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COMMENTARY

Dietary Recommendations for the Management of Gastrointestinal Symptoms in Patients Treated with GLP-1 Receptor Agonist

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Abstract: GLP-1 receptor agonist (GLP-1RA) have been developed to address the global burden of obesity and are renowned for their safety and efficacy. These medications influence hunger and satiety, reducing energy intake and promoting weight loss. Despite their benefits, GLP-1RAmay cause a slowed gastric emptying, leading to gastrointestinal symptoms. This study examines how food properties and meal composition affect these symptoms. Dietary recommendations are provided, particularly for evening meals, focusing on how different foods and nutrients can influence the rate of gastric emptying, to improve patient compliance and prevent interruption in weight loss.

Keywords: obesity, GLP-1 receptor agonist, gastric emptying, nausea, food viscosity

Introduction

As reported by the World Health Organization (WHO) in 2022, globally, 43% of the adult population is overweight and 16% experience obesity.[1] The global spread of obesity and the resulting burden on public health have prompted the development of new approaches to treat individuals with this condition. Although lifestyle interventions are effective and the first approach for managing obesity, they may not be sufficient, necessitating pharmacological therapy.[2,3] There are different types of drugs that have been developed through the years; among these, GLP-1 receptor agonists (GLP-1RAs) are known for their safety and efficacy[4] due to their ability to act at the hypothalamic influencing hunger and fullness, and consequently reducing caloric intake.[5] Despite their benefits, GLP-1RAs may cause a slowdown in gastric emptying, leading to temporary gastrointestinal symptoms such as nausea, diarrhea, and constipation.[6] The effects of GLP-1RAs on gastric emptying do not fully account for the occurrence of diarrhea or constipation, which are likely mediated by different mechanisms. Additionally, GLP-1RAs significantly impact central nausea centers, contributing to their gastrointestinal side effects.[7]

Providing specific dietary and behavioral guidelines is crucial to improve patient compliance and avoid interruption of weight loss. Recently, an expert consensus has been published, offering practical advice on managing gastrointestinal adverse events in individuals with type 2 diabetes mellitus (T2DM) and obesity who are treated with GLP-1RAs.[8] Nevertheless, there is a lack of precise recommendations concerning meal composition and food selection. This study aims to propose practical dietary advice to manage gastrointestinal symptoms caused by GLP-1RAs, intended for clinicians and patients. The analysis included a review of the existing literature on food consistency, viscosity, meal composition, and lifestyle factors that may contribute to gastric emptying delay.

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Material and Methods

The relevant literature was revised to develop dietary recommendation for the management of gastrointestinal symptoms in patient treated with GLP-1RAs. Searches were conducted in the electronic databases PubMed and Web of Science (WoS) using the following keywords (alone or in various combinations): "obesity", "GLP-1 receptor agonist", "gastric emptying", "nausea", "gastrointestinal symptoms" "food composition and charateristics" and "food viscosity". Boolean operators (AND; OR) were also applied. To refine the search strategy, filters used were: English language, human studies, and publications from the last 20 years (time range: 2004–2024). Studies were included if they focused on individuals treated with GLP-1RAs or on the physiology of gastric emptying. After conducting an initial search, two authors assessed the titles and abstracts of the relevant studies and reviewed the full texts. Authors also examined the reference lists of all manuscripts to identify additional relevant studies. Any disagreements that occurred were resolved through consultation with a third author.

