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Comparative Efficacy of Surgical and Endoscopic Interventions for Primary Achalasia: A Systematic Review and Bayesian Network Meta-Analysis

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Abstract

Background

Multiple treatments exist for primary achalasia, yet their comparative efficacy remains uncertain. We conducted a systematic review and network meta-analysis (NMA) to compare all available interventions.

Methods

Randomized controlled trials comparing any intervention for primary achalasia were included. A Bayesian random-effects NMA was performed as the primary analysis, with a frequentist NMA as sensitivity analysis. Outcomes were treatment failure and mean change in Lower Esophageal Sphincter (LES) pressure. Treatments were ranked using SUCRA. Consistency was assessed via node-splitting and the unrelated mean effects model.

Results

Thirty-two RCTs encompassing 10 treatments were included. Convergence was satisfactory and between-study heterogeneity was low (I^2=0%). All active treatments significantly outperformed Placebo on both outcomes, with findings consistent across Bayesian and frequentist analyses. For treatment failure, Heller's Myotomy with Nissen Fundoplication (87.7%) and Heller's Myotomy alone (SUCRA 79.6%) ranked highest, while Botulinum Toxin ranked lowest among active treatments (SUCRA 11.1%). For LES pressure reduction, Pneumatic Dilation (PD) + Botulinum Toxin achieved the greatest reduction (MD − 28 mmHg, 95% CrI − 40 to − 15; SUCRA 93.5%), followed by Anterior POEM (SUCRA 77.1%) and Heller's Myotomy (62.5%). PD (23.3%) ranked lowest in LES pressure reduction. PD ranked lowest among active treatments for LES pressure reduction.

Conclusion

Heller's Myotomy with Nissen Fundoplication and a combination of PD with Botox ranked highest in terms of treatment success and LES pressure reduction, respectively. Anterior POEM ranked high for both treatment failure and LES pressure reduction, these findings extend prior pairwise evidence by quantifying relative efficacy across all modalities simultaneously.

Introduction

Primary achalasia is a rare progressive esophageal motility disorder characterized by failure of lower esophageal sphincter (LES) relaxation and absent peristalsis, resulting in functional obstruction at the gastroesophageal junction [1]. Its global incidence is estimated at 0.78 per 100,000 person-years, with prevalence of 10.82 per 100,000 persons, affecting men and women equally with peak onset between 30 and 60 years [1, 2].

Since no treatment restores physiological peristalsis, available therapies aim to relieve esophageal outflow obstruction by lowering or disrupting LES tone. Current modalities span pharmacological, endoscopic, and surgical approaches. Botulinum toxin injection offers short-term efficacy but limited durability, making it most suitable as bridge therapy or for high-risk patients. Pneumatic dilation provides durable outcomes through forceful disruption of LES muscle fibers [5]. Laparoscopic Heller myotomy (LHM) with partial fundoplication has long been considered the gold standard surgical approach [6]. Peroral endoscopic myotomy (POEM), first described in 2009, has gained increasing global acceptance as a minimally invasive alternative with comparable efficacy to LHM.

Despite this breadth of options, optimal treatment strategy remains debated [7] [8, 9]. Network meta-analysis (NMA) overcomes the limitations of pairwise comparisons by integrating direct and indirect evidence to enable simultaneous ranking of all interventions [10]. This study therefore conducts a comprehensive systematic review and Bayesian NMA of all relevant randomized controlled trials, with primary objectives of comparing treatment failure rates, mean change in LES pressure, and generating treatment rankings using the SUCRA framework.

Methodology

Study Design

This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Network Meta-Analysis (PRISMA-NMA) guidelines [11]. The protocol was prospectively registered on PROSPERO (registration number: CRD420261368082). The analysis focused on synthesizing evidence from randomized controlled trials (RCTs) comparing the efficacy of different surgical, endoscopic, laparoscopic, and pharmacological modalities for patients with primary achalasia, with predefined outcomes of mean lower esophageal sphincter (LES) pressure change and treatment failure. Bayesian approach was employed given the small evidence size, backed by frequentist sensitivity analysis [12].

