



Endoscopic functional luminal imaging probe for intraprocedural guidance of achalasia treatment: a systematic review and meta-analysis

Matyas Fehervari, PhD, FRCS^{a,b}, Isla Middleton, MBBS^c, Emma Rose McGlone, PhD, FRCS^{b,c}, Michael G. Fadel, MRCS^{b,c}, James Brewer, FRCS^c, Pranav Patel, PhD, FRCS^{d,e}, Majid Hashemi, MD, FRCS^f, Naim Fakh-Gomez, FRCS^c, Sacheen Kumar, PhD, FRCS^{d,e,g,*}

Background: Functional luminal imaging probes (EndoFLIP) have shown potential as both diagnostic tools and intraoperative guides during achalasia interventions. This systematic review and meta-analysis aim to evaluate the intraoperative use of EndoFLIP during surgical procedures for achalasia, with a focus on its impact on the distensibility index (DI) and treatment outcomes.

Materials and methods: A literature search of Medline, Embase, and the Cochrane Library was conducted for studies reporting the use of EndoFLIP and DI in achalasia treatment from January 2000 to January 2024. Meta-analysis was performed using random-effect models to assess treatment effects, with heterogeneity between studies evaluated.

Results: A total of 32 studies with 2681 patients were included in the qualitative synthesis, and 17 studies with 1734 patients were included in the quantitative synthesis. A pooled random-effects analysis demonstrated a significant reduction in DI following myotomy, with a weighted mean difference (WMD) of -3.72 (95% CI: -4.16 to -3.28 ; $I^2 = 90\%$). The Eckardt score analysis, including data from 1009 patients, showed a significant reduction by -5.21 (95% CI: -5.8 to -4.6 ; $P < 0.001$, $I^2 = 89.4\%$). The random-effects analysis of DI pre- and post-myotomy without an endoscope demonstrated a significant increase with a WMD of -2.402 (95% CI: -3.175 to -1.6 ; $P < 0.001$, $I^2 = 85.6\%$). A larger WMD was observed with endoscope placement above the FLIP device, measuring -4.14 (95% CI: -5.4 to -2.8 ; $P < 0.001$, $I^2 = 91.2\%$). For the 30 mL balloon fill, the WMD in the DI post-myotomy was -2.89 (95% CI: -3.2 to -2.4 ; $P < 0.001$). For the 40 mL balloon fill, the WMD was -4.02 (95% CI: -4.8 to -3.1 ; $P < 0.001$).

Conclusions: EndoFLIP enhances achalasia treatment by offering real-time feedback on the DI, allowing for more tailored interventions and improved outcomes. A standardized protocol for EndoFLIP usage is necessary to further validate its role in clinical practice and ensure consistent, comparable measurements.

Keywords: achalasia, distensibility index, EndoFLIP, gastro-esophageal reflux disease, myotomy

^aBariatric Surgery Department, Maidstone and Tunbridge Wells NHS Trust, Kent, United Kingdom, ^bDepartment of Surgery and Cancer, Imperial College London, United Kingdom, ^cDepartment of Bariatric and Metabolic Surgery, Chelsea and Westminster Hospital, London, United Kingdom, ^dDepartment of Upper GI Academic Surgery, the Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom, ^eUpper Gastrointestinal Surgical Oncology Research Group, Institute of Cancer Research, London, United Kingdom, ^fUniversity College London Hospitals NHS Foundation Trust, London, United Kingdom and ^gDepartment of Upper GI Surgery, Digestive Disease & Surgery Institute, Cleveland Clinic London Hospital, London, United Kingdom

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Upper GI Academic Surgery, Royal Marsden Hospital NHS Foundation Trust, London SW36JJ, United Kingdom. E-mail: (sacheen.kumar@rmh.nhs.uk) (S. Kumar).

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-ShareAlike License 4.0, which allows others to remix, tweak, and build upon the work, even for commercial purposes, as long as the author is credited and the new creations are licensed under the identical terms.

International Journal of Surgery (2025) 111:4165–4176

Received 8 October 2024; Accepted 1 April 2025

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.ijw.com/international-journal-of-surgery.

Published online 20 May 2025

<http://dx.doi.org/10.1097/JS9.0000000000002397>

HIGHLIGHTS

- Endoscopic functional luminal imaging probe for intra-procedural guidance of achalasia treatment: A systematic review and meta-analysis
- EndoFLIP Accuracy: EndoFLIP provides real-time accurate measurements of esophagogastric junction distensibility during achalasia procedures.
- Intraoperative Guidance: EndoFLIP is highly beneficial for intraoperative decision-making, enabling tailored myotomies based on real-time feedback on distensibility index (DI).
- Improvement in Outcomes: Use of EndoFLIP during procedures is associated with a significant improvement in postoperative outcomes, including a reduction in Eckardt scores.
- Comparison of Balloon Pressures: The study reveals that a 40 mL balloon fill provides more accurate and sensitive DI measurements compared to a 30 mL fill.
- Standardization Needs: Despite its advantages, there is a need for standardized EndoFLIP protocols to ensure consistent clinical results and facilitate comparisons across studies.

Introduction

Achalasia is a motility disorder characterized by the selective loss of inhibitory neurons from the esophageal myenteric plexus, resulting in a failure of the lower esophageal sphincter (LES) to relax on swallowing^[1,2]. It has a global prevalence estimated at 10 cases per 100 000 person-years, usually presenting with progressive dysphagia, regurgitation and weight loss^[3]. Diagnostic modalities for achalasia include esophagogastric-duodenoscopy (EGD), barium swallow, and gold standard high-resolution manometry (HRM)^[2]. Achalasia is defined via HRM as an abnormally high median integrated pressure at the LES and failure of peristalsis during swallowing^[4].

Management strategies for achalasia aim to reduce lower esophageal pressures, so that food boluses can pass freely through the LES. There are two definitive approaches with long-term efficacy to achieve this objective: via laparoscopic surgery, in the form of a Heller's cardiomyotomy (LHC), or endoscopically with per-oral endoscopic myotomy (POEM), which involves formation of a submucosal tunnel and division of the inner circular muscle layer of the LES^[5,6]. Both procedures are highly effective with comparable success rates of around 90% at 2 years^[7] and 80% at 5 years^[8,9]. A major limitation of disturbing the muscular integrity of the LES is the development of post-procedural gastro-esophageal reflux disease (GERD). For this reason, LHC is invariably complemented with an anti-reflux procedure, most typically an anterior (Dor) fundoplication. Patients treated with POEM are at much greater risk of developing symptomatic and objective GERD than those undergoing LHC with partial fundoplication^[7], although early indications suggest that the novel procedure of POEM and fundoplication could mitigate this complication^[10,11].

In some cases, for example, where there is a co-existing hiatus hernia, HRM findings do not correlate with symptoms or are difficult to interpret. Endoscopic functional luminal imaging probe (EndoFLIP) may be helpful in such cases to assess achalasia^[12]. EndoFLIP consists of an endoscopic probe which is covered by an 8 cm-long balloon. This is sited across the LES, before being distended by injection of a predetermined volume. Simultaneous impedance planimetry is used to assess the cross-sectional area (CSA) at 16 equally-spaced points along the length of the balloon. This enables simulation of a 3D representation of the region, including sphincter length and width. The distensibility index (DI) is defined as the minimum CSA (narrowest area) divided by the intrabag pressure, representing compliance of the LES. Patients with achalasia have a lower DI than healthy volunteers and DI negatively correlates to Eckardt score (self-reported symptomatic severity score for achalasia)^[13,14]. Patients with a DI <0.8 have >99% probability of having achalasia^[15], and therefore treatment of achalasia is associated with an increase in DI^[13].

EndoFLIP can be utilized intraprocedurally to calibrate extent of myotomy^[16]. DI decreases with each myotomy increment, thus intraoperative EndoFLIP can be used to calibrate myotomy length^[17]. However, determining a DI that correlates to clinical success has been more difficult to achieve. Some reports indicate that the ideal DI to balance dysphagia and GERD symptoms is within the range of 4.5–8.5 mm³/mmHg following intervention^[18,19], while Pandolfino, *et al*^[20] showed good treatment response for patients with a post-procedure median DI of 3.4 mm³/mmHg.

Achalasia is a rare condition and most studies investigating EndoFLIP as an intraprocedural guiding device present a limited number of measurements. The absence of procedural guidance and standardized techniques for using EndoFLIP leads to a wide variability in measurement outcomes^[12]. Current controversies include whether to place the probe “blindly” post-endoscopy, or alongside the endoscope and what volume to inflate the balloon to (e.g. 20–60 ml).

