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ULTRASONIDO GÁSTRICO PARA LA ESTRATIFICACIÓN DEL RIESGO DE ASPIRACIÓN EN PACIENTES TRATADOS CON AGONISTAS GLP-1: REVISIÓN SISTEMÁTICA INTEGRADA Y ACTUALIZACIÓN DE EVIDENCIA SOBRE HALLAZGOS ULTRASONOGRÁFICOS, ENDOSCÓPICOS Y DESENLACES ANESTÉSICOS

GASTRIC ULTRASOUND FOR ASPIRATION-RISK STRATIFICATION IN PATIENTS RECEIVING GLP-1 RECEPTOR AGONISTS: AN INTEGRATED SYSTEMATIC REVIEW AND EVIDENCE UPDATE OF ULTRASONOGRAPHIC, ENDOSCOPIC, AND ANESTHETIC OUTCOMES

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Resumen

Introducción: Los agonistas del receptor GLP-1 y los agonistas duales GLP-1/GIP retrasan el vaciamiento gástrico. Los estudios endoscópicos muestran de manera consistente mayor contenido gástrico residual (CGR), pero la aspiración pulmonar es infrecuente y el papel del ultrasonido gástrico como herramienta individualizada de estratificación no se ha integrado adecuadamente con los hallazgos endoscópicos y anestésicos. Métodos: Se realizó una revisión sistemática integrada y actualización estructurada de evidencia. La evidencia endoscópica se ancló a una revisión sistemática con búsqueda hasta el 7 de julio de 2025 (24 estudios comparativos). Se efectuó una actualización dirigida en PubMed y rastreo de citas hasta el 27 de agosto de 2026 para incorporar estudios de ultrasonido gástrico y nueva evidencia endoscópica/anestésica. Se realizó un metaanálisis exploratorio de efectos aleatorios con cuatro cohortes ecográficas controladas y definiciones compatibles de CGR elevado/estómago lleno. Resultados: Se integraron 35 estudios primarios. En la síntesis endoscópica previa (184.707 participantes), los agonistas GLP-1 se asociaron con mayor CGR (OR 4,82; IC95% 3,66-6,35) y mayor interrupción del procedimiento (OR 3,93; IC95% 2,42-6,39), sin aumento estadísticamente significativo de aspiración (OR 1,10; IC95% 0,84-1,48). En cuatro cohortes ecográficas controladas (n=461), la exposición a GLP-1 se asoció con CGR elevado/estómago lleno (OR combinado 9,31; IC95% 3,68-23,57; I^2=60,0%). El ensayo aleatorizado OCULUS de 2026 (n=60) encontró volumen gástrico residual clínicamente significativo en 25,0% al continuar el tratamiento frente a 3,1% al omitir una dosis. No se identificó un estudio de exactitud diagnóstica que comparara, en los mismos pacientes tratados con GLP-1, ultrasonido gástrico preprocedimiento con hallazgos posteriores de EGD. Conclusiones: La terapia basada en GLP-1 se asocia fuertemente con CGR detectado por ultrasonido y endoscopia; la evidencia sobre aspiración clínica sigue siendo inconsistente por la baja frecuencia del evento. El ultrasonido gástrico es

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una herramienta prometedora para estratificación individualizada, pero requiere validación pareada frente a endoscopia y estudios de impacto clínico.

Palabras claves: agonistas GLP-1; semaglutida; ultrasonido gástrico; POCUS; contenido gástrico residual; endoscopia digestiva alta; aspiración; anestesia; sedación.

Abstract

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual GLP-1/GIP agonists delay gastric emptying. Observational endoscopy data consistently show more retained gastric content (RGC), but pulmonary aspiration remains rare and the role of gastric ultrasound as an individualized preprocedural triage tool has not been integrateld with endoscopic and anesthetic outcomes. Methods: We performed an integrated systematic review and structured evidence update. The endoscopy evidence base was anchored to a systematic review that searched MEDLINE and the Cochrane Library through 7 July 2025 and included 24 comparative studies. A targeted PubMed/citation update through 27 August 2026 expanded eligibility to gastric-ultrasound studies and newly published endoscopy/anesthesia studies. Adults receiving GLP-1 RA or GLP-1/GIP therapy were eligible when objective gastric content was assessed by ultrasound or upper endoscopy, or when aspiration/anesthetic outcomes were reported. A random-effects exploratory meta-analysis pooled four controlled gastric-ultrasound cohorts with compatible definitions of increased RGC/full stomach. Results: The integrated evidence set comprised 35 primary studies (24 carried forward and 11 newly integrated). The predecessor endoscopy synthesis (184,707 participants) found higher RGC (OR 4.82, 95% CI 3.66-6.35) and procedure discontinuation (OR 3.93, 95% CI 2.42-6.39), without a statistically significant increase in aspiration (OR 1.10, 95% CI 0.84-1.48). In four controlled ultrasound cohorts (n=461), GLP-1 RA exposure was associated with increased RGC/full stomach (pooled crude OR 9.31, 95% CI 3.68-23.57; I^2=60.0%). The 2026 OCULUS randomized trial (n=60) found clinically significant residual gastric volume in 25.0% of patients continuing therapy versus 3.1% withholding one dose. No eligible same-patient diagnostic-accuracy study directly validated gastric ultrasound against subsequent EGD findings in GLP-1-treated patients. Conclusions: GLP-1-based therapy is strongly associated with RGC detected by both ultrasound and endoscopy, whereas evidence for increased aspiration is inconsistent and limited by rare events. Gastric ultrasound is a promising individualized risk-stratification adjunct, but its diagnostic agreement with endoscopic findings and its ability to reduce clinically important aspiration events require prospective paired validation.

Keywords: GLP-1 receptor agonist; semaglutide; gastric ultrasound; POCUS; retained gastric content; upper gastrointestinal endoscopy; aspiration; anesthesia; sedation.

1. Introduction

GLP-1 receptor agonists are now widely prescribed for type 2 diabetes and obesity, and dual GLP-1/GIP agonists are increasingly encountered in patients presenting for procedural sedation or general anesthesia. Their pharmacologic effect on gastric motility has created a clinically important tension: the surrogate marker of risk—retained gastric content—is consistently increased, while the clinically decisive event—pulmonary aspiration—remains uncommon and difficult to study. Recent endoscopy meta-analyses have therefore converged on a strong association with RGC and procedure interruption but have produced discordant estimates for aspiration [1-3].

The practical challenge is particularly relevant to upper gastrointestinal endoscopy. Deep sedation can diminish protective airway reflexes, while endoscopic visualization provides direct confirmation of gastric contents only after sedation has begun. Gastric point-of-care ultrasound (POCUS), in contrast, can be performed before induction and can identify solid content or estimate clear-fluid volume. Contemporary multidisciplinary recommendations increasingly include a 24-hour clear-fluid strategy and gastric ultrasound when residual-content risk remains uncertain [4,5].

However, the evidence supporting gastric ultrasound and the evidence derived from endoscopic cohorts have largely evolved in parallel. Ultrasound studies typically involve perioperative surgical populations rather than patients proceeding directly to EGD, whereas endoscopy studies rely on intraprocedural visual or suction-based definitions of RGC. Consequently, it is not yet clear whether a preprocedural ultrasound finding in a GLP-1-treated patient accurately predicts what the gastroenterologist will encounter during subsequent EGD, or whether ultrasound-guided changes in anesthetic management reduce aspiration events.

The objective of this review was therefore to integrate three clinically connected evidence domains—gastric ultrasound, upper endoscopy, and anesthetic outcomes—in patients receiving GLP-1-based therapy. We specifically aimed to: (1) quantify the association between GLP-1 exposure and a full stomach/increased RGC on gastric ultrasound; (2) contextualize these findings against the established endoscopic evidence base; (3) summarize aspiration and airway-management outcomes; and (4) identify whether direct same-patient ultrasound-to-endoscopy validation exists.

2. Methods

2.1 Design and reporting framework

This manuscript is an integrated systematic review and structured evidence update, reported according to PRISMA 2020 principles where applicable [33]. It was designed as a modality expansion of a recent

systematic review of upper-GI endoscopy outcomes rather than as a de novo recreation of that review's database search. This distinction is explicit in the flow diagram and is important for reproducibility.

The review was not prospectively registered. The endoscopy evidence base through 7 July 2025 was carried forward from Malandris et al. [1], whose review included 24 comparative observational studies. A targeted update and modality-expansion search was then performed to identify gastric-ultrasound studies and newer endoscopy/anesthesia studies through 27 August 2026.

2.2 Eligibility criteria

Population: adults (≥18 years) receiving a GLP-1 receptor agonist or dual GLP-1/GIP agonist and undergoing upper gastrointestinal endoscopy, procedural sedation/general anesthesia, or preprocedural gastric ultrasound. Exposure: current or recent GLP-1-based therapy, including semaglutide, liraglutide, dulaglutide, exenatide, lixisenatide, tirzepatide, or class-level exposure. Comparator: patients not receiving a GLP-1-based agent, an alternative glucose-lowering drug, or an alternative withholding strategy when available. Outcomes: objectively assessed RGC/full stomach by gastric ultrasound or EGD, procedure interruption, aspiration/regurgitation, urgent airway intervention/intubation, or other clinically relevant anesthetic outcomes.

Comparative cohort, case-control, cross-sectional, and randomized studies were eligible. Noncomparative cohorts were retained only for descriptive synthesis of rare adverse outcomes or ultrasound-based risk stratification. Case reports, case series without an analyzable cohort, editorials, comments, guidelines, narrative reviews, and systematic reviews were excluded from the primary evidence set, although high-quality secondary sources were used to contextualize the findings.

2.3 Information sources and search strategy

The legacy endoscopy branch was based on the MEDLINE/PubMed and Cochrane Library search reported by Malandris et al. through 7 July 2025 [1]. For the present modality

expansion and update, PubMed-indexed records and backward/forward citation links were searched through 27 August 2026. A core search concept was: ("glucagon-like peptide-1 receptor agonist" OR GLP-1 OR GLP-1RA OR semaglutide OR liraglutide OR dulaglutide OR exenatide OR lixisenatide OR tirzepatide) AND ("gastric ultrasound" OR ultrasonography OR POCUS OR "residual gastric content" OR "retained gastric content" OR "gastric residue" OR esophagogastroduodenoscopy OR EGD OR "upper endoscopy" OR aspiration OR regurgitation).