Search Strategy and Database

A comprehensive literature search was performed from database inception till March 4th, 2026, across multiple electronic databases, including PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus and Clinicaltrials.gov. The search strategy incorporated Medical Subject Headings (MeSH) terms and free-text keywords such as “Achalasia”, “Peroral endoscopic myotomy”, “Heller’s myotomy”, “Botulinum

toxin", "Randomized controlled trial", and "placebo-controlled". Boolean operators (AND, OR) were used to combine terms, with no language restrictions applied. Grey literature was searched via conference proceedings and major gastroenterology societies (e.g., American College of Gastroenterology). Reference lists of included studies and relevant reviews were hand-searched for additional trials. The complete search strategy has been provided in the supplementary table 1.

Eligibility Criteria

We included comparative randomized clinical trials that evaluated any endoscopic, surgical or medical intervention for adult patients with achalasia. We excluded studies without the outcomes of interest (mean change in LES pressure, treatment failure), single arm trials, observational studies, studies with achalasia due to secondary cause such as esophageal cancer.

Data Screening and Extraction

Two independent reviewers screened individual titles and abstracts of the identified studies and excluded studies that did not address the research question of interest. The full texts of the remaining studies were assessed to determine whether they met the inclusion and exclusion criteria. Any disagreements were resolved through consensus with a third reviewer. Relevant data from the selected articles were then extracted and organized into a standardized Excel spreadsheet. All relevant data was extracted independently by two, capturing study characteristics (author, year, design, sample size), participant demographics (age, sex, disease etiology), and outcome data (event counts, totals). Discrepancies were reconciled by consensus. Corresponding authors were not contacted for missing data.

Quality and Certainty Assessment

The risk of bias for each included RCT was evaluated independently by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool [13]. All discrepancies were reconciled by consensus.

The certainty of evidence for each NMA estimate was assessed using the CINeMA (Confidence In Network Meta-Analysis) framework [14]. CINeMA evaluates confidence in pairwise comparisons derived from the NMA across six domains: (1) within-study bias; (2) reporting bias; (3) indirectness; (4) imprecision; (5) heterogeneity; and (6) incoherence. Each domain was rated as no concern, some concern, or major concern, and the overall confidence in each NMA estimate was graded as High, Moderate, Low, or Very Low, following the principles of the GRADE framework adapted for network meta-analysis [14]. All comparisons were assessed relative to Placebo as the reference treatment.

Outcomes:

The primary outcome was treatment failure (clinical non-response or re-intervention), while mean change in LES pressure (mmHg) from baseline till follow-up served as the secondary outcome.

Statistical Analysis

A Bayesian random-effects NMA [15, 16] was performed as the primary analysis using the gemtc package in R (version 4.5.0) [17], with a frequentist NMA (netmeta) as sensitivity analysis. A binomial likelihood with logit link was specified for treatment failure, yielding posterior odds ratios (OR) with 95% credible intervals (CrI); a normal likelihood with identity link was used for mean LES pressure change, yielding mean differences (MD) with 95% CrI. Where studies did not report change scores, mean change was derived by subtracting baseline from follow-up means, and SD of change was imputed using a correlation coefficient of 0.5 per Cochrane Handbook guidance [18].

Markov Chain Monte Carlo (MCMC) sampling [19] was conducted across four parallel chains (10,000 adaptation; 100,000 sampling iterations; thinning factor 10), yielding 10,000 effective posterior samples per chain. Convergence was confirmed visually via trace and density plots and formally via the Gelman-Rubin statistic (threshold < 1.05) [20].

Between-study heterogeneity was quantified by τ (Bayesian, 95% CrI) and I^2 (frequentist) [21].

Consistency was assessed using the unrelated mean effects (UME) model with DIC comparison and node-splitting analysis [22].

Treatments were ranked using SUCRA, with lower failure rates and greater LES pressure reduction considered favorable [10]. Further detail can be found in supplementary materials.

Results

Study Selection

The search strategy yielded a total of 1002 records. After removal of 452 duplicates and exclusion of 516 studies from title/abstract screening, 34 full-text studies were reviewed. Out of the 34 studies, 32 [23–53] were included in the review, of which 26 contributed to the statistical analysis (Fig. 1). Six

studies were excluded from the quantitative synthesis for LES pressure because they did not provide sufficient data to calculate variance (e.g., missing ranges, standard deviations, or confidence intervals) or did not report results as a mean change from baseline.

Study Characteristics

Of the 26 studies (1,842) in the network meta-analysis, 22 trials reported treatment failure and 16 trials reported mean change in LES pressure, with 12 trials contributing to both outcomes. Follow-up duration ranged from short-term (≤ 3 months) to long-term (≥ 5 years) across studies, though follow-up definitions varied considerably between trials. Mean participant age ranged from approximately 34 to 54 years across study arms, with broadly comparable baseline demographics between intervention and control groups. The proportion of male participants varied widely (25%–80%). Baseline LES pressure ranged from approximately 22 to 53 mmHg. Symptom duration and baseline Eckardt scores were incompletely reported. BMI data were available in only one study. The baseline characteristics of all included studies are summarized in Table 1.

Table 1

Baseline Characteristics of Included Studies (* Boeckxstaens 2011, Borges 2013, Khashab 2020, Kim 1993, Nabi 2021, and Torquati 2005 were included in the systematic review but not in the network meta-analysis due to missing outcome data for the predefined endpoints. Int. = Intervention arm; Ctrl. = Control arm; PD = Pneumatic Dilation; HM = Heller's Myotomy; BotTox = Botulinum Toxin; Ant-POEM = Anterior POEM; Post-POEM = Posterior POEM; LES = Lower Esophageal Sphincter; NR = Not Reported. Values are Mean ± SD unless stated otherwise.)

Study	Comparison	N (Int/Ctrl)	Age (Mean ± SD)		Male (%)		Baseline LES Pressure (mmHg, Mean ± SD)		Symptom Duration (months, Mean ± SD)		Baseline Eckardt Score (Mean ± SD)		BMI (kg/m², Mean ± SD)	
			Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.
Annese 1996	BotTox vs Placebo	8 / 8	34.1 ± 9.1	35.5 ± 21.8	55.3%	43.8%	31.3 ± 9.7	33 ± 8.6	50	33.3	12.94 ± 3.2	12.19 ± 2.9	NR	NR
Bakhshipour 2010	PD+BotTox vs PD	16 / 18	49.8 ± 3.7	51.8 ± 3.4	43.8%	66.7%	37.9 ± 3	30.1 ± 2.7	23.5	33.6	5.8 ± 0.5	6 ± 0.5	NR	NR
Bansal 2003	PD vs BotTox	95 / 106	46.4 ± 4.8	45.4 ± 4.1	63.2%	53.8%	24.6 ± 3.9	25 ± 5.19	33 ± 5.3	31 ± 3.8	7 ± 0.5	7.4 ± 0.6	NR	NR
Boeckxstaens 2011	PD vs HM + Dor	48 / 44	54.6 ± 14	50.2 ± 12.8	52.8%	45.8%	26.1 ± 5.7	26.1 ± 5.3	53	36.4	NR	NR	NR	NR
Borges 2013	PD vs HM	25 / 25	NR	NR	25%	25%	34.2 ± 15.7	34.8 ± 13.4	NR	NR	NR	NR	NR	NR
Chrystoja 2016	PD vs HM	20 / 20	44.9 ± 14.6	44.2 ± 13.2	47.7%	41.3%	NR	NR	NR	NR	NR	NR	NR	NR
Conte 2020	Post-POEM vs HM	12 / 14	34.6 ± 11.3	29.4 ± 9.8	70%	50%	NR	NR	NR	NR	8 ± 1.7	8.5 ± 1.9	NR	NR
Falkenback 2003	HM vs HM+Nissen	10 / 10	49 ± 43.9	51.5 ± 30.1	25%	25%	NR	NR	32	30.8	NR	NR	NR	NR
Hamdy 2015	HM vs PD	25 / 25	39.8 ± NR	37.4 ± NR	44%	44%	52.3 ± 21	51.2 ± 16	73	77	NR	NR	NR	NR
Ichkhanian 2020	Ant-POEM vs Post-POEM	46 / 60	NR	NR	53.3%	50.3%	24.5 ± 4.5	23.5 ± 3.5	NR	NR	8 ± 7	7 ± 8	NR	NR
Khashab 2020	Ant-POEM vs Post-POEM	71 / 77	50.5 ± 25.5	49.6 ± 19.6	52%	56%	24 ± 4.5	23.3 ± 3.7	NR	NR	NR	NR	NR	NR
Kim 1993	BotTox vs PD	13 / 55	NR	NR	64%	NR%	43 ± 22	52.18	NR	NR	NR	NR	NR	NR
Kostic 2007	PD vs HM	26 / 25	49 ± 50.4	46.9 ± 44.4	NR%	NR%	22.9 ± 4.2	23.8 ± 3.3	19	22	NR	NR	NR	NR
Kumagai 2014	HM + Dor vs HM+Toupet	11 / 14	NR	NR	27%	27%	33.2 ± 16.4	37.6 ± 18	NR	NR	NR	NR	NR	NR
Mikaeli 2006	PD vs PD+BotTox	27 / 27	NR	NR	46.2%	61.5%	47.4 ± 18	56 ± 18.8	NR	NR	NR	NR	NR	NR
Moonen 2015	PD vs HM + Dor	105 / 96	45.7 ± 14.3	46.4 ± 15.8	53%	64%	24.6 ± 4.9	23.9 ± 3.6	30.5 ± 13	33.4 ± 16.6	8.4 ± 2.1	17 ± 1.75	NR	NR
Muehldorfer 1999	PD vs BotTox	12 / 12	43.3 ± 40.3	47.2 ± 41.1	58%	58%	37.7 ± 37	39.7 ± 40.2	NR	NR	NR	NR	NR	NR
Nabi 2021	Ant-POEM vs Post-POEM	55 / 34	40.1 ± 16.8	41.3 ± 14.5	37%	37%	52.9 ± NR	46.9 ± NR	36	NR	6.02 ± 1.33	6.75 ± 1.32	NR	NR
Novais 2010	PD vs HM + Dor	47 / 47	52.3 ± 13.6	46.5 ± 14.3	53%	38%	28.3 ± 13.7	30.3 ± 12.2	NR	NR	NR	NR	NR	NR

Study	Comparison	N (Int/Ctrl)	Age (Mean ± SD)		Male (%)		Baseline LES Pressure (mmHg, Mean ± SD)		Symptom Duration (months, Mean ± SD)		Baseline Eckardt Score (Mean ± SD)		BMI (kg/m², Mean ± SD)	
			Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Ctrl.
Pasricha 1995	BotTox vs Placebo	11 / 10	47 ± 16.6	54 ± 16.8	NR%	NR%	NR	NR	NR	NR	NR	NR	NR	NR
Perrson 2014	PD vs HM+Toupet	15 / 45	NR	NR	40%	45%	NR	NR	NR	NR	7.1 ± 1.2	5.9 ± 1.6	NR	NR
Ponds 2019	Ant-POEM vs PD	63 / 63	NR	NR	48%	57.6%	NR	NR	28	25	NR	NR	NR	NR
Ramchandani 2018	Ant-POEM vs Post-POEM	30 / 30	38 ± 13.4	43.9 ± 15.7	50%	60%	38.7 ± 16.2	34.2 ± 17.5	52.2	35.6	7.3 ± 1.3	7.03 ± 1.13	NR	NR
Rawlings 2012	HM + Dor vs HM+Toupet	36 / 24	46.8 ± 12.4	51.7 ± 13.7	52.8%	62.5%	35.4 ± 15.2	45.1 ± 27.9	21	22	NR	NR	NR	NR
Richards 2004	HM vs HM + Dor	21 / 22	50 ± 13	50 ± 12.75	52.4%	45.5%	35 ± 28.5	33 ± 26.2	NR	NR	NR	NR	NR	NR
Saleh 2023	Post-POEM vs PD	45 / 45	53 ± 36.8	52 ± 41.4	40%	35.6%	22.7 ± 16.4	25.4 ± 20.9	NR	NR	6 ± 3.06	5.33 ± 1.53	NR	NR
Tan 2018	Ant-POEM vs Post-POEM	31 / 32	45.8 ± 12.2	42.4 ± 13.3	48.4%	43.8%	38.7 ± 7.5	36.2 ± 5.5	80.4	74.4	6.3 ± 1.3	6.2 ± 1.3	NR	NR
Torquati 2005	HM vs HM + Dor	21 / 22	40.9 ± 14.3	40.1 ± 15.5	42%	37%	25.9 ± 5.0	23.4 ± 4.6	39.7 ± 27.1	41.5 ± 22.9	24.7	24.7	8.89 ± 2.3	9.43 ± 3.7
Torres-Villalobos 2018	HM + Dor vs HM+Toupet	11 / 9	48.6 ± 14.9	48.6 ± 14.6	60.7%	55%	24.8 ± 4.6	24.5 ± 4.5	26.8 ± 11.4	26 ± 10.9	6.8 ± 2.0	6.7 ± 2.0	NR	NR
Werner 2019	Ant-POEM vs HM + Dor	112 / 109	45.6 ± 40.7	49 ± 41.5	45%	45%	29.6 ± 30.7	38 ± 39.9	24	18	NR	NR	NR	NR
Zaninotto 2004	BotTox vs HM + Dor	40 / 40	36.7 ± 10.4	38.2 ± 9.9	44.8%	42.9%	30.4 ± 12.8	32.2 ± 11.7	29	28	NR	NR	NR	NR
Zhu 2010	BotTox vs PD vs PD+BotTox	29 / 28	NR	NR	NR%	NR%	NR	NR	NR	NR	NR	NR	NR	NR

Ten treatment modalities were evaluated across the network:

Placebo (2 studies), Botulinum Toxin injection (6 studies), Pneumatic Dilation (11 studies), Pneumatic Dilation + Botulinum Toxin (3 studies), Anterior POEM (4 studies), Posterior POEM (4 studies), Heller's Myotomy (6 studies), Heller's Myotomy + Dor Fundoplication (6 studies), Heller's Myotomy + Toupet Fundoplication (4 studies), Heller's Myotomy + Nissen Fundoplication (1 study)

Risk of Bias

Overall, the majority of included trials were judged to have some concerns regarding risk of bias. The most commonly flagged domain was blinding of participants and personnel, which was inherently difficult to achieve given the procedural nature of the interventions under comparison (e.g., surgical vs. endoscopic vs. pharmacological). Several studies also raised concerns around allocation concealment and selective outcome reporting. Five trials were rated as high risk of bias, primarily due to absence of blinding in outcome assessment or incomplete reporting of randomization procedures. Six trials demonstrated low risk of bias across all domains. A detailed summary of the RoB 2 assessments for each included study is presented (Supplementary Figs. 1 & 2). Given the procedural nature of the interventions, open-label designs were considered an inherent limitation across the body of evidence rather than a study-specific flaw.

Network Geometry

The network plot for treatment failure comprised 10 nodes and 15 direct pairwise comparisons. The most replicated direct comparisons were Heller's Myotomy + Nissen Fundoplication vs Heller's Myotomy and Pneumatic Dilation vs Botulinum Toxin, each supported by 3 direct trials. Pneumatic Dilation was the most connected node, serving as the primary evidence hub. Two studies compared anterior versus posterior POEM directly. Placebo

and Heller's Myotomy + Toupet Fundoplication were peripheral nodes with limited direct connections, meaning their comparisons with most other treatments relied predominantly on indirect evidence (Fig. 2.1).

The network plot for mean change in LES pressure comprised 9 nodes and 15 direct pairwise comparisons. Botulinum Toxin and Pneumatic Dilation were the most connected nodes. The most replicated direct comparison was Botulinum Toxin vs Pneumatic Dilation, supported by 3 direct trials. Placebo remained a peripheral node (Fig. 2.2).

Convergence and Model Fit

All models converged satisfactorily (Rhat < 1.05; ESS > 400 for all parameters).

Inconsistency

No significant inconsistency was detected in either network. DIC comparison between the consistency and inconsistency (UME) models favored the consistency model for both outcomes, supporting the validity of the transitivity assumption. Node-splitting analysis demonstrated compatible direct and indirect estimates across all closed loops, