]	↓↓ [89,90]
	Lipolysis	↑ [86]	↓/↔ [91]	↑/↔ [92]
Skeletal muscle	Glucose uptake	↑/↔ [62,93]	↓/↔ [94]	↔ [95]
	Glycogenolysis	↓/↔ [96]	↔ [94]	↔ [97]

Mechanisms of Action

- Non-weight loss health benefits:
  - Improves cardiac function
  - Lowers risk of stroke, myocardial infarction
  - Lowers risk of mortality
  - Lowers LDL
  - Increases HDL



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Glycemic control	Lowers blood sugar Stimulates insulin secretion Stimulates insulin biosynthesis Increases insulin sensitivity Suppresses glucagon
Cardiovascular	Lowers blood pressure Increased cardiac output Lowers risk of stroke Lowers risk of myocardial infarction Lowers risk of mortality
Lipid profile	Lowers LDL Increases HDL Lowers triglyceride levels

Mechanism of Action

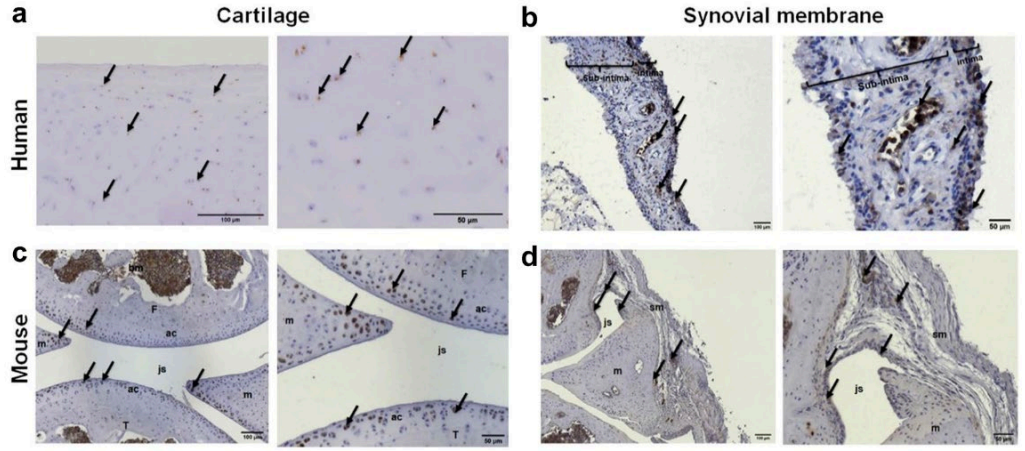
- GLP-1 receptor is present in human articular cartilage and the synovial membrane
- In an osteoarthritis mouse model, liraglutide displayed potent anti-inflammatory
- Liraglutide treatment led to a decrease in several pro-inflammatory cytokines implicated in the progression and pathogenesis of osteoarthritis including nitrite, prostaglandin E2, and interleukin 6

Liraglutide, a glucagon-like peptide 1 receptor agonist, exerts analgesic, anti-inflammatory and anti-degradative actions in osteoarthritis

C. Meurot[1], C. Martin[1], L. Sudre[1], J. Breton[1], C. Bougault[2], R. Rattenbach[1,3], K. Bismuth[1], C. Jacques[2] & F. Berenbaum[3,4]✉

scientific reports

nature



Expression of GLP-1 receptor in human and mouse

Primary Hip and Knee Arthroplasty

Decreased Risk of Readmission and Complications With Preoperative GLP-1 Analog Use in Patients Undergoing Primary Total Joint Arthroplasty

Anirudh Buddhiraju, MD, Whitney Kagabo, MD, Harpal S. Khanuja, MD, Julius K. Oni, MD, Lucas E. Nikkel, MD, Vishal Hegde, MD *

Department of Orthopaedic Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland

Journal of Arthroplasty, 2024

As Few as Three Months of Preoperative Semaglutide Exposure Prior to Total Knee Arthroplasty Is Associated With Reduced Postoperative Adverse Events in Patients Who Have Type II Diabetes

Anthony E. Seddio, MD, Rajiv S. Vasudevan, MD, Michael J. Gouzoulis, MD, Jeremy K. Ansah-Twum, MD *, Jonathan N. Grauer, MD *, Lee E. Rubin, MD

Department of Orthopaedics and Rehabilitation, Yale School of Medicine, New Haven, Connecticut

Journal of Arthroplasty, 2025

Glucagon-Like Peptide-1 Receptor Agonists Decrease Medical and Surgical Complications in Morbidly Obese Patients Undergoing Primary TKA

Billy I. Kim, MD, Scott M. LaValva, MD, Michael L. Parks, MD, Peter K. Sculco, MD, Alejandro G. Della Valle, MD, and Gwo-Chin Lee, MD

Investigation performed at the Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY

Journal of Bone and Joint Surgery, 2024

2024 AAHKS Proceedings

Utilization of Glucagon-Like Peptide-1 Receptor Agonist at the Time of Total Hip Arthroplasty for Patients Who Have Morbid Obesity

Billy I. Kim, MD [a], Tyler K. Khilnani, MD [a], Scott M. LaValva, MD [a], Susan M. Goodman, MD [b], Alejandro G. Della Valle, MD [a], Gwo-Chin Lee, MD [a,*]

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[b] *Hospital for Special Surgery, Department of Rheumatology, New York, New York*

Journal of Arthroplasty, 2025

Proceedings of The Hip Society 2024

GLP-1 Agonists for Weight Loss: Do They Increase Complications in Non-diabetic Patients Undergoing Primary Total Hip Arthroplasty?

Jens T. Verhey, MD [a,*], Roman P. Austin, BS [b], Saad Tarabichi, MD [a], Benjamin Paul, BS [a], David G. Deckey, MD [a], Zachary K. Christopher, MD [a], Mark J. Spangehl, MD [a], Joshua S. Bingham, MD [a]

Journal of Arthroplasty, 2025

GLP-1 agonists are protective against postoperative complications following total knee arthroplasty

Rachel Ranson [a,*], Philip M. Parel [a], Julia Kirkland [b], Jackson W. Durbin [a], Jordan C. Villa [a], Robert Sterling [a]

[a] *Department of Orthopaedic Surgery, The George Washington University School of Medicine and Health Sciences, Washington,*
[b] *Kansas City University College of Osteopathic Medicine, Kansas City, MO, United States*

Knee, 2025

Considerations for the Arthroplasty Surgeon

- **Risk of pulmonary aspiration during anesthesia**:
  - GLP-1 mediated delayed gastric emptying
  - Likely dose and medication dependent
  - Highest risk during dose-escalation phase

  - Stop GLP-1 and dual receptor agonists 2 weeks prior to elective surgery
  - Gastric ultrasound can be used to identify gastric contents prior to non-elective cases
  - Rapid sequence intubation & nasogastric tube evacuation of gastric contents

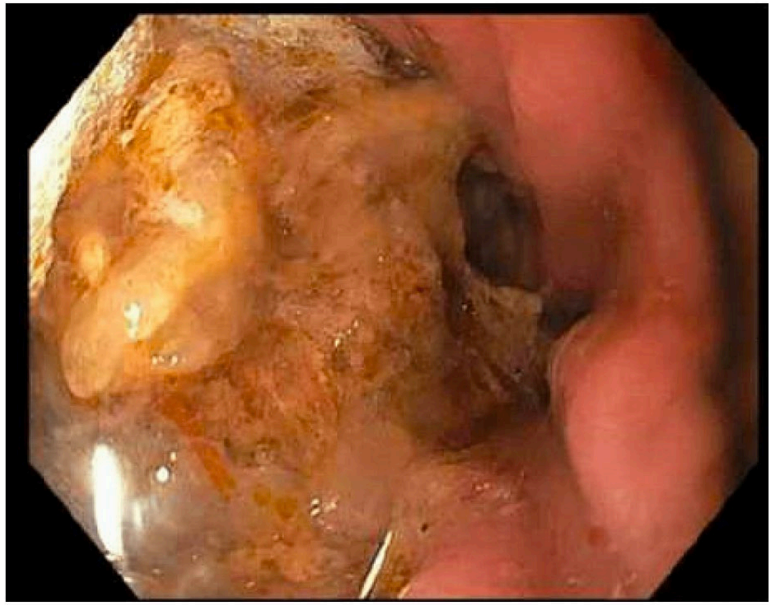
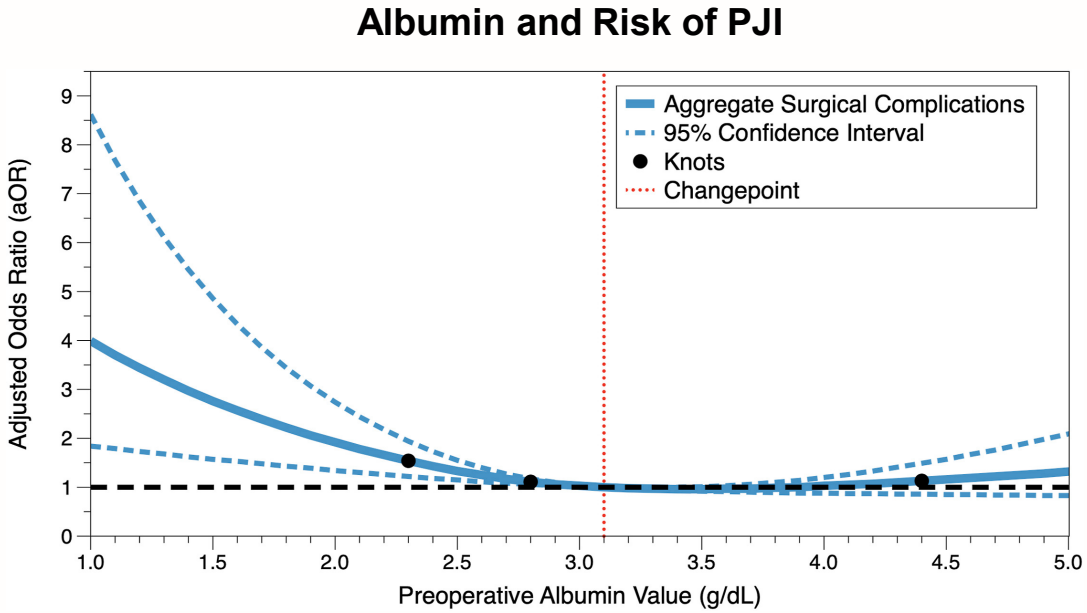


FIGURE 1: EGD showing the presence of food in the stomach despite fasting to solids for over 10 hours.