The aims of this systematic review and meta-analysis are as follows:

- To summarize the available data on intraoperative use of EndoFLIP during interventional procedures for achalasia;
- To determine if the change in DI following the procedure differs depending on the volume of balloon distension or if the device is placed with or without endoscope.

Materials and methods

A systematic literature search was conducted based on a prospectively developed protocol and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement^[21] and the AMSTAR (Assessing the methodological quality of systematic reviews) guidelines^[22]. The review was registered on PROSPERO Centre for Reviews and Dissemination (registration number CRD42024589079).

Search strategy

A systematic literature search was performed in the following electronic medical databases PubMed/Medline, Embase/Ovid and the Cochrane library between 1 January 2000 and 1 January 2024. The exact search strategy has been provided as supplementary material. <http://links.lww.com/JS9/E187> (Supp. 1. <http://links.lww.com/JS9/E187>). Specific research equations were formulated for each database using the following Medical Subject Heading terms: *oesophageal achalasia, achalasia cardia, cardiospasm, oesophageal aperistalsis, FLIP, functional luminal imaging probe, EndoFlip, impedance planimetry, laparoscopy Heller Myotomy, and per-oral endoscopic myotomy*. Studies identified from the search strategy were entered into Covidence (Victoria, Australia) for bibliographic management and removal of duplicates.

Inclusion and exclusion criteria

The following criteria were applied for inclusion in the study:

- Randomized controlled trials (RCT), prospective or retrospective cohort studies, case-control studies and cross-sectional studies;
- Articles reporting on interventional treatment of achalasia with the use of intraoperative EndoFLIP;
- Reported outcome of interest including resolution of achalasia symptoms and perioperative complications;
- Original, full-length publications published in English.

Animal studies, reviews, abstracts, conference presentations, case reports, editorials, and unpublished studies were excluded from the analysis.

Screening of articles and data extraction

Three authors (MF, IM, and ERM) independently screened to identify relevant studies and any discrepancies were resolved by consensus with the help of a fourth author (SK). Two authors (MF and IM) independently extracted all relevant data and metadata, including study design, sample size, gender, age, modality of treatment, resolution of achalasia and post-procedural complications and DI pre-and post-procedure. Any discrepancy was resolved by SK.

Risk of bias assessment

The quality of all observational studies was assessed using the Newcastle–Ottawa Scale (NOS)^[23]. This was calculated by examining method of patient selection, comparability of the study groups, and assessment of outcomes reported. The full score was nine stars, and studies that had a score of seven stars or more were considered high quality. All studies were rated independently by two authors (MF and IM), with any differences resolved by consensus. The strength of clinical data and subsequent recommendations were also graded according to the Oxford Centre for Evidence-Based Medicine^[24]. Levels of evidence were as follows: level 1, properly powered and conducted RCT or systematic review with meta-analysis; level 2, well-designed controlled trial without randomization or prospective comparative cohort trial; level 3, case-control study or retrospective cohort study and level 4, case series or cross-sectional study.

Statistical analysis

Meta-analysis was completed using STATA version 13. Where studies investigated cohorts of patients undergoing LHC and POEM data for each group was considered separately. Weighted mean differences (WMD) and mass effect were calculated for each treatment cohort using random-effects analysis. The distension pressures of 30 and 40 mmHg values used in the analysis were based on those reported in the original studies. Data were summarized using a random effects inverse-variance model and is presented as WMD (95% confidence interval). Statistical heterogeneity was estimated with I^2 : we considered an I^2 of 30% or less as low, between 30% and 60% to be moderate, and 60% or over as high heterogeneity^[25].

Results

Study selection

The search identified 1588 relevant citations and one additional article was included from a manual search. After removing duplicate results, 1191 articles were screened for titles and abstracts and 125 studies were included for full-text review. A total of 96 articles were excluded after full-length review due to reasons outlined in (Fig. 1). Thus, 32 studies^[15–19,26–51] were eligible for inclusion for critical appraisal and 17^[15–19,26,27,29,31,33,35,36,38,41,47,49–51] studies for quantitative synthesis. All studies were cohort studies, of which six were prospective but non-randomized and 23 were retrospective (Table 1). Twenty-two studies scored 7 or above on the NOS quality assessment; the remaining studies scored 6.

Treatment effect on EndoFlip readings

EndoFLIP can be used to evaluate real-time motility changes during intervention for achalasia. Overall, our search detected 34 cohorts of patients undergoing either LHC or POEM in 32 studies. The baseline study characteristics are displayed in Table 1. In total, data from 2681 subjects were included in the qualitative synthesis, with data from 1734 subjects were included in the meta-analysis. Across 17 studies involving 1173 patients, a pooled random-effects analysis of the WMD in the DI demonstrated a reduction of -3.72 (95% CI: -4.16 to -3.28 ; $I^2 = 90\%$) following myotomy (Fig. 2).

Campagna, *et al*^[41] compared achalasia subtypes, demonstrating that intraoperative contractility was uncommon in patients with types I and II achalasia but occurred in 100% of patients with type III achalasia. Following completion of LHC, there was an immediate reduction in the frequency of repetitive retrograde contractions and contractile vigor in those with type III achalasia.

Intraoperative EndoFLIP measurements in patients with achalasia showed a significant increase in DI following LHC compared to prior to surgery and a subsequent significant decrease in DI following completion of Dor fundoplication compared to after LHC^[15]. Furthermore, Hsing, *et al*^[29] also showed that the presence of contractility on manometry post-POEM is associated with the presence of repetitive antegrade contractions (RACs) with EndoFLIP. These findings further support the utility on EndoFLIP as a potential intraoperative tool to help when there is diagnostic uncertainty and to provide an objective measure to assess outcome following intervention for achalasia.

Treatment effect on Eckardt score

Our search identified 13 cohorts in 12 studies, where an Eckardt score was measured pre- and post-EndoFLIP-guided myotomy. The data comprised 1009 patients with achalasia. Random-effects analysis demonstrated a significant reduction in Eckardt score by -5.21 (95% CI -5.8 to -4.6 ; $P < 0.001$, $I^2 = 89.4\%$) (Fig. 3).

In a study of patients undergoing POEM, those who underwent intraoperative FLIP (65% of whom had additional myotomy performed following the initial post-myotomy FLIP) had significantly more clinical success (Eckardt score 3 or lower) than those without intraoperative FLIP^[16]. Compliance may be a better measure than DI to predict postoperative Eckardt score^[26].

Use of EndoFlip to calibrate myotomy

EndoFLIP can be used to intraoperatively measure the effect of variable distal myotomy lengths on oesophago-gastric junction (OGJ) distensibility^[18,19]. A creation of the submucosal tunnel close to myotomy resulted in a marked improvement in OGJ physiology. Myotomy extension across the LES and to 2 cm onto the gastric wall resulted in the normalization of OGJ distensibility. Further extension to 3 cm distal to the OGJ did not increase compliance further. Similar findings were described by Knowles, *et al*^[17] whom also evaluated change in DI with short and long myotomies. They found similar outcomes of DI for most patients following a short (2–4 cm) myotomy than with a long myotomy (8 cm). Findings of these studies suggest that