GLP- 1 Receptor Agonists and Their Adverse Events

GLP-1RAs are medications initially used to treat diabetes and, more recently, for overweight and obesity. GLP-1 is a hormone mainly produced by endocrine L-cells in the distal ileum and colon, as well as by some neurons in the brain.[9] It is released in response to meal intake leading to increased satiety and better glucose metabolism regulation. GLP-1RAs reduce plasma glucose levels through glucose-dependent mechanisms by stimulating insulin secretion and inhibiting glucagon secretion. They also delay gastric emptying, slowing nutrient absorption.[6] While GLP-1 has a brief half-life due to rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4), GLP-1RAs have been developed with a prolonged half-life. Liraglutide and Semaglutide are examples of GLP-1RAs used for weight management, showing effectiveness in reducing body weight and improving cardiovascular risk factors.[10] However, gastrointestinal side effects, such as nausea and diarrhea, are common.[11] The secretion of GLP-1 is partly mediated by nutrient binding to G-protein-coupled receptors (GPCRs) or by absorption via membrane transporters. Peptides, amino acids, monounsaturated fatty acids, polyunsaturated fatty acids, and short chain fatty acids (SCFAs) can increase GLP-1 levels.[12] Simple sugars and indigestible, fermentable dietary fiber can be involved in this mechanism. On the other hand, plasma levels of GLP-1 are reduced in the fasting state, and these levels increase after food ingestion.[12] GLP-1 exhibits a brief half-life due to rapid degradation by DPP-4, approximately 1.5 minutes.[13] This rapid degradation limits its potential as a viable pharmacological intervention, despite its numerous effects.[13] Over the years, compounds with a prolonged half-life have been developed. These GLP-1RAs are not identical to native GLP-1 but can activate the GLP-1 receptor.[13] GLP-1RAs include exendin-based molecules and human GLP-1 analogues. Exendin-4, derived from lizards, is naturally resistant to DPP-4.15 degradation.[14] Human GLP-1 analogues are modified versions of the GLP-1 peptide,[15,16] available in several sizes and structures, influencing their mechanism of action and half-life.[13,15] *Liraglutide*, the first GLP-1RAs approved for weight management, acts as a long-acting agonist on its receptor, reducing appetite, delaying gastric emptying, and increasing pancreatic insulin secretion.[13] Several studies show that treatment with Liraglutide, along with a proper diet and healthy lifestyle, helps reduce body fat, especially visceral fat, and may improve cardiovascular risk factors.[10,11] *Semaglutide* shares 94% structural homology with native GLP-1.[13] A 2021 double-blind showed that Semaglutide effectively managed weight in patients with obesity. After 20 weeks, patients treated with Semaglutide had an average body weight reduction of 9.9% compared to 0.4% in the placebo group. They also reported decreased hunger and increased feelings of fullness and satisfaction.[17] An increased incidence of gallstones has been reported in patients treated with Liraglutide, along with a potential association between mild pancreatitis and rapid weight loss.[18]

The Process of Gastric Emptying

The adverse effects observed in patients treated with GLP-1RAs are primarily gastrointestinal.[11,18] Therefore, understanding the mechanisms underpinning these issues is crucial. Gastric emptying involves the transfer of stomach contents into the duodenum for subsequent digestion and nutrient assimilation.[19] This process is divided into four phases: tonic contractions, peristaltic contractions, retropulsion, and emptying.[19] Researchers have focused on the physiology of motility and gastric emptying, showing the existence of two parallel neuronal circuits able of regulating stomach emptying speed: the gastric

inhibitory vagal motor circuit and the gastric excitatory vagal motor circuit.[20,21] Hormones like cholecystokinin and GLP-1 may slow down gastric emptying by acting on the gastric inhibitory vagal motor circuit, while hormones like ghrelin and motilin can speed it by stimulating the gastric excitatory vagal motor circuit.[22] Factors such as age, pathophysiological states, and emotions can also affect the rate of gastric emptying. As people age, changes in the gastrointestinal physiology and reduced peristaltic movements can result in a slower digestive process.[23] Conditions such as gastroesophageal reflux, gastritis, allergies, and certain drugs may also significantly affect digestion[24] as well as emotions such as anger, anxiety, and stress,[25] revealing the role of the gut as a "second brain".