The update branch was intentionally focused on evidence that could materially change the imaging–endoscopy–anesthesia interpretation. It is therefore best described as a structured evidence update rather than a new, fully independent multi-database search. The search log and evidence-assembly counts are provided in Supplementary Table S1 and Figure 1.

Supplementary Table S1. *Update/modality-expansion search log*

Stage	n	Explanation
Candidate reports identified in targeted PubMed/citation search	28	All candidate reports logged before evidence-set adjudication.
Known legacy/duplicate reports	9	Already represented in the 24-study predecessor endoscopy review.
Records screened after removal	19	Title/abstract relevance to ultrasound, new endoscopy, or anesthetic outcomes.
Excluded at title/abstract	6	Systematic/meta-analyses, guideline/consensus documents, or secondary reviews.
Full-text reports assessed	13	Original-research eligibility checked.
Full-text reports excluded	2	Comment/reply; not original research.
New primary studies included	11	6 gastric-ultrasound studies + 5 newer endoscopy/anesthesia studies.
Total integrated primary studies	35	24 legacy + 11 newly integrated.

2.4 Outcomes and definitions

The primary imaging outcome was increased RGC or “full stomach” on gastric ultrasound. When available, this was defined as visible solid/thick content or estimated clear-fluid volume >1.5 mL/kg in the right lateral

decubitus position. Endoscopic RGC definitions varied and included visible solid food, retained liquid, “poor preparation,” or measured/aspirated fluid above study-specific thresholds. Because these constructs are related but not identical, ultrasound and endoscopy estimates were not pooled together.

Secondary outcomes were pulmonary aspiration/aspiration pneumonia, regurgitation, procedure discontinuation, urgent endotracheal intubation or change in airway plan, and the influence of withholding interval, clear-liquid preparation, or concurrent colonoscopy.

2.5 Data synthesis

The 24-study endoscopy meta-analysis from the predecessor review was treated as a validated benchmark rather than recomputed, because its study-level extraction, overlap adjudication, and random-effects modeling had already been completed [1]. New post-update endoscopy evidence was integrated narratively. Gastric-ultrasound studies were synthesized separately.

Four controlled ultrasound cohorts with compatible binary definitions of full stomach/increased RGC were pooled in an exploratory random-effects meta-analysis using crude event counts (Sen et al. [10], Nersessian et al. [19], Queiroz et al. [22], and Vlaeminck et al. [28]). DerSimonian-Laird between-study variance was used; heterogeneity was expressed with I^2. Sherwin et al. [9] was not pooled because it was a very small volunteer study focused on solid-content prevalence by position rather than the same composite full-stomach threshold. Pai et al. [27] lacked a non-exposed comparator and was synthesized descriptively.

2.6 Methodological quality

For the legacy endoscopy evidence, we relied on the formal ROBINS-I v2 and GRADE assessments reported by Malandris et al. [1]. Most studies were judged at low risk for the primary outcome, with four studies at serious risk mainly because of residual confounding and four abstract-only studies at moderate risk; the certainty of evidence was rated very low. For the 11 newly integrated reports, we performed a structured single-reviewer methodological appraisal focused on confounding, exposure classification,

outcome ascertainment, selection, and reporting. Because a second independent reviewer did not repeat this update appraisal, these ratings are presented as methodological concerns rather than formal duplicate-review ROBINS-I judgments.

3. Results

3.1 Study selection and evidence set

The predecessor endoscopy review screened 255 records, assessed 58 full-text reports, and included 24 observational studies [1]. In the present update/modality branch, 28 candidate reports were logged. Nine represented known legacy/duplicate reports, leaving 19 records for screening. Six secondary reviews/guidelines were excluded at title/abstract level. Thirteen reports were assessed in full text; two were comments/replies rather than original research, leaving 11 newly integrated primary studies. The final integrated evidence set therefore comprised 35 primary studies (Figure 1). Eight legacy studies were available only as conference abstracts; 27 full-text primary reports are summarized in Table 1.

Figure 1. *PRISMA-informed evidence assembly flow for the integrated systematic review and structured update*

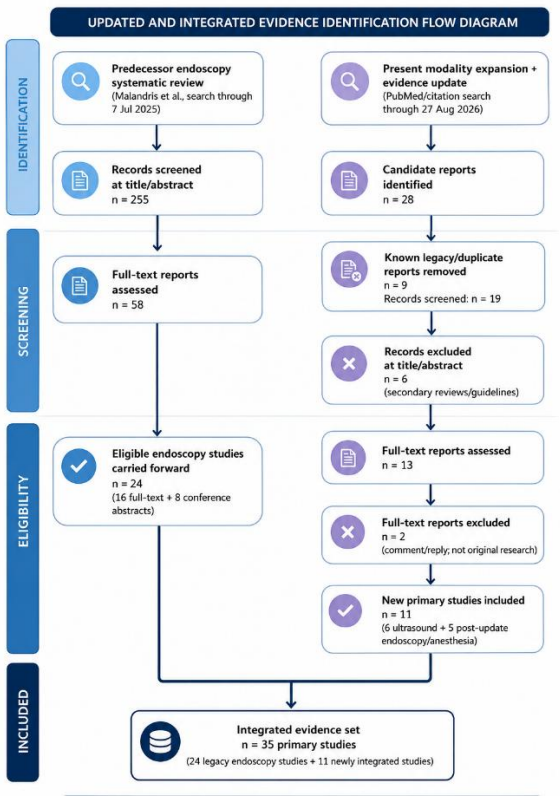


Table 1. *Characteristics and key findings of 27 full-text primary studies*

Study	Design / setting	Sample	Exposure	Outcome	Key finding
Stark 2022 [6]	Retrospective matched EGD	177 (59 vs 118)	GLP-1 RA class	Endoscopic retained food	6.8% vs 1.7%; early signal, not statistically definitive
Kobori 2023 [7]	Matched case-control EGD	410 matched (205 pairs)	GLP-1 RA class; T2D	Gastric residue on EGD	5.4% vs 0.49%; P=0.004
Silveira 2023 [8]	Retrospective EGD	404 (33 vs 371)	Semaglutide	Increased RGC; aspiration	24.2% vs 5.1%; adjusted OR 5.15; 1 aspiration in exposed
Sherwin 2023 [9]	Prospective volunteer ultrasound	20 (10 vs 10)	Semaglutide	Residual solids after fasting	Supine solids 70% vs 10%; lateral 90% vs 20%
Sen 2024 [10]	Prospective cross-sectional ultrasound	124 (62 vs 62)	Weekly GLP-1 RA	Increased RGC on ultrasound	56% vs 19%; adjusted prevalence ratio 2.48
Wu 2024 [11]	Historical cohort EGD	192 (90 vs 102)	GLP-1 RA class	Visible contents; airway events	18.9% vs 4.9%; adjusted OR 5.8; urgent intubation 5 vs 1
Nadeem 2024 [12]	Large retrospective EGD	35,183 (922 exposed)	GLP-1 RA class	RGC; aborted/repeat EGD	~4-fold higher RGC and aborted EGD; ~2-fold repeat EGD
Nasser 2024 [13]	Cross-sectional EGD	141 (47 vs 94)	GLP-1 RA class	Food retention	Solid retention 8.5% vs 0% in reported comparison
Chapman 2024 [14]	Case-control EGD	168 (84 pairs)	GLP-1 RA class	Visibility; RGC; abortion	RGC 13.1% vs 4.8%; adjusted OR 4.62; no anesthesia AEs
Abu-Freha 2024 [15]	Multicenter retrospective EGD	120,879 (1,671 exposed)	GLP-1 RA class	Gastric residue	5.6% vs 2.0%; GLP-1 use independent risk factor
Yeo 2024 [16]	Claims-based cohort	~30,177 matched	GLP-1 RA class	Aspiration pneumonia	Reported increased aspiration-pneumonia signal; contrasts with other large cohorts
Alkabbani 2024 [17]	Comparative cohort EGD	43,365	GLP-1 RA vs SGLT2 inhibitor	Aspiration; discontinuation	Aspiration RR 0.98 (0.73-1.31); discontinuation RR 1.99
Santos 2024 [18]	Retrospective EGD	1,094 (123 semaglutide)	Semaglutide	RGC by withholding interval	20.3% vs 3.2%; symptoms and shorter interruption associated with RGC
Nersessian 2024 [19]	Prospective ultrasound	220 (107 vs 113)	Semaglutide	Increased RGC	40% vs 3%; weighted OR 36.97; no aspiration
Elimihele 2024 [20]	Retrospective EGD	Full-text cohort	GLP-1 RA class	RGC in asymptomatic patients	Confounding-sensitive association; highlights comorbidity effects
Anazco 2024 [21]	Retrospective upper endoscopy cohort	4,000+ GLP-1-treated EGDs	GLP-1 RA class	Pulmonary aspiration	Very low absolute aspiration incidence
Queiroz 2025 [22]	Prospective volunteer ultrasound	30 (15 vs 15)	Semaglutide	Full stomach	73% vs 7%; P<0.001
Firkins 2025 [23]	Clinical outcomes EGD cohort	Full-text cohort	GLP-1 RA class	RGC/safety outcomes	Supports low absolute severe-event rate despite retention concern

Study	Design / setting	Sample	Exposure	Outcome	Key finding
Gu 2025 [24]	Retrospective matched EGD	304 (152 vs 152)	Semaglutide	RGC	12.5% vs 1.3%; several RGC EGDs aborted
Dev 2025 [25]	Large retrospective EGD	32,275 (1,179 exposed)	GLP-1 RA class	Aborted EGD due to food	0.6% vs 0.096%; no aspiration among retained-food cases reported
Le 2025/2026 [26]	Retrospective GLP-1 cohort	218 exposed	GLP-1 RA class	RGC; complications	RGC 20.6%; 9 terminated; 1 aspiration; 1 intraprocedural intubation
Pai 2026 [27]	Prospective ultrasound cohort	316 exposed	GLP-1 RA class	High RGC; withholding interval	High RGC 35.8%; shorter hold/solid fast associated with high RGC
Vlaeminck 2026 [28]	Prospective multicenter matched ultrasound	87 analyzable (43 vs 44)	Semaglutide	Full stomach; solids	Full stomach 49% vs 18% (OR 4.29); solids 42% vs 7%
Ahmad/OCULUS 2026 [29]	Randomized EGD trial	60	GLP-1/GLP-1-GIP; hold vs continue	Clinically significant residual volume	25.0% continue vs 3.1% hold one dose; no aspiration/intubation/hospitalization
Dong 2026 [30]	Retrospective EGD	16,067 (103 continue; 62 hold 2 wk)	GLP-1 RA class	RGC	0.4% no use; 5.83% continue; 1.61% 2-week hold
Chang 2026 [31]	Retrospective case-control EGD	3,746	GLP-1 RA class	Increased RGC	GLP-1 use independently associated with RGC; concurrent colonoscopy evaluated
Patel 2026 [32]	Retrospective EGD; TiGR scale	150 (73 vs 77)	GLP-1 RA class	Food retention grading	No significant binary GLP-1 association in this small cohort; illustrates definition heterogeneity

Abbreviations: EGD, esophagogastroduodenoscopy; GLP-1 RA, glucagon-like peptide-1 receptor agonist; RGC, retained/residual gastric content; T2D, type 2 diabetes; AE, adverse event. Eight additional legacy studies were available only as conference abstracts and contribute to the predecessor pooled benchmark [1] but are not re-extracted here.

3.2 Overview of the evidence

The integrated evidence domains, principal outcomes, and key estimates are summarized in Table 2.

Table 2. *Integrated overview of ultrasonographic, endoscopic, randomized, and anesthetic evidence*

Evidence domain	Evidence base	Primary outcome	Key estimate/finding	Interpretation
Upper-GI endoscopy (legacy benchmark)	24 observational studies; 184,707 participants	Endoscopic RGC, aspiration, discontinuation	RGC OR 4.82 (3.66-6.35); discontinuation OR 3.93 (2.42-6.39); aspiration OR 1.10 (0.84-1.48)	Strong surrogate signal; aspiration rare; very-low certainty [1]
Controlled gastric ultrasound	4 pooled cohorts; n=461	Full stomach / increased RGC	Pooled crude OR 9.31 (3.68-23.57); I^2=60.0%	Consistent direction; heterogeneous populations and definitions

Evidence domain	Evidence base	Primary outcome	Key estimate/finding	Interpretation
Other gastric ultrasound	Sherwin n=20; Pai n=316	Solids, volume, withholding interval	Semaglutide associated with more residual solids; Pai found high RGC in 35.8% of GLP-1 users	Useful for triage; limited direct endoscopy linkage
Randomized withholding evidence	OCULUS RCT; n=60	Clinically significant residual gastric volume on EGD	25.0% continuing vs 3.1% withholding one dose	First randomized endoscopy evidence; small and stopped early
Post-update endoscopy cohorts	Le, Dong, Chang, Patel (2025-2026)	RGC, interruption, aspiration	Generally confirms higher RGC, with heterogeneity by obesity, preparation, and grading	No consistent demonstration of increased aspiration

Across modalities, the direction of effect was consistent for the surrogate endpoint of gastric retention. The magnitude varied because ultrasound studies used a physiologic full-stomach threshold, whereas EGD studies used visual, suction-based, or report-derived definitions. This distinction precluded a single combined meta-analysis.

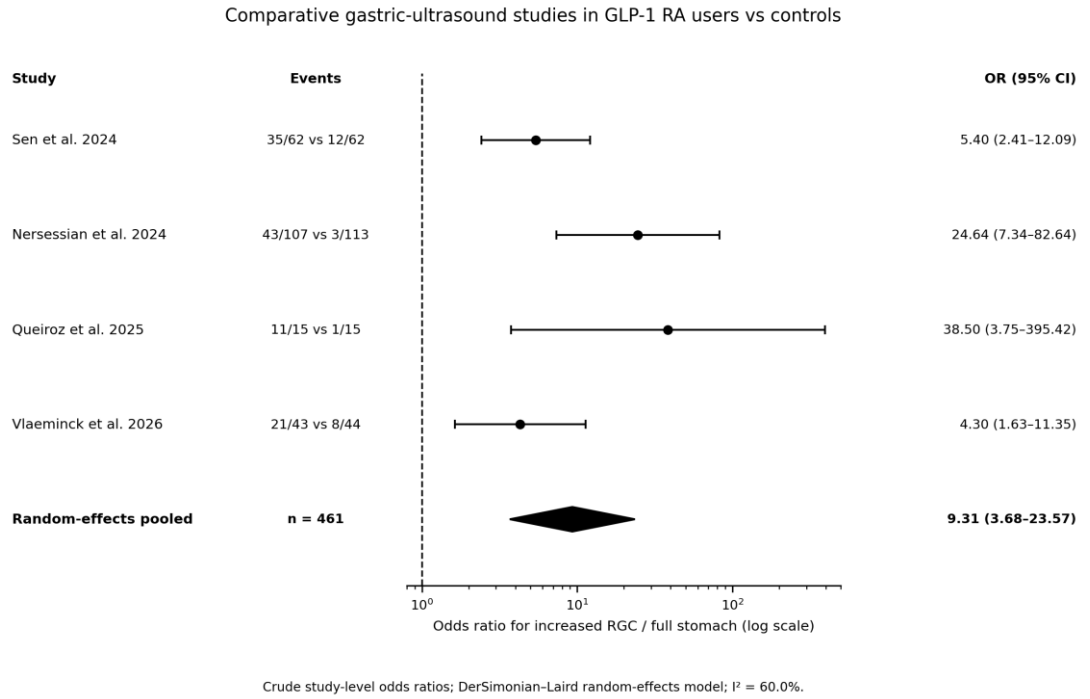
3.3 Gastric ultrasound findings

Six newly integrated ultrasound studies were identified [9,10,19,22,27,28]. Sherwin et al. prospectively evaluated 20 volunteers and found residual solids after an 8-hour fast in 70% of semaglutide users versus 10% of controls in the supine position and 90% versus 20% in the lateral position [9]. Sen et al. prospectively enrolled 124 fasted procedural patients; increased RGC was present in 56% of GLP-1 RA users and 19% of controls, with an adjusted prevalence ratio of 2.48 [10].

Nersessian et al. studied 220 surgical patients and found increased RGC in 40% of patients exposed to semaglutide within 10 days versus 3% of controls; there were no aspiration events [19]. Queiroz et al. reported a full stomach in 73% of semaglutide-exposed volunteers versus 7% of controls despite standard fasting [22]. In the 2026 multicenter matched study by Vlaeminck et al., a full stomach was present in 49% of semaglutide users versus 18% of controls, and solid content in 42% versus 7% [28]. Pai et al. assessed 316 GLP-1 RA users before anesthesia and found high RGC in 35.8%, with shorter withholding intervals and shorter solid fasting associated with higher risk [27].

Pooling the four controlled ultrasound studies with compatible full-stomach/increased-RGC definitions (n=461) yielded a crude random-effects OR of 9.31 (95% CI 3.68-23.57), with substantial heterogeneity (I^2=60.0%) (Figure 2). This estimate should be interpreted as an exploratory class-level association rather than diagnostic accuracy.

Figure 2. *Exploratory random-effects synthesis of controlled gastric-ultrasound studies. Events represent study-specific full-stomach/increased-RGC definitions.*



3.4 Endoscopic retained gastric content

The most comprehensive endoscopy synthesis through July 2025 included 24 observational studies and 184,707 participants, 59,095 of whom were receiving GLP-1 RAs [1]. RGC occurred in approximately 11.0% of GLP-1 RA users versus 2.7% of controls, corresponding to OR 4.82 (95% CI 3.66-6.35; I^2=63%). The association remained in propensity-matched analyses (OR 3.79, 95% CI 2.96-4.84; I^2=10%) [1].

The study-level literature shows clinically relevant heterogeneity. Silveira et al. reported increased RGC in 24.2% of semaglutide users versus 5.1% of controls [8]. Wu et al. documented visible gastric contents in 18.9% versus 4.9% and reported five urgent intubations among GLP-1-exposed procedures versus one in controls [11]. Abu-Freha et al.

analyzed 120,879 EGDs and found gastric residue in 5.6% of GLP-1 RA users versus 2.0% of nonusers [15]. Conversely, more recent studies using alternative grading systems have shown lower or nonsignificant binary retention differences, emphasizing the need for standardized definitions [32].

3.5 Withholding strategies and bowel-preparation effect

The 2026 OCULUS randomized clinical trial provides the strongest causal evidence to date. In the preplanned interim analysis of 60 patients undergoing elective upper endoscopy, clinically significant residual gastric volume occurred in 25.0% of those who continued GLP-1/GLP-1-GIP therapy versus 3.1% of those who withheld one dose [29]. The trial was stopped early after the interim difference. Importantly, participants undergoing EGD with concurrent colonoscopy and clear-liquid preparation had no clinically significant residual-volume events in either group, supporting the biologic plausibility of prolonged clear-liquid preparation as a mitigation strategy.

Santos et al. found that semaglutide interruption intervals shorter than 8 days and 8-14 days remained associated with RGC, while longer interruption in asymptomatic patients approached the risk of nonusers [18]. Dong et al. reported RGC rates of 5.83% with continued GLP-1 therapy, 1.61% after a 2-week hold, and 0.4% in nonusers; obesity remained an independent risk factor [30]. These studies should not be interpreted as establishing a universal cessation interval because drug formulation, dose escalation, symptoms, diabetes, obesity, and baseline gastroparesis differ across patients.