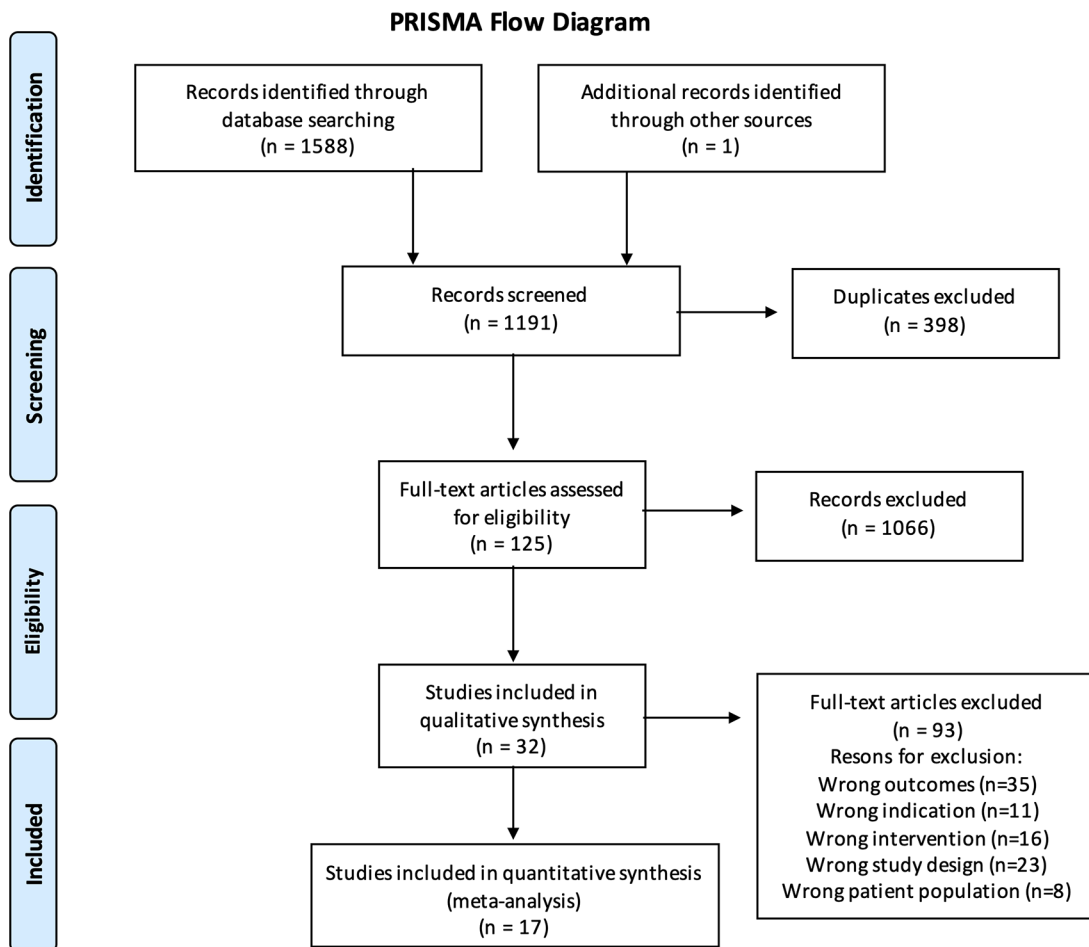


Figure 1. PRISMA flowchart of study selection.

a shorter myotomy may be appropriate for selected patients, and the use of the EndoFLIP intraoperatively may allow for a tailored myotomy length.

Attaar, *et al* evaluated long-term changes in EndoFLIP measurements by comparing values from the time of surgery and at follow-up EGD^[33], suggesting that esophageal remodeling may cause changes in LES geometry after POEM. They concluded that postoperative EndoFLIP targets immediately post-myotomy should be adjusted to account for these changes. Amundson, *et al*^[26] focused on improving intraprocedural measurements with EndoFLIP, with utilization of post-myotomy compliance. They concluded that pressure over 125 mm³/mmHg at a 40 ml fill is more closely associated with normal Eckardt scores than defined DI and CSA scores. Jain, *et al*^[42] looked at esophageal anatomy versus DI as predictors of treatment response and found that the EndoFLIP DI is the most useful metric for assessing the effect of achalasia treatment. However, atypical anatomy is also an important factor for predicting therapeutic outcomes.

DeHaan, *et al*^[48] aimed to define the changes in OGJ distensibility during Heller's Myotomy with Dor fundoplication using the EndoFLIP device. Their findings suggested that Heller myotomy leads to significant changes in the distensibility of the OGJ. Minimum esophageal diameter and OGJ distensibility increased significantly with Heller's myotomy. Knight, *et al*^[19] supported

the use of EndoFLIP in measuring esophageal distensibility in order to customize myotomy length intraoperatively. Tailored myotomies of ≤6 cm were shown to be effective and were associated with reduced proton-pump inhibitor use postoperatively. Holmstrom, *et al*^[16] and Sloan, *et al*^[34] also demonstrated a role for EndoFLIP in the tailoring of myotomy, with an additional myotomy lengthening procedure being required in more than 50% of patients following EndoFLIP measurement.

DI with different balloon fills

The distension pressures of 30 and 40 mmHg in the EndoFLIP system are used to assess esophageal distensibility. At 40 mmHg, the balloon exerts more force on the esophagogastric junction, potentially revealing greater distension, which can highlight areas of increased stiffness or reduced elasticity that may not be as apparent at 30 mmHg. There were nine studies across 12 cohorts, with a total of 391 patients, demonstrated a significant change in the DI before and after myotomy using a 40 mmHg balloon pressure. The random-effects analysis showed a marked reduction in DI of -4.02 (95% CI: -4.8 to -3.1; $P < 0.001$) (Fig. 4). Similarly, a significant increase in DI was reported in 12 studies involving 586 patients using 30 mmHg balloon pressure, with a reduction of -2.89 (95% CI: -3.2 to -2.4; $P < 0.001$) (Fig. 5). This analysis showed greater DI improvement with

Table 1

Baseline study characteristics and quality assessment scoring of studies included in systematic review. BTI, botulinum toxin injection; LHC, laparoscopic Heller's cardiomyotomy; NOS, Newcastle–Ottawa scale; PD, pneumatic dilatation; POEM, per-oral endoscopic myotomy; SD, standard deviation; – = information not available

Author, year	Country	Study design (level of evidence)	Number of patients	Age ± SD	Number of female patients	Endoscopic/operative procedure	Specific procedure type	Balloon fill (ml)	Number of patients with achalasia	Eckardt score pre-treatment	Eckardt score post-treatment	NOS
Amundson, et al ^[51]	USA	Retrospective (3)	919	66 ± 12	243	Both	POEM, POP, ZPOEM, LHM	30 and 40	919	-	-	8
Howk, et al ^[50]	USA	Retrospective (3)	10	13.3 ± 3.3	7	Operative	Oesophagectomy	10	10	-	-	6
Rafeeqi, et al ^[49]	USA	Retrospective (3)	33	14 (10-16)	12	Endoscopic	POEM	40	33	7	1	7
Amundson, et al ^[26] 2022	USA	Retrospective (3)	35	61 ± 19	18	-	POEM	30 and 40	35	5.5	1.3	7
Attaar, et al ^[27] 2022	USA	Retrospective (3)	97	63 ± 18	67	Endoscopic	POEM	-	97	6.5	1.6	8
Knowles, et al ^[7] 2022	USA	Retrospective (3)	16	49 ± 14	6	Endoscopic	POEM	40	16	-	-	6
Ichkhanian, et al ^[28] 2022	USA, Europe and Asia	Retrospective (3)	123	53 ± 21	62	Both	POEM and LHM	-	-	-	-	8
Hsing, et al ^[29] 2022	Korea	Retrospective (3)	68	52 ± 17	35	Endoscopic	POEM	-	68	6.48	1.16	7
DeWitt, et al ^[30] 2022	USA	Retrospective (3)	87	51 ± 17	36	Endoscopic	POEM	-	87	-	-	7
Law, et al ^[15] 2022	USA	Retrospective (3)	169	54.5 ± 8	17	Operative	LHM	30	36	4.5	0	8
Knight, et al ^[9] 2022	UK	Retrospective (3)	142	-	-	Endoscopic	POEM	-	142	-	-	8
Holmstrom, et al ^[31] 2021	USA	Prospective (2)	46	53 ± 8	19	Both	POEM and LHM	-	53	7	2	8
Moran, et al ^[32] 2021	USA	Retrospective (3)	290	47.2 ± 17.4	154	Endoscopic	POEM	-	290	8	1	8
Attaar, et al ^[33] 2021	USA	Retrospective (3)	43	65 ± 16	20	Endoscopic	POEM	-	43	6.9	1.6	7
Holmstrom, et al ^[6] 2021	USA	Retrospective (3)	143	58 ± 7.5	43	Endoscopic	POEM	-	58	6 and 7	1	8
Sloan, et al ^[34] 2020	USA	Retrospective (3)	51	54 ±	25	Endoscopic	Balloon dilatation	-	37	5	1.5	7
Schnurre, et al ^[35] 2020	Switzerland	Prospective (2)	28	43 ± 15.7	8	Endoscopic	Balloon dilatation	-	28	7	2	6
Kim, et al ^[36] 2020	Korea	Retrospective (3)	89	42 ± 15.5	-	Endoscopic	POEM	-	89	6.5	1.5	7
Su, et al ^[37] 2020	USA	Retrospective (3)	402	-	-	Both	-	-	-	-	-	8
Su, et al ^[38] 2020	USA	Retrospective (3)	77	65 ± 16	-	Both	POEM and LHM	-	77	-	-	7
Bianca, et al ^[39] 2020	Switzerland	Retrospective (3)	93	62 ±	47	Endoscopic	-	-	-	5	-	7
Carlson, et al ^[40] 2020	USA	Prospective (2)	160	52 ± 18	20	-	-	-	140	-	-	8
Campagna, et al ^[41] 2020	USA	Retrospective (3)	32	50 ± 15	13	Both	POEM and LHM	-	-	7	-	6
Jain, et al ^[42] 2019	USA	Prospective (2)	79	49 ± 16	-	-	-	-	-	-	-	7
Yoo, et al ^[43] 2019	Korea	Retrospective (3)	52	42 ± 14.8	25	Endoscopic	POEM	30 and 40	-	6.4	1.3	7
Carlson, et al ^[44] 2019	USA	Prospective (2)	40	64 ± 14	24	-	-	-	-	-	-	7
Carlson, et al ^[45] 2016	USA	Retrospective (3)	145	60 ± 16.7	-	-	-	-	-	-	-	8
Ahuja, et al ^[46] 2017	USA	Retrospective (3)	70	54 ± 16	-	-	-	-	-	-	-	6
Ponds, et al ^[47] 2017	Netherlands	Retrospective (3)	13	48 ± 10	-	Both	BTI, PD and LHM	30 and 40	-	7	2	6
Carlson, et al ^[40] 2015	USA	Retrospective (3)	61	60 ± 15.7	27	-	-	-	51	-	-	7
DeHaan, et al ^[48] 2016	USA	Prospective (2)	14	-	-	-	-	-	-	-	-	6
Teitelbaum, et al ^[18] 2016	USA	Retrospective (3)	16	53 ± 15	-	Endoscopic	POEM	-	-	-	-	6

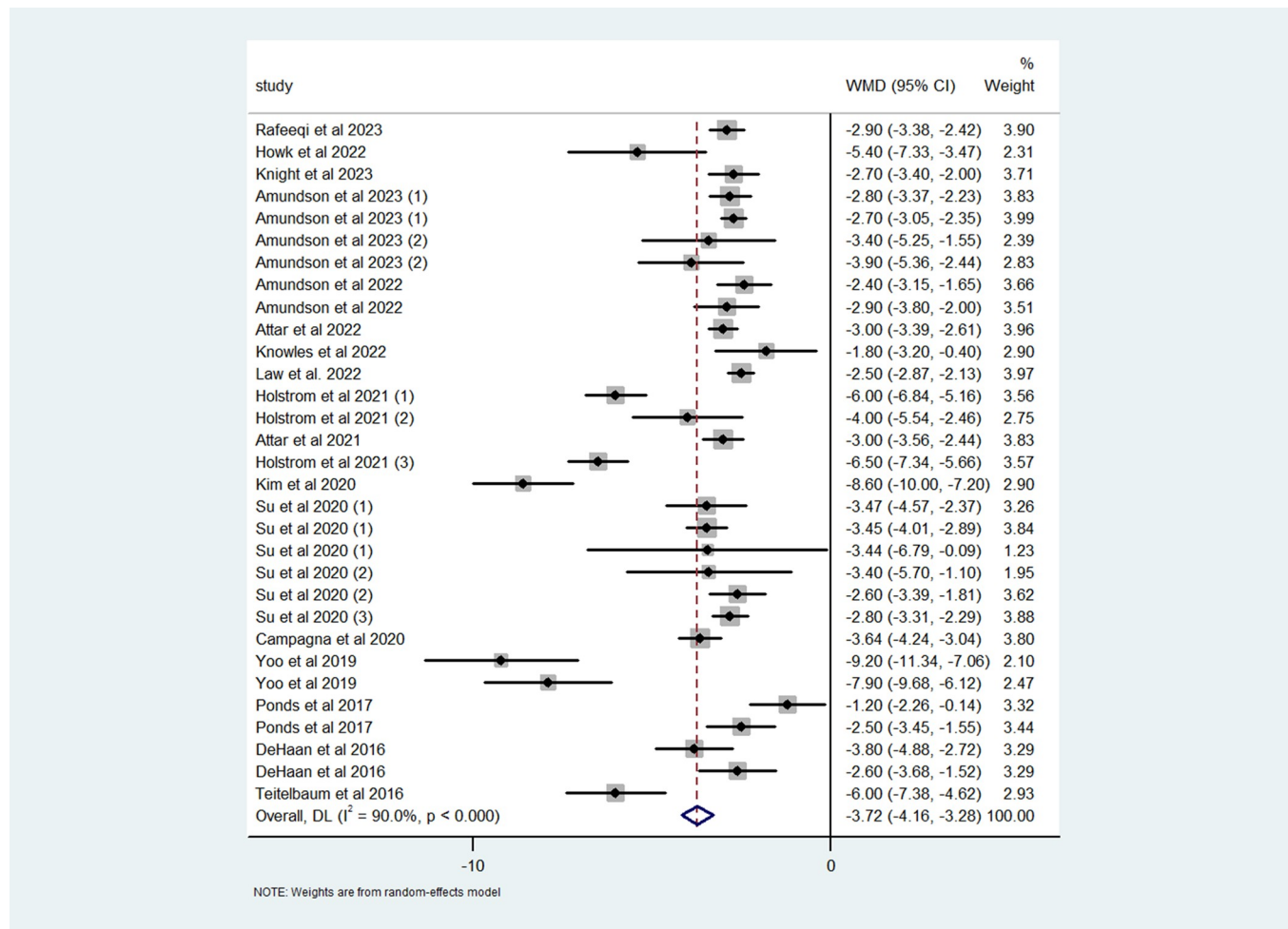


Figure 2. Forest plot showing the WMD in DI before and after myotomy. The analysis demonstrates the overall change across studies, with 95% CI indicated for each.

a 40 mL balloon (216% increase from baseline) compared to a 30 mL balloon (170% increase from baseline).

DI with and without flexible endoscope

Bianca, *et al*^[39] observed a significant difference in EndoFLIP measurements when the endoscope was present in the esophagus during DI measurements, positioned above the balloon but below the upper esophageal sphincter. In contrast, other studies removed the endoscope completely during DI assessment. Three studies, which involved 200 patients across four cohorts, published data on DI measurements without concurrent endoscopic assessment. Additionally, three other studies included 121 patients from four cohorts where the endoscope was present during DI measurement. A random-effects analysis of DI pre- and post-myotomy without the endoscope demonstrated a significant increase in DI, with a mean difference of -2.402 (95% CI: -3.175 to -1.6 ; $P < 0.001$, $I^2 = 85.6\%$). Similarly, a significant increase in DI was observed with the endoscope in place, showing a greater mean difference of -4.14 (95% CI: -5.4 to -2.8 ; $P < 0.001$, $I^2 = 91.2\%$) (Figs 6 and 7). We also calculated the percentage change in DI following myotomy with both

methods. The weighted mean of percentage improvement with endoscope placement was 529% and 314% without endoscope. Comparing the percentage change between these groups demonstrated significantly higher change in DI measurements with concomitant endoscope placement ($P = 0.019$).

Prediction of post-procedural GERD with EndoFLIP

Holmstrom, *et al*^[31] reported that DI measurements taken intraoperatively post-LHC were predictive of erosive esophagitis on endoscopy at 12 months postoperatively. Similarly, Attaar, *et al*^[27] found that patients with a final DI ≥ 2.7 and CSA ≥ 83 intraoperatively with POEM were significantly more likely to develop esophageal inflammation on postoperative EGD. However, other groups have not found intraoperative EndoFLIP to be predictive of post-procedural GERD. Amundson, *et al*^[26] looked at using EndoFLIP compliance measurements to determine therapeutic success rather than the more commonly cited DI and CSA measurements. They showed that whilst compliance is predictive of post-treatment Eckardt scores, its use in prediction of postoperative GERD is unreliable. Moran, *et al*^[32] investigated patients undergoing POEM and

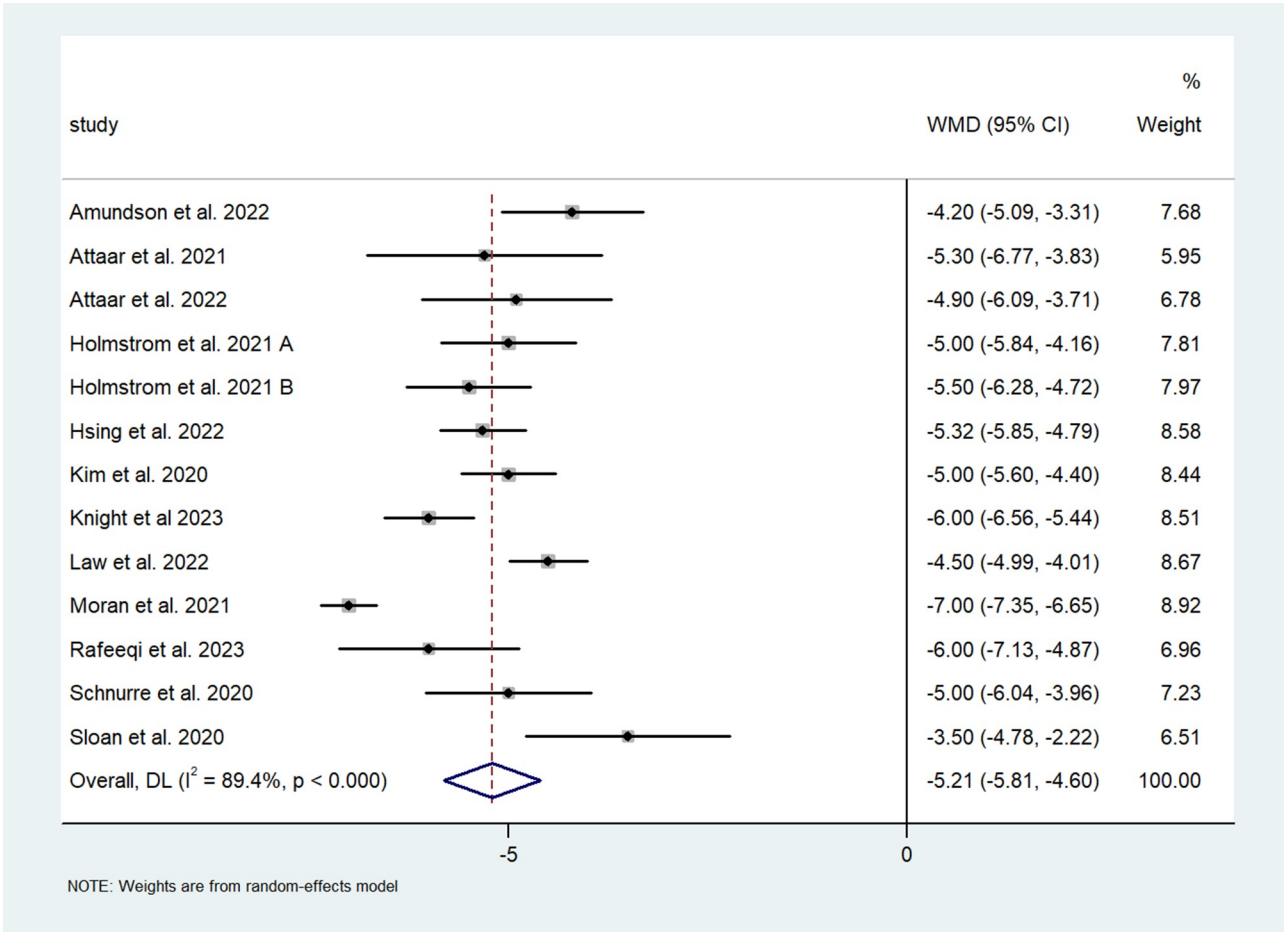


Figure 3. Forest plot showing the WMD in Eckardt score before and after EndoFLIP-guided myotomy. The analysis presents the overall change across studies, with 95% CI provided for each.

demonstrated that intraoperative EndoFLIP values had low predictive value for reflux with area under the curve ranging from 0.40 to 0.62.

Discussion

The EndoFLIP has been shown to be a potentially effective diagnostic device in achalasia and dysmotility. Some studies demonstrated that EndoFLIP can be complementary to manometry or utilized as an alternative to identify dysmotility patterns where HRM is inadequate. This is also the case for hiatal hernia detection where the EndoFLIP was able to differentiate achalasia from hiatus hernia using DI measurements^[15]. More recently, EndoFLIP has been used as an intraoperative device to guide myotomy. It can be highly beneficial for determining the myotomy length that alleviates achalasia symptoms whilst minimizing GERD symptoms. Our random-effects analysis suggested a significant drop in Eckardt score when EndoFLIP was used as an adjunct to myotomy, regardless of the surgical technique being used, translating to a significant improvement in achalasia symptoms. However, the literature differs in the role of EndoFLIP in specifically predicting GERD postoperatively. Whilst some suggest that the topography could be used for predicting erosive esophagitis, others found that this predictive

value was weak^[26,32]. Theoretically, an optimal DI is the value where the procedure is of therapeutic benefit to a patient with minimal reflux postoperatively. This is yet to be defined and it appears from early studies that this may be difficult to assess, suggesting a greater number of studies are required. The most clinically beneficial measurement that the EndoFLIP topography offers is the DI. The DI provides excellent predictive value for clinical outcome, however, there is currently no standardized optimal DI measurement and no consistent protocol for the EndoFLIP technique, with variability on the final measurements as shown in our results. The distension pressures of 30 and 40 mmHg in the EndoFLIP system are essential for assessing esophageal distensibility, providing insight into the mechanical properties of the OGJ. At 40 mmHg, the balloon applies greater force, which may reveal increased distension, highlighting areas of stiffness or reduced elasticity that are not as evident at 30 mmHg. It is likely that after myotomy, a 30 ml fill is simply not enough to obtain valid readings as the balloon would not adequately occupy the entire intraluminal space. Su, *et al*^[38] suggest that the optimal fill of the balloon may be 40 ml and this is also what is recommended by the company making the devices. The differences that this study described between the 30 and 40 mmHg balloon pressures highlight the incremental utility of higher pressures in evaluating esophageal distensibility.

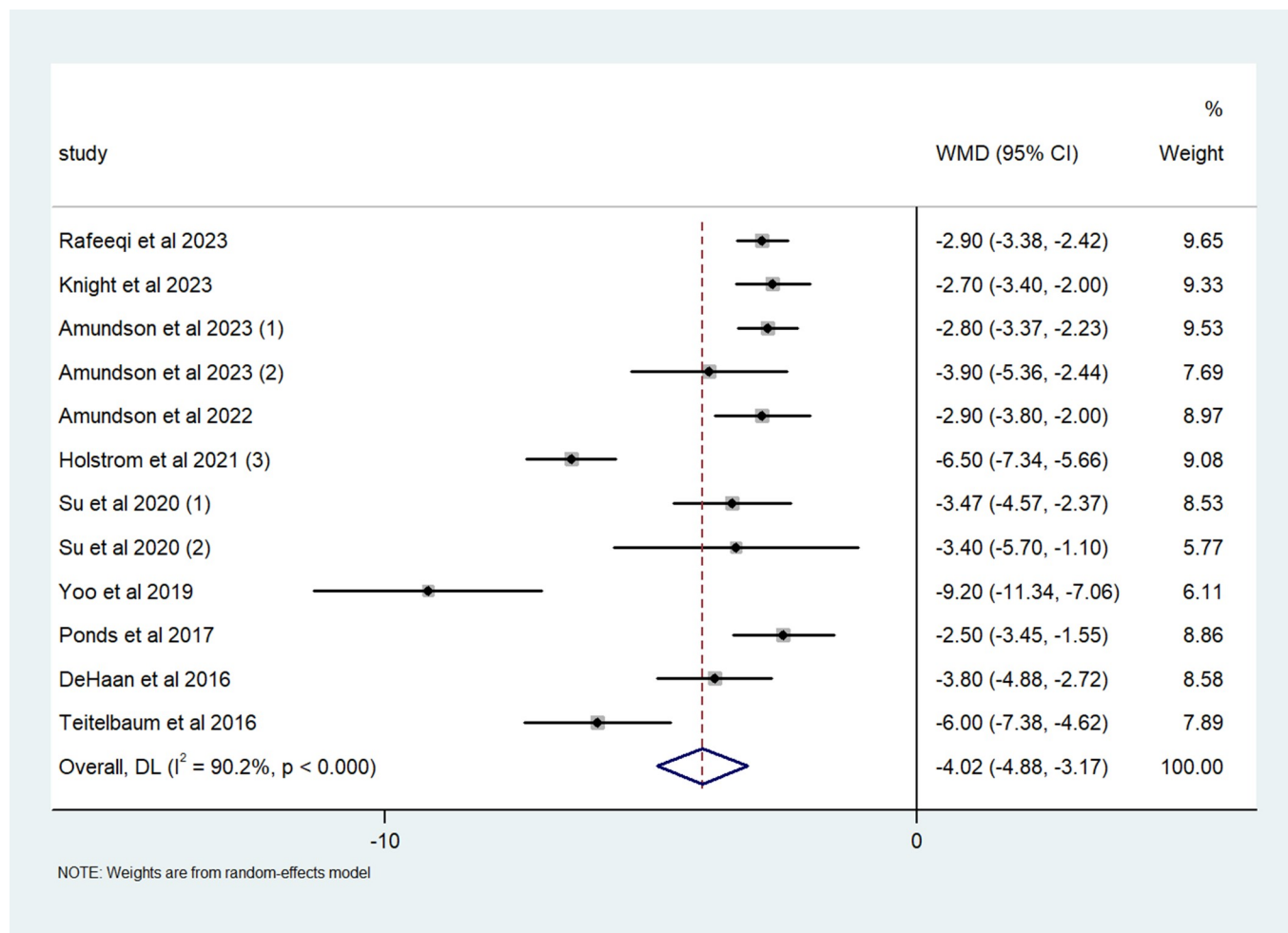


Figure 4. Distensibility index before and after myotomy for the treatment of achalasia with EndoFLIP balloon pressure set to 40 mmHg. The analysis presents the overall change across studies, with 95% CI provided for each.

While both pressures yielded significant changes in the DI post-myotomy, the greater reduction observed at 40 mmHg suggests that this higher pressure might provide more sensitive detection of changes in esophageal stiffness. This could be particularly relevant in cases of severe achalasia or other conditions where tissue stiffness is a significant factor. The smaller reduction at 30 mmHg might indicate that some structural changes are not fully captured at lower pressures, making 40 mmHg a more comprehensive choice for detailed assessments. However, it is also important to consider patient comfort and procedural safety, as higher pressures may introduce more discomfort or risk of injury. Therefore, while the 40 mmHg pressure provides more diagnostic sensitivity, the choice of balloon pressure should balance the need for diagnostic accuracy with patient tolerance and safety considerations. The presence of the endoscope during EndoFLIP measurements appears to affect the results, potentially leading to greater changes in the DI. The studies comparing DI with and without the endoscope reveal a larger reduction in DI when the endoscope is in place. This suggests that the physical presence of the endoscope might artificially increase the esophageal pressure or alter the distensibility readings. This finding raises important considerations for the

standardization of EndoFLIP procedures, as differing protocols (with or without the endoscope) may lead to variability in DI outcomes. For more accurate comparisons across studies and in clinical practice, a standardized approach, potentially favoring endoscope removal, may reduce this variability. However, further research is needed to determine the clinical relevance of these differences and to establish the most reliable protocol for DI measurement, balancing accuracy and patient comfort.

Furthermore, the use of EndoFLIP as a dilator for therapeutic purposes has been described before. This is highly feasible according to Schnurre, *et al*^[35] providing an alternative to pneumatic dilatation (PD) without the topography measurements. The EndoFLIP device enhances an already widely accepted procedure by allowing expansion of the sphincter to a DI that is known to provide a patient with symptomatic relief. This technique may also be used to minimize the rate of esophageal rupture, a significant risk with PD. It may be possible to do this by only dilating the esophagus to a point where there is adequate change in DI and no further. This technique requires a target DI which currently is not cited in literature, which highlights again the importance of having an operational protocol and therefore a defined value to guide dilatation.

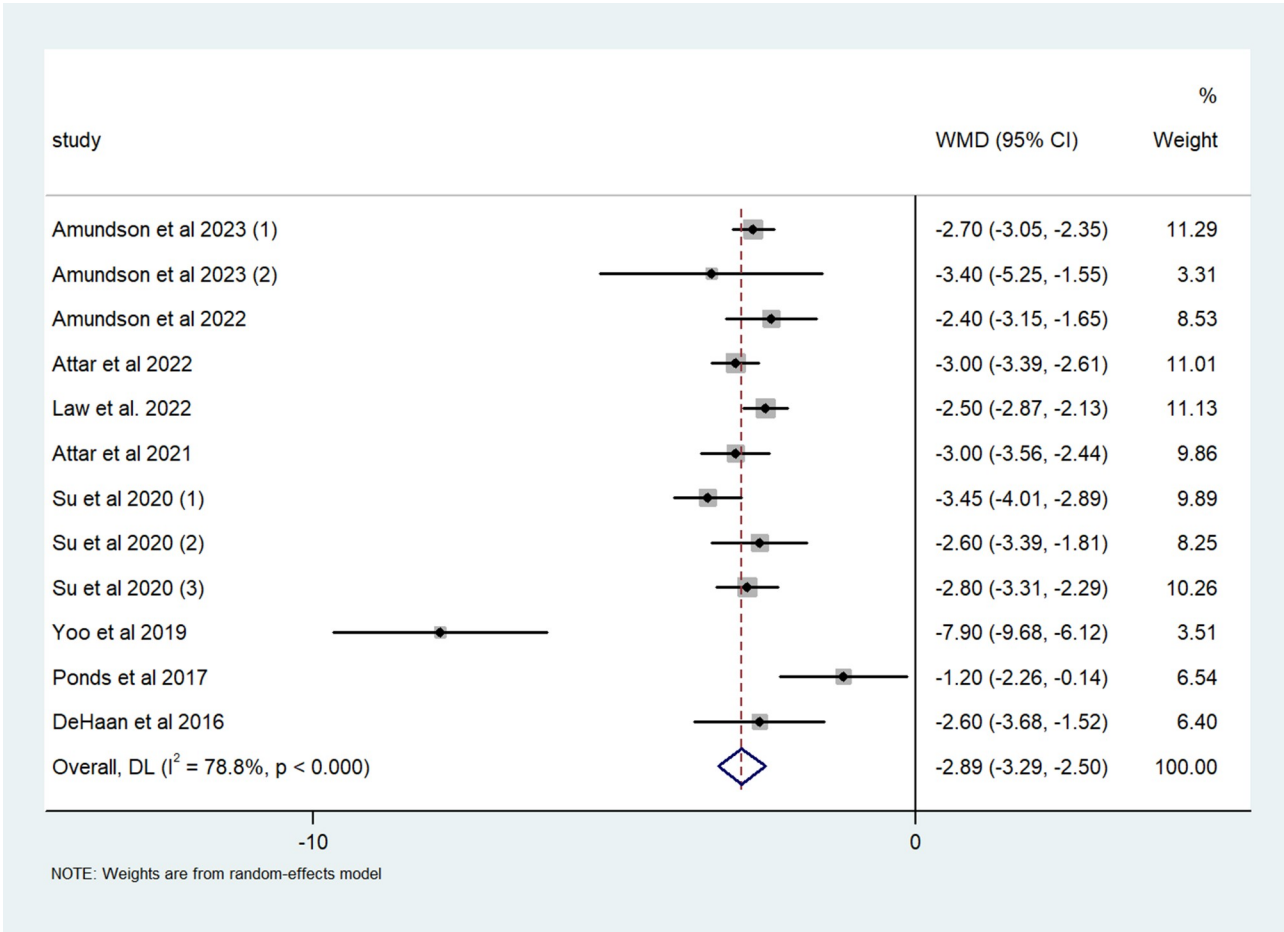


Figure 5. Distensibility index before and after myotomy for the treatment of achalasia with EndoFLIP balloon pressure set to 30 mmHg. The analysis presents the overall change across studies, with 95% CI provided for each.

EndoFLIP has also been shown to evaluate esophageal dysmotility in the literature. Diagnostically, by comparing HRM and EndoFLIP in patients with non-obstructive dysphagia, Carlson, *et al*^[45] showed that all the patients with achalasia that were picked up with HRM were also detected with EndoFLIP. In addition, EndoFLIP was found to detect abnormal esophageal motility that was undetected with manometry. The same group carried out a prospective multicenter study to assess real-time EndoFLIP at the endoscopic encounter in patients planned for future HRM^[44]. Consistent with their previous findings, all patients with a HRM diagnosis of achalasia had an abnormal real-time EndoFLIP at endoscopy. When compared to healthy controls, the frequency of RAC in response to esophageal distention in patients with achalasia was found to be significantly higher^[40]. Also, when comparing patients with known achalasia who have a normal and an abnormal integrated relaxation pressure (IRP), EndoFLIP shows a higher DI and CSA in those with a normal IRP^[36].

In addition, some centers have used EndoFLIP to guide their endoscopic dilatation. Schnurre, *et al*^[35] found that an EndoFLIP could be used for dilatation to successfully reduce the Eckardt score in the short-term for those with achalasia. Sloan, *et al*^[34] looked at dilatation with EndoFLIP device as treatment for those with achalasia and those with esophagoesophageal

junction outflow obstruction (EGJOO). They discovered that with balloon dilatation the Eckardt score of those with achalasia was significantly decreased whereas in patients with EGJOO, there was no significant change. The authors concluded that hydrostatic balloon dilatation was a safe and efficacious method of treatment for achalasia.

Limitations

This systematic review and meta-analysis was subject to important limitations which should be addressed. The majority of studies were retrospective or prospective in nature, with no RCTs identified. Not all studies assessed every aspect reviewed by this meta-analysis and between-study heterogeneity was present, for example, when analyzing change in DI following myotomy. It should also be noted that the use of EndoFLIP is a relatively new procedure, which some surgeons may be technically invested in which may ultimately lead to publication bias and publication of optimal outcomes.

Conclusions

Diagnostic uncertainties and therapeutic interventions for achalasia were often previously associated with failed symptom

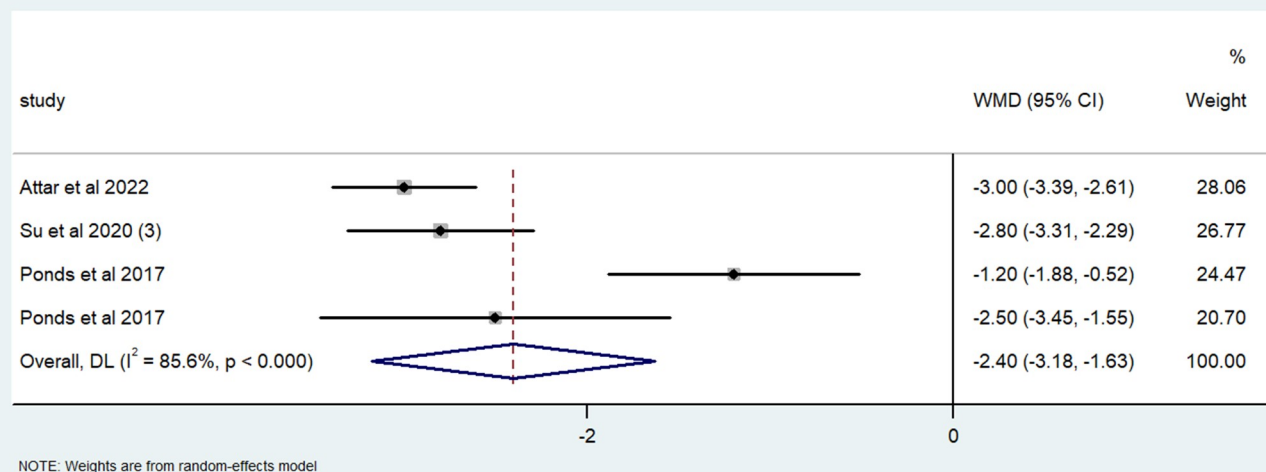


Figure 6. Distensibility index before and after myotomy for the treatment of achalasia using EndoFLIP without concurrent endoscope placement.

resolution and exacerbated GERD. The current treatment options for achalasia include LHC, POEM, and PD, and each has their advantages and disadvantages, with not one method being clearly superior. The use of EndoFLIP appears to enhance these techniques, potentially offering patients a more tailored therapy with a reduction in adverse effects. As a relatively novel device, a defined EndoFLIP protocol needs to be standardized in order for valid and comparable measurements to be obtained in future studies to help with outlining the guidelines for clinical practice.

Ethical approval

No ethical approval required.

Consent

No participants and therefore no written consent required.

Sources of funding

No funding relevant for this research.

Author contributions

M.F. was the primary writer and editor of manuscript, involved in data collection and curation, study design and project administration. I.M. and E.R.M. participated in study data collection and analysis as well as writing of the manuscript. M.G. F. participated in study data collection and analysis as well as proof reading of the manuscript. J.B.P.P.M.H.N.F.-Gomez participated equally in draft writing and editing as well as study design and critical appraiser of the manuscript. S.K. is a senior author leading study design and administration, writing, and supervision.

Conflicts of interest disclosure

The authors declare no conflict of interest.

Guarantor

Sacheen Kumar and Matyas Fehervari are guarantors of this work.

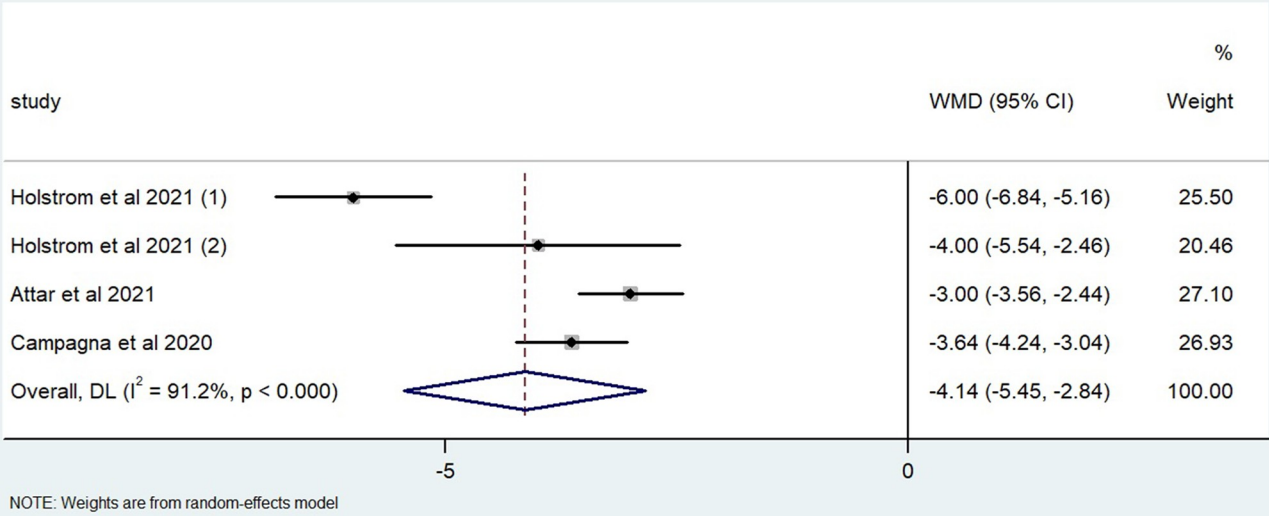


Figure 7. Distensibility index before and after myotomy for the treatment of achalasia using EndoFLIP with concurrent endoscope placement.

Research registration unique identifying number (UIN)

PROSPERO 2024 (CRD42024589079).

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

Research data regarding studies included and analysis are available on request.

References

[1] Walther B. Treatment of achalasia—from whale bone to poem. The biggest success so far within transluminal surgery. *Lakart* 2014;111:2022–23.

[2] Markar S, Zaninotto G. Management of oesophageal achalasia in POEM (and GOOGLE) times. *Br J Surg* 2022;109:150–51.

[3] Lee K, Hong SP, Yoo IK, *et al.* Global trends in incidence and prevalence of achalasia, 1925–2021: a systematic review and meta-analysis. *United Eur Gastroenterol J* 2024;12:504–15.

[4] Yadlapati R, Kahrilas PJ, Fox MR, *et al.* Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterol Motil* 2021;33:e14058.

[5] Inoue H, Tianle KM, Ikeda H, *et al.* Peroral endoscopic myotomy for esophageal achalasia: technique, indication, and outcomes. *Thorac Surg Clin* 2011;21:519–25.

[6] Haskins IN, Lombardi ME, Overby DW, Farrell TM. The endoscopic management of achalasia: less may lead to more. *Am Surg* 2021;87:1953–55.

[7] Schlottmann F, Luckett DJ, Fine J, Shaheen NJ, Patti MG. Laparoscopic Heller myotomy versus peroral endoscopic myotomy (POEM) for achalasia. *Ann Surg* 2018;267:451–60.

[8] Moonen A, Annese V, Belmans A, *et al.* Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. *Gut* 2016;65:732–39.

[9] McKay SC, Dunst CM, Sharata AM, *et al.* POEM: clinical outcomes beyond 5 years. *Surg Endosc* 2021;35:5709–16.

[10] Inoue H, Ueno A, Shimamura Y, *et al.* Peroral endoscopic myotomy and fundoplication: a novel NOTES procedure. *Endoscopy* 2019;51:161–64.

[11] Bapaye A, Dashatwar P, Dharamsi S, Pujari R, Gadhikar H. Single-session endoscopic fundoplication after peroral endoscopic myotomy (POEM+F) for prevention of post gastroesophageal reflux – 1-year follow-up study. *Endoscopy* 2021;53:1114–21.

[12] Desprez C, Roman S, Leroi AM, Gourcerol G. The use of impedance planimetry (endoscopic functional lumen imaging probe, EndoFLIP®) in the gastrointestinal tract: a systematic review. *Neurogastroenterol Motil* 2020;32:e13980.

- [13] Teitelbaum EN, Soper NJ, Pandolfino JE, *et al.* Esophagogastric junction distensibility measurements during Heller myotomy and POEM for achalasia predict postoperative symptomatic outcomes. *Surg Endosc* 2015;29:522–28.
- [14] Pandolfino JE, de Ruigh A, Nicodème F, Xiao Y, Boris L, Kahrilas PJ. Distensibility of the esophagogastric junction assessed with the functional lumen imaging probe (FLIP™) in achalasia patients. *Neurogastroenterol Motil* 2013;25:496–501.
- [15] Law YY, Nguyen DT, Meisenbach LM, *et al.* Intraoperative diagnosis and treatment of achalasia using EndoFLIP during Heller myotomy and Dor fundoplication. *Surg Endosc* 2022;36:2365–72.
- [16] Holmstrom AL, Campagna RAJ, Cirera A, *et al.* Intraoperative use of FLIP is associated with clinical success following POEM for achalasia. *Surg Endosc* 2021;35:3090–96.
- [17] Knowles TB, Jackson AS, Chang SC, *et al.* Changes in distensibility index during an incremental POEM myotomy. *J Gastrointest Surg* 2022;26:1140–46.
- [18] Teitelbaum EN, Sternbach JM, El Khoury R, *et al.* The effect of incremental distal gastric myotomy lengths on EGJ distensibility during POEM for achalasia. *Surg Endosc* 2016;30:745–50.
- [19] Knight W, Kandiah K, Vrakopoulou Z, *et al.* Early outcomes following EndoFLIP-tailored peroral endoscopic myotomy (POEM): the establishment of POEM services in two UK centers. *Dis Esophagus* 2023;36:doac110.
- [20] Pandolfino JE, Gawron AJ. Achalasia. *JAMA* 2015;313:1841.
- [21] Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg* 2021;88:105906.
- [22] Shea BJ, Grimshaw JM, Wells GA, *et al.* Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol* 2007;7:10.
- [23] Wells GA, Shea B, O'Connell D, *et al.* The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses. Oxford; 2000.
- [24] Oxford centre for evidence-based medicine - levels of evidence (March 2009). Available online: <http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/>.
- [25] Yeung KTD, Penney N, Ashrafian L, Darzi A, Ashrafian H. Does sleeve gastrectomy expose the distal esophagus to severe reflux?: a systematic review and meta-analysis. *Ann Surg* 2020;271:257–65.
- [26] Amundson JR, Wu H, VanDruff V, *et al.* Esophagogastric junction compliance on impedance planimetry (EndoFLIP™) following peroral endoscopic myotomy (POEM) predicts improvement in postoperative Eckardt score. *Surg Endosc* 2023;37:1493–500.
- [27] Attaar M, Wong HJ, Wu H, *et al.* Changes in impedance planimetry (EndoFLIP) measurements at follow-up after peroral endoscopic myotomy (POEM). *Surg Endosc* 2022;36:9410–15.
- [28] Ichkhanian Y, Brewer Gutierrez O, Roman S, *et al.* Role of functional luminal imaging probe in the management of postmyotomy clinical failure. *Gastrointest Endosc* 2022;96:9–17.e3.
- [29] Hsing LC, Choi K, Jung KW, *et al.* The predictive value of intraoperative esophageal functional luminal imaging probe panometry in patients with achalasia undergoing peroral endoscopic myotomy: a single-center experience. *J Neurogastroenterol Motil* 2022;28:474–82.
- [30] DeWitt JM, Siwec R, Kessler WR, *et al.* Comparison of functional lumen imaging probe and high-resolution manometry to assess response after peroral endoscopic myotomy. *Gastrointest Endosc* 2022;95:855–63.
- [31] Holmstrom AL, Campagna RJ, Carlson DA, *et al.* Comparison of pre-operative, intraoperative, and follow-up functional luminal imaging probe measurements in patients undergoing myotomy for achalasia. *Gastrointest Endosc* 2021;94:509–14.
- [32] Moran RA, Brewer Gutierrez OI, Rahden B, *et al.* Impedance planimetry values for predicting clinical response following peroral endoscopic myotomy. *Endoscopy* 2021;53:570–77.
- [33] Attaar M, Su B, Wong HJ, *et al.* Intraoperative impedance planimetry (EndoFLIP™) results and development of esophagitis in patients undergoing peroral endoscopic myotomy (POEM). *Surg Endosc* 2021;35:4555–62.
- [34] Sloan JA, Triggs JR, Pandolfino JE, *et al.* Treatment experience with a novel 30-mm hydrostatic balloon in esophageal dysmotility: a multicenter retrospective analysis. *Gastrointest Endosc* 2020;92:1251–57.
- [35] Schnurre L, Murray FR, Schindler V, *et al.* Short-term outcome after singular hydraulic EsoFLIP dilation in patients with achalasia: a feasibility study. *Neurogastroenterol Motil* 2020;32:e13864.
- [36] Kim E, Yoo IK, Yon DK, Cho JY, Hong SP. Characteristics of a subset of achalasia with normal integrated relaxation pressure. *J Neurogastroenterol Motil* 2020;26:274–80.
- [37] Su B, Callahan ZM, Kuchta K, *et al.* Use of impedance planimetry (Endoflip) in foregut surgery practice: experience of more than 400 cases. *J Am Coll Surg* 2020;231:160–71.
- [38] Su B, Callahan ZM, Novak S, Kuchta K, Ujiki MB. Using impedance planimetry (EndoFLIP) to evaluate myotomy and predict outcomes after surgery for achalasia. *J Gastrointest Surg* 2020;24:964–71.
- [39] Bianca A, Schindler V, Schnurre L, *et al.* Endoscope presence during endoluminal functional lumen imaging probe (FLIP) influences FLIP metrics in the evaluation of esophageal dysmotility. *Neurogastroenterol Motil* 2020;32:e13823.
- [40] Carlson DA, Lin Z, Kahrilas PJ, *et al.* The functional lumen imaging probe detects esophageal contractility not observed with manometry in patients with achalasia. *Gastroenterology* 2015;149:1742–51.
- [41] Campagna RAJ, Carlson DA, Hungness ES, *et al.* Intraoperative assessment of esophageal motility using FLIP during myotomy for achalasia. *Surg Endosc* 2020;34:2593–600.
- [42] Jain AS, Carlson DA, Triggs J, *et al.* Esophagogastric junction distensibility on functional lumen imaging probe topography predicts treatment response in achalasia-anatomy matters! *Am J Gastroenterol* 2019;114:1455–63.
- [43] Yoo IK, Choi SA, Kim WH, Hong SP, Cakir OO, Cho JY. Assessment of clinical outcomes after peroral endoscopic myotomy via esophageal distensibility measurements with the endoluminal functional lumen imaging probe. *Gut Liver* 2019;13:32–39.
- [44] Carlson DA, Gyawali CP, Kahrilas PJ, *et al.* Esophageal motility classification can be established at the time of endoscopy: a study evaluating real-time functional luminal imaging probe panometry. *Gastrointest Endosc* 2019;90:915–923.e1.
- [45] Carlson DA, Kahrilas PJ, Lin Z, *et al.* Evaluation of esophageal motility utilizing the functional lumen imaging probe. *Am J Gastroenterol* 2016;111:1726–35.
- [46] Ahuja NK, Agnihotri A, Lynch KL, *et al.* Esophageal distensibility measurement: impact on clinical management and procedure length. *Dis Esophagus* 2017;30:1–8.
- [47] Ponds FA, Bredenoord AJ, Kessing BF, Smout AJ. Esophagogastric junction distensibility identifies achalasia subgroup with manometrically normal esophagogastric junction relaxation. *Neurogastroenterol Motil* 2017;29:e12908.
- [48] DeHaan RK, Frelich MJ, Gould JC. Intraoperative assessment of esophagogastric junction distensibility during laparoscopic Heller myotomy. *Surg Laparosc Endosc Percutan Tech* 2016;26:137–40.
- [49] Rafeeqi T, Salimi-Jazi F, Cunningham A, Wall J. The utility of endoscopic functional luminal imaging (EndoFLIP) in the diagnosis and management of children with achalasia. *J Pediatr Surg* 2023;58:639–42.
- [50] Howk AA, Clifton MS, Garza JM, Durham MM. Impedance planimetry (EndoFLIP) assisted laparoscopic esophagomyotomy in pediatric population. *J Pediatr Surg* 2022;57:1000–04.
- [51] Amundson JR, Kuchta K, VanDruff VN, *et al.* Experience with impedance planimetry for surgical foregut disease in 1,097 cases. *J Am Coll Surg* 2023;237:35–48.