Food Composition and Characteristics

The composition, physical characteristics, and energy content of foods affect gastric emptying. These factors can either accelerate or delay gastric emptying, with substantial implications for digestion, satiety, and overall metabolic control. Liquid foods empty from the stomach faster than solid foods, but high-calorie liquids may delay gastric emptying due to nutrient interaction with intestinal receptors.[22] Non-caloric liquid saline solutions are characterized by an emptying initial linear phase followed by a late linear phase, whereas high-calorie liquids show a lag phase during gastric emptying. This may be due to the interaction between nutrient-rich liquids and the receptors in the small intestine mucosa, potentially leading to a greater inhibition of gastric emptying.[26] The pressure disparity between the stomach and the duodenum can also affect the speed of emptying of liquid foods.[27] Moreover, energy content modulates gastric emptying rate. Research indicates that low-energy foods tend to empty from the stomach faster than high-energy foods. For instance, water has a brief gastric residence time, while a nutrient-dense solid meal remains in the stomach for a longer period.[28] Additionally, there is a connection between blood glucose levels and gastric emptying. Higher blood glucose concentrations are associated with slower gastric emptying, while lower levels lead to a faster emptying process.[28] Viscosity is another crucial property with high viscosity inhibiting gastric emptying and affecting transit time in the digestive tract; it is closely related to food digestion regulation, nutrient absorption, and physiological responses such as glycemic response and appetite regulation.[27] However, the impact of food viscosity on physiological responses remains a topic of ongoing debate and incomplete comprehension, primarily due to the non-Newtonian behavior of most foods and its consequential impact on digestion. While several studies suggest that viscosity exerts negligible influence on gastric emptying, the prevailing view is that high viscosity can inhibit gastric emptying and, as a result, affect food transit time in the digestive tract.[27] According to Camps et al, gastric emptying is observed to decelerate with increasing viscosity of ingested food.[29] This phenomenon could regulate the postprandial glycemic response and prolong the sense of satiety, as food needs to be digested for a longer period to reduce its viscosity.[30] Recent research conducted by Liu et al supports this thesis.[31] They utilized nutritious model meals based on peanut butter, with viscosity manipulated through the addition of guar gum, to investigate the effects of food viscosity on gastric emptying, gastric motility, and physiological responses in human volunteers. The findings indicate that nearly 55% of the stomach content in both the control and low viscosity groups were emptied after 30 minutes of digestion. In contrast, only approximately 25% of the chyme in the high viscosity group was emptied from the stomach at the same interval ($p < 0.05$), which corresponded with significantly elevated fullness scores.[31] Nevertheless, several factors such as temperature may influence food viscosity itself and its impact on gastric motility. Colder foods tend to have a higher viscosity, which can delay gastric emptying. A study by Dimitreli et al, demonstrated that the viscosity of processed cheese, for instance, is increased at lower temperatures, leading to slower gastric emptying.[32] Moreover, gastric emptying is influenced by different nutrients entering the gastrointestinal tract: proteins, fats, and fibers, affect gastric emptying rates. As far as proteins are concerned, a recent randomized controlled trial investigated the effects of different preloads (strawberry milkshake) high in protein, fat, or carbohydrates while maintaining equal energy content (~300 kcal) and volume (250 mL).[33] The results revealed a significant difference in the gastric emptying latency phase (Tlat), which was shorter after consuming the high-protein preload compared to the other types of preloads. However, the gastric emptying ascension time (Tasc) was notably longer after consuming the high-protein preload when compared to the high-fat preload.[33] Concerning the viscosity of cheese, it decreases as the temperature rises due to a decrease in the force of attraction between the molecules.[32] Moisture also plays a crucial role in protein-rich foods. An increase in moisture weakens protein-protein interaction, leading to reduced food viscosity.[34] As for fats, their high molecular cohesion results in high viscosity. However, elevated temperatures can reduce this cohesion, leading to decreased viscosity.[35] Regarding fiber,

research shows that a high consumption can slow down the rate at which the stomach empties. This is because certain components of fiber, such as lignin, are resistant to digestion, leading to a delayed gastric emptying process.[36]