3.6 Aspiration and anesthetic outcomes

Despite a consistent increase in RGC, clinically documented aspiration was rare. In the predecessor meta-analysis, aspiration occurred in approximately 0.4% of GLP-1 RA users and 0.1% of controls; the pooled association was not statistically significant (OR 1.10, 95% CI 0.84-1.48; I^2=9%) [1]. Similar null estimates were reported by Baig et al. [2], although another 2025 meta-analysis reported an increased aspiration signal [3]. The discrepancy reflects rare events, differing outcome definitions, claims-based coding, and cohort overlap.

At the individual-study level, Silveira et al. and Wu et al. each reported one aspiration event among exposed patients [8,11], whereas large claims-based studies produced conflicting results. Yeo et al. reported an association with aspiration pneumonia after endoscopic procedures [16], while Alkabbani et al. found a weighted aspiration risk of approximately 4.15 versus 4.26 per 1000 for GLP-1 RA versus SGLT-2 inhibitor users (RR 0.98, 95% CI 0.73-1.31) [17]. Anazco et al. likewise reported a low absolute incidence of aspiration among thousands of GLP-1-treated upper endoscopies [21].

3.7 Direct ultrasound-to-endoscopy correlation

No eligible study was identified that prospectively performed gastric ultrasound immediately before EGD in the same GLP-1-treated cohort and then evaluated prespecified diagnostic-accuracy measures (sensitivity, specificity, likelihood ratios, or agreement) against endoscopic gastric contents as the reference standard. This is the central evidence gap revealed by the integrated review. Existing ultrasound and endoscopy studies therefore support triangulation of the same biologic phenomenon—delayed gastric emptying—but do not yet establish a validated ultrasound threshold that predicts the subsequent endoscopic field in GLP-1-treated patients.

3.8 Methodological quality of newly integrated studies

The structured appraisal of the 11 newly integrated studies identified serious methodological concerns in three studies, moderate concerns in seven, and some concerns in the randomized OCULUS trial. The principal concerns were small or convenience samples, residual confounding, nonrandomized exposure or withholding strategies, exposed-only designs, and early trial stopping. These judgments are summarized in Table 3 and should be interpreted as single-reviewer structured concerns rather than duplicate-review formal ROBINS-I or RoB 2 assessments.

Table 3. *Methodological concerns in the 11 newly integrated studies*

Study	Design	Overall concern	Main rationale
Sherwin 2023	Prospective volunteer US	Serious concern	Very small convenience sample; recent semaglutide initiation; limited generalizability.
Sen 2024	Prospective US	Moderate concern	Adjusted analysis but residual confounding and single-center selection remain.
Nersesian 2024	Prospective US	Moderate concern	Strong association; nonrandomized exposure and perioperative selection.
Queiroz 2025	Prospective volunteer US	Serious concern	n=30; volunteer design; wide imprecision.
Pai 2026	Prospective US cohort	Moderate concern	No unexposed comparator; useful for risk-factor/withholding analysis.
Vlaeminck 2026	Prospective matched US	Moderate concern	Multicenter and matched; residual confounding and small sample.
Le 2025/2026	Retrospective exposed-only EGD	Serious concern	No comparator; adverse events descriptive only.
Ahmad/OCULUS 2026	Randomized EGD trial	Some concerns	Randomized design; small interim sample and early stopping may inflate effect size.
Dong 2026	Retrospective EGD	Moderate concern	Large reference group; withholding not randomized; obesity interaction.
Chang 2026	Retrospective case-control EGD	Moderate concern	Large screened population; residual confounding and case-control sampling.
Patel 2026	Retrospective EGD	Moderate concern	Small cohort; novel grading scale; limited power for rare outcomes.

These ratings reflect a structured single-reviewer appraisal of the update and should not be interpreted as duplicate-review formal ROBINS-I or RoB 2 judgments.

4. Discussion

4.1 Principal findings

This integrated review yields four clinically important conclusions. First, the association between GLP-1-based therapy and residual gastric content is robust across two independent measurement modalities. The effect is large on gastric ultrasound and remains consistently elevated in endoscopic cohorts. Second, the strength of association with RGC does not translate directly into a proven increase in pulmonary aspiration, an event that is both rare and vulnerable to misclassification. Third, randomized evidence now suggests that withholding can reduce residual volume in some patients, while clear-liquid preparation may substantially modify risk. Fourth, the key translational link remains missing: direct paired validation of preprocedural gastric ultrasound against subsequent EGD findings.

4.2 Why ultrasound may be clinically valuable

Gastric ultrasound has an important temporal advantage over

endoscopy: it can be performed before sedation or induction. In a patient with uncertain medication timing, ongoing nausea/bloating, obesity, diabetes, or suspected gastroparesis, a clear demonstration of solids or a large fluid volume can meaningfully alter the risk-benefit calculation before airway reflexes are suppressed. The 2025 ADS/ANZCA/GESA/NACOS recommendations explicitly endorse a 24-hour clear-fluid diet followed by standard fasting and recommend gastric ultrasound or minimally sedated gastroscopy when that preparation has not been completed [4]. Multisociety guidance similarly supports individualized risk assessment rather than automatic discontinuation for every patient [5].

However, ultrasound should not be framed as a proven aspiration-prevention intervention. Current studies validate association with gastric content, not a reduction in aspiration events. Operator dependence, body habitus, altered gastric anatomy, and inconsistent volume equations also limit universal implementation. A positive scan may appropriately prompt postponement or airway protection, but the threshold at which those actions improve net outcomes remains uncertain.

4.3 Endoscopy and anesthesia implications

For gastroenterologists, the consequences of RGC extend beyond aspiration. Retained food may impair mucosal visualization, trigger procedure abortion, and require repeat EGD [12-15]. For anesthesiologists, the same finding changes the airway-risk profile and may favor deferral, rapid-sequence induction with tracheal intubation, or other individualized strategies depending on urgency and patient comorbidity. The decision should therefore be shared across the procedural team rather than reduced to a medication hold/no-hold rule.

The apparent protective effect of concurrent colonoscopy seen in several cohorts and in the OCULUS trial is mechanistically plausible because bowel preparation usually imposes a prolonged clear-liquid period. This signal supports research into preparation-based mitigation rather than simply extending drug-withholding intervals, particularly for long-acting agents whose

pharmacodynamic effects may persist beyond one missed weekly dose.

An evidence-informed framework for multidisciplinary decision-making before upper endoscopy is presented in Table 4. It is intended to support individualized discussion between gastroenterology and anesthesia teams rather than to function as a validated prediction rule.

Table 4. *Evidence-informed clinical interpretation framework for GLP-1-treated patients undergoing upper endoscopy*

Step	Action	Interpretation
1	Identify exposure	Ask specifically about GLP-1 RA/GLP-1-GIP agent, dose, escalation phase, last dose, indication, GI symptoms, diabetes, obesity, gastroparesis, opioid use.
2	Optimize preparation	When feasible, use a 24-hour clear-fluid strategy plus standard fasting according to local guidance.
3	Use gastric POCUS when uncertainty remains	Visible solid/thick content or clearly elevated fluid volume indicates a higher-risk stomach; an apparently empty/low-volume stomach lowers but does not eliminate aspiration risk.
4	Coordinate endoscopy + anesthesia plan	If high-risk content is detected, individualize deferral versus protected-airway general anesthesia according to urgency and patient risk.
5	Avoid overreliance on symptoms	Absence of nausea/bloating does not reliably exclude increased gastric content in GLP-1-treated patients.

This table summarizes current evidence and multidisciplinary guidance [4,5]; it is not a validated clinical prediction rule.

4.4 Proposed research agenda

The highest-priority next study is a prospective paired diagnostic-accuracy cohort in GLP-1-treated adults undergoing elective EGD. Gastric ultrasound should be performed immediately before sedation using a prespecified qualitative/quantitative protocol; the gastroenterologist should then grade solid and liquid gastric content using a standardized endoscopic scale while blinded to the ultrasound result whenever feasible. Primary analyses should estimate sensitivity, specificity, likelihood ratios, calibration of estimated gastric volume, and agreement. Secondary analyses should evaluate whether ultrasound changes anesthetic management, procedure completion, and airway events.

A subsequent pragmatic trial should compare ultrasound-guided management with a standardized preparation strategy (for example, 24-hour clear liquids plus standard fasting) using clinically relevant outcomes and decision-impact measures. Given the rarity of

aspiration, multicenter recruitment or a composite endpoint including regurgitation, urgent airway intervention, and procedure interruption may be required.

4.5 Strengths and limitations

A key strength of this work is its explicit integration of imaging, gastroenterology, and anesthesia evidence, including new 2026 randomized and prospective ultrasound data that are not the central focus of prior endoscopy meta-analyses. The separate quantitative synthesis of compatible ultrasound cohorts avoids inappropriate pooling of ultrasound and endoscopic definitions. The evidence-update design also minimizes unnecessary duplication of a recent 24-study endoscopy meta-analysis.

Several limitations are important. First, this is a structured update anchored to a predecessor systematic review, not an independently repeated search of every bibliographic database. Second, the update screening and methodological appraisal were not independently duplicated by two reviewers, which increases susceptibility to reviewer-dependent classification. Third, most evidence remains observational, with heterogeneous fasting protocols, exposure definitions, GLP-1 agents, and RGC thresholds. Fourth, the exploratory ultrasound meta-analysis uses crude event counts and includes small cohorts. Fifth, aspiration events are too rare for precise effect estimates. Finally, the absence of a paired ultrasound-EGD validation study prevents claims of diagnostic accuracy or direct correlation between modalities.

5. Conclusiones

GLP-1 receptor agonist and dual GLP-1/GIP therapy is strongly associated with retained gastric content detected by both gastric ultrasound and upper gastrointestinal endoscopy. In controlled ultrasound cohorts, GLP-1 exposure was associated with approximately ninefold higher crude odds of a full stomach/increased RGC, while the established endoscopy evidence shows approximately fivefold higher odds of RGC. In contrast, the absolute incidence of aspiration is low and

current studies do not provide a consistent estimate of excess clinical risk. Gastric ultrasound is therefore best viewed as a promising individualized risk-stratification adjunct—not yet a validated surrogate for endoscopic findings or a proven aspiration-prevention strategy. Direct same-patient ultrasound-to-EGD validation is the critical next step.

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