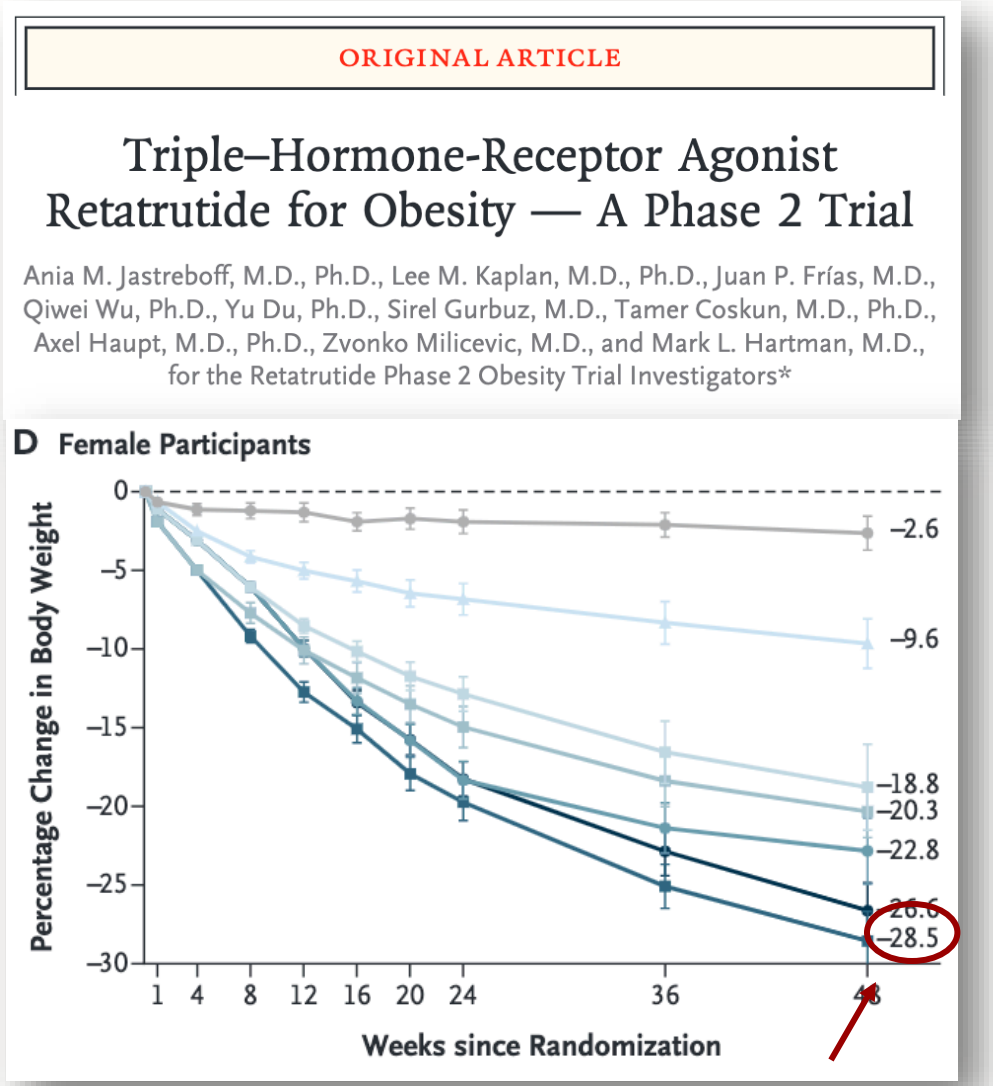
Considerations for the Arthroplasty Surgeon

- **Malnutrition & Catabolic States**:
  - GLP-1 agonists may allow patients to enact anorectic deleterious behaviors
  - Rapid weight loss may lead to catabolic state
  - Consider checking albumin to screen for malnutrition (cutoff 3.0-3.5 g/dL)
  - Encourage increased caloric/protein consumption in the weeks prior to surgery and the weeks afterward
  - Delay surgery until weight has plateaued



Conclusion

- GLP-1 and dual receptor agonists are effective weight loss tools
- Utilization will continue to increase given efficacy and other health benefits
- Newer, more effective medications are on the horizon
- Surgeons should identify utilization among their patients and develop a strategy to manage these patients


ORIGINAL ARTICLE

Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

Ania M. Jastreboff, M.D., Ph.D., Lee M. Kaplan, M.D., Ph.D., Juan P. Frías, M.D., Qiwei Wu, Ph.D., Yu Du, Ph.D., Sirel Gurbuz, M.D., Tamer Coskun, M.D., Ph.D., Axel Haupt, M.D., Ph.D., Zvonko Milicevic, M.D., and Mark L. Hartman, M.D., for the Retatrutide Phase 2 Obesity Trial Investigators*

THANK YOU!!!