Gastrointestinal Effects Management

Effective management of gastrointestinal side effects from GLP-1RAs is crucial for treatment adherence. Gradual dose escalation is recommended to mitigate symptoms.[8,37,38] If gastrointestinal adverse events occur, clinicians should prolong the titration period or avoid dose increases until the effects subside.[39] If side effects appear when transitioning to a higher dose, the recommendation is to revert to the previous dose and then gradually increase it, or to establish a maximum tolerated dose for maintenance.[39] However, these side effects often occur in patients with an inadequate diet. Hence, adjusting the medication dosage and investigating the patient's eating habits can help manage symptoms. So far, there is no specific guidance on caloric restriction and type of foods to prefer or to avoid with GLP-1RAs treatment. A personalized dietary approach is essential, considering the individual's preferences and lifestyle to ensure compliance.[8] In this regard, a group of medical experts, including endocrinologists, nephrologists, general practitioners, cardiologists, internal medicine specialists, and nurses, recently have developed dietary and behavioral guidelines to prevent or minimize gastrointestinal effects and avoid medication interruption.[8]

Results

While the literature provides insights into managing gastrointestinal events in patients treated with GLP-1RAs, specific guidance on meal composition remains unavailable. This study presents an adapted version (Figure 1) of the Harvard Healthy Plate[40] as a practical tool for managing gastrointestinal symptoms. Since adverse effects, such as nausea and vomiting,[38] often occur in the evening, the tool focuses on offering practical advice for dinner composition. The approach emphasizes the inclusion of all three macronutrients while addressing the gastric slowing commonly experienced by patients.

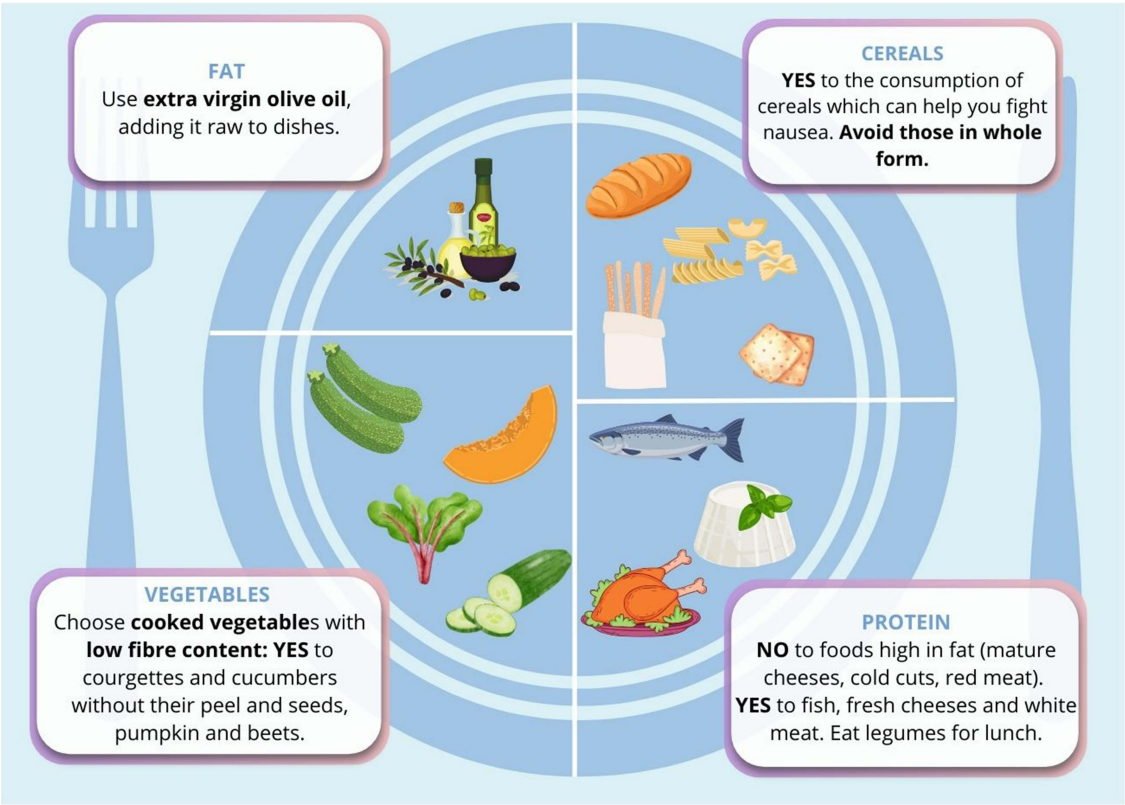

Figure 1 The dinner of the patient treated with GLP-1 receptor agonist.

The tool does not specify precise food quantities, as these must be personalized with the guidance of a healthcare professional, tailored to the individual's specific needs and goals. The selection of food items was informed by a thorough review of relevant scientific literature and current dietary guidelines. Key considerations include:

Cereals

To manage the impact of fiber and glucose levels on gastric emptying, it is recommended to include complex carbohydrates such as pasta, bread, and crackers, while avoiding whole grain products and foods high in simple sugars. Furthermore, portion sizes should be moderate to support digestion.

Protein

Since protein consumption is associated to delayed gastric emptying, it is advisable to choose low-fat protein sources, including white meats and blue fish, while avoiding red meats and processed cold cuts. Fresh cheeses are acceptable, if consumed at moderate temperatures, whereas mature cheeses, which are higher in fat, should be avoided. Legumes, due to their high fiber content, should not be included in the evening meal; instead, they are best consumed during lunch, preferably in peeled form.

Fats

Despite their potential to delay gastric emptying due to high viscosity, fats are essential for overall health. Moderation is key, with a preference for extra virgin olive oil, which is rich in unsaturated fatty acids, fat-soluble vitamins, and polyphenols that offer anti-inflammatory and cardioprotective benefits.[41]

Vegetables

Fiber's role in slowing gastric emptying and promoting satiety makes vegetable inclusion important. However, to manage fiber content, low-fiber vegetables are recommended, avoiding those with peels and seeds, while maintaining appropriate portion sizes. Portion sizes should be kept appropriate to maintain digestive comfort, although fiber is recognized for its role it is essential to include vegetables in meals, also for educational purposes. Therefore, it is recommended to select vegetables with low fiber content.

In addition to these dietary considerations, the following recommendations are suggested: consume small, frequent meals; use simple cooking methods and avoid complex dishes, spicy foods, and alcohol; stay well- hydrated; choose fruit as a snack, and avoid lying down or engaging in vigorous activity after meals (Box 1).

Box 1 Behavioral Advice for Meal Management

Recommendations
Eat small, frequent meals, and eat slowly.
Use simple cooking methods such as steaming, baking, and boiling, avoiding frying and sautéing.
Avoid complex or heavily seasoned dishes, spicy foods, and alcoholic drinks.
Avoid consuming liquid foods like soups, and broths during the evening meal, as they may slow down digestion and increase symptoms.
Stay hydrated by drinking water in small sips, avoiding excessive intake during meals.
Choose fruit as a mid-morning or mid-afternoon snack and avoid their consumption during lunch or dinner in order to avoid an abundant meal.
Avoid lying down or vigorous activity after meals.
Avoid wearing tight clothes or belts.
If symptoms persist, consult your doctor.

Discussion

GLP-1RAs are highly effective for the obesity treatment but can cause gastrointestinal symptoms due to delayed gastric emptying. This study analyzes how food properties and meal composition influence these symptoms and provide guidelines for managing them. Educating patients on diet management can enhance treatment outcomes and prevent therapy interruption. The influence of GLP-1RAs in delaying gastric emptying is well known and of great interest to the scientific literature. Further research is needed to explore food properties and lifestyle factors affecting gastric emptying to develop personalized patient management strategies.

Author Contributions

All authors made a significant contribution to the work reported, in the conception, execution, acquisition of data, and interpretation; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Silvia Gentinetta is affiliated with Novo Nordisk Italia SpA, a company involved in the development and marketing of GLP-1 receptor agonists. This affiliation is disclosed to maintain transparency, and the author affirms that the views expressed in this manuscript are independent and based solely on scientific evidence. The authors report no other conflicts of interest in this work.

References

1. World Health Organization (WHO), Obesity and overweight, Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight#:~:text=In%202022%2C%201%20in%208,million%20were%20living%20with%20obesity. Accessed Jun 11, 2024.
2. Yumuk V, Tsigos C, Fried M, et al. Obesity Management Task Force of the European Association for the Study of Obesity. *European Guidelines for Obesity Management in Adults Obes Facts*. 2015;8(6):402–424. doi:10.1159/000442721. Epub 2015 Dec 5. Erratum in: Obes Facts. 2016;9(1):64. PMID: 26641646; PMCID: PMC5644856.
3. Ryan DH, Kahan S. Guideline Recommendations for Obesity Management. *Med Clin North Am*. 2018;102(1):49–63. doi:10.1016/j.mcna.2017.08.006. PMID: 29156187.
4. Popoviciu MS, Păduraru L, Yahya G, Metwally K, Cavalu S. Emerging Role of GLP-1 Agonists in Obesity: a Comprehensive Review of Randomised Controlled Trials. *Int J Mol Sci*. 2023;24(13):10449. doi:10.3390/ijms241310449. PMID: 37445623; PMCID: PMC10341852.
5. Purnell JQ, le Roux CW. Hypothalamic control of body fat mass by food intake: the key to understanding why obesity should be treated as a disease. *Diabetes Obes Metab*. 2024;26(Suppl 2):3–12. doi:10.1111/dom.15478. Epub 2024 Feb 14. PMID: 38351898.
6. Maselli DB, Camilleri M. Effects of GLP-1 and Its Analogs on Gastric Physiology in Diabetes Mellitus and Obesity. *Adv Exp Med Biol*. 2021;1307:171–192. doi:10.1007/5584_2020_496. PMID: 32077010.
7. Wan J, Ferrari C, Tadros M. GLP-1RA Essentials in Gastroenterology: side Effect Management, Precautions for Endoscopy and Applications for Gastrointestinal Disease Treatment. *Gastroenterology Insights*. 2024;15(1):191–212. doi:10.3390/gastroent15010014
8. Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, et al. Clinical Recommendations to Manage GastrointestinalAdverse Events in Patients Treated with Glp-1 Receptor Agonists: a Multidisciplinary Expert Consensus. *J Clin Med*. 2022;12(1):145. doi:10.3390/jcm12010145. PMID: 36614945; PMCID: PMC9821052.
9. Müller TD, Finan B, Bloom SR, et al. Glucagon-like peptide 1 (GLP-1). *Mol Metab*. 2019;30:72–130. doi:10.1016/j.molmet.2019.09.010. Epub 2019 Sep 30. PMID: 31767182; PMCID: PMC6812410.
10. Neeland IJ, Marso SP, Ayers CR, et al. Effects of liraglutide on visceral and ectopic fat in adults with overweight and obesity at high cardiovascular risk: a randomised, double-blind, placebo-controlled, clinical trial. *Lancet Diabetes Endocrinol*. 2021;9(9):595–605. doi:10.1016/S2213-8587(21)00179-0. Epub 2021 Aug 3. PMID: 34358471.
11. SCALE Obesity and Prediabetes NN8022-1839 Study Group. Pi-Sunyer X, Astrup A, Fujioka K, et al. A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. *N Engl J Med*. 2015;373(1):11–22. doi:10.1056/NEJMoa1411892. PMID: 26132939.
12. Huber H, Schieren A, Holst JJ, Simon MC. Dietary impact on fasting and stimulated GLP-1 secretion in different metabolic conditions - a narrative review. *Am J Clin Nutr*. 2024;119(3):599–627. doi:10.1016/j.ajcnut.2024.01.007. Epub 2024 Jan 11. PMID: 38218319; PMCID: PMC10972717.
13. Knudsen LB, Lau J. The Discovery and Development of Liraglutide and Semaglutide. *Front Endocrinol*. 2019;10:155. doi:10.3389/fendo.2019.00155. PMID: 31031702; PMCID: PMC6474072.
14. Andersen A, Lund A, Knop FK, Vilsbøll T. Glucagon-like peptide 1 in health and disease. *Nat Rev Endocrinol*. 2018;14(7):390–403. doi:10.1038/s41574-018-0016-2. PMID: 29728598.

15. Brown E, Cuthbertson DJ, Wilding JP. Newer GLP-1 receptor agonists and obesity-diabetes. *Peptides*. 2018;100:61–67. doi:10.1016/j.peptides.2017.12.009. PMID: 29412833.
16. Gentilella R, Pechtner V, Corcos A, Consoli A. Glucagon-like peptide-1 receptor agonists in type 2 diabetes treatment: are they all the same? *Diabetes Metab Res Rev*. 2019;35(1):e3070. doi:10.1002/dmrr.3070. Epub 2018 Oct 4. PMID: 30156747.
17. Friedrichsen M, Breitschaft A, Tadayon S, Wizert A, Skovgaard D. The effect of semaglutide 2.4 mg once weekly on energy intake, appetite, control of eating, and gastric emptying in adults with obesity. *Diabetes Obes Metab*. 2021;23(3):754–762. doi:10.1111/dom.14280. Epub 2021 Jan 3. PMID: 33269530; PMCID: PMC7898914.
18. Bettge K, Kahle M, El Aziz MS A, Meier JJ, Nauck MA. Occurrence of nausea, vomiting and diarrhoea reported as adverse events in clinical trials studying glucagon-like peptide-1 receptor agonists: a systematic analysis of published clinical trials. *Diabetes Obes Metab*. 2017;19(3):336–347. doi:10.1111/dom.12824. Epub 2016 Dec 19. PMID: 27860132.
19. Janssen P, Vanden Berghe P, Verschueren S, Lehmann A, Depoortere I, Tack J. Review article: the role of gastric motility in the control of food intake. *Aliment Pharmacol Ther*. 2011;33(8):880–894. doi:10.1111/j.1365-2036.2011.04609.x. Epub 2011 Feb 22. PMID: 21342212.
20. Zhou SY, Lu YX, Yao H, Owyang C. Spatial organization of neurons in the dorsal motor nucleus of the vagus synapsing with intragastric cholinergic and nitric oxide/VIP neurons in the rat. *Am J Physiol Gastrointest Liver Physiol*. 2008;294(5):G1201–9. doi:10.1152/ajpgi.00309.2006. PMID: 18460697; PMCID: PMC3221413.
21. Travagli RA, Hermann GE, Browning KN, Rogers RC. Brainstem circuits regulating gastric function. *Annu Rev Physiol*. 2006;68(1):279–305. doi:10.1146/annurev.physiol.68.040504. 094635. PMID: 16460274; PMCID: PMC3062484.
22. Goyal RK, Guo Y, Mashimo H. Advances in the physiology of gastric emptying. *Neurogastroenterol Motil*. 2019;31(4):e13546. doi:10.1111/nmo.13546. Epub 2019 Feb 10. PMID: 30740834; PMCID: PMC6850045.
23. Brogna A, Loreno M, Catalano F, et al. Radioisotopic assessment of gastric emptying of solids in elderly subjects. *Aging Clin Exp Res*. 2006;18(6):493–496. doi:10.1007/BF03324849. PMID: 17255638.
24. Kamiya T, Adachi H, Joh T. Relationship between gastric motility and the pathophysiology of GERD. *Nihon Rinsho*. 2007;65(5):836–839. Japanese. PMID: 17511221.
25. Holtmann G, Talley NJ. The stomach-brain axis. *Best Pract Res Clin Gastroenterol*. 2014;28(6):967–979. doi:10.1016/j.bpg.2014.10.001. Epub 2014 Oct 8. PMID: 25439064.
26. Maurer AH. Advancing gastric emptying studies: standardization and new parameters to assess gastric motility and function. *Semin Nucl Med*. 2012;42(2):101–112. doi:10.1053/j.semnuclmed.2011.10.001. PMID: 22293165.
27. Liu W, Jin Y, Wilde PJ, Hou Y, Wang Y, Han J. Mechanisms, physiology, and recent research progress of gastric emptying. *Crit Rev Food Sci Nutr*. 2021;61(16):2742–2755. doi:10.1080/10408398.2020.1784841. Epub 2020 Jun 30. PMID: 32602780.
28. Mackie A. The role of food structure in gastric-emptying rate, absorption and metabolism. *Proc Nutr Soc*. 2024;83(1):35–41. doi:10.1017/S0029665123003609. Epub 2023 Sep 6. PMID: 37671658.
29. Camps G, Mars M, de Graaf C, Smeets PA. Empty calories and phantom fullness: a randomized trial studying the relative effects of energy density and viscosity on gastric emptying determined by MRI and satiety. *Am J Clin Nutr*. 2016;104(1):73–80. doi:10.3945/ajcn.115.129064. Epub 2016 Jun 8. PMID: 27281305.
30. Zhu Y, Hsu WH, Hollis JH. The impact of food viscosity on eating rate, subjective appetite, glycemic response and gastric emptying rate. *PLoS One*. 2013;8(6):e67482. doi:10.1371/journal.pone.0067482. PMID: 23818981; PMCID: PMC3688614.
31. Liu W, Jin W, Wilde PJ, Jin Y, Pan Y, Han J. Understanding the mechanism of high viscosity food delaying gastric emptying. *Food Funct*. 2024;15(10):5382–5396. doi:10.1039/d4fo00319e
32. Dimitreli G, Thomareis AS. Effect of temperature and chemical composition on processed cheese apparent viscosity. *Journal of Food Engineering*. 2004;64(2):265–271. doi:10.1016/j.jfoodeng.2003.10.008
33. Dericioglu D, Oldham S, Methven L, Shafat A, Clegg ME. Macronutrients effects on satiety and food intake in older and younger adults: a randomised controlled trial. *Appetite*. 2023;189:106982. doi:10.1016/j.appet.2023.106982
34. Masson LMP, Rosenthal A, Calado VMA, Deliza R, Tashima L. Effect of ultra-high pressure homogenization on viscosity and shear stress of fermented dairy beverage. *LWT Food Sci Technol*. 2011;44(2):495–501. doi:10.1016/j.lwt.2010.07.012
35. Rahmati NF, Tehrani MM, Daneshvar K, Koocheki A. Influence of selected gums and pregelatinized corn starch on reduced fat mayonnaise: modeling of properties by central composite design. *Food Biophys*. 2015;10(1):39–50. doi:10.1007/s11483-014-9356-1
36. Yu K, Ke MY, Li WH, Zhang SQ, Fang XC. The impact of soluble dietary fibre on gastric emptying, postprandial blood glucose and insulin in patients with type 2 diabetes. *Asia Pac J Clin Nutr*. 2014;23(2):210–218. doi:10.6133/apjcn.2014.23.2.01. PMID: 24901089.
37. Sodhi M, Rezaeianzadeh R, Kezouh A, Etminan M. Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss. *JAMA*. 2023;330(18):1795–1797. doi:10.1001/jama.2023.19574. PMID: 37796527; PMCID: PMC10557026.
38. Liu L, Chen J, Wang L, Chen C, Chen L. Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: a real-world disproportionality study based on FDA adverse event reporting system database. *Front Endocrinol*. 2022;13:1043789. doi:10.3389/fendo.2022.1043789. PMID: 36568085; PMCID: PMC9770009.
39. Wharton S, Davies M, Dicker D, et al. Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice. *Postgrad Med*. 2022;134(1):14–19. doi:10.1080/00325481.2021.2002616. Epub 2021 Nov 29. PMID: 34775881.
40. Harvard TH. *Healthy Eating Plate, Chan School of Public Health*. Harvard University; 2011.
41. Kiani AK, Medori MC, Bonetti G, et al. Modern vision of the Mediterranean diet. *J Preventive Med Hygiene*. 2022;63(2 Suppl 3):E36–E43. doi:10.15167/2421-4248/jpmh2022.63.2S3.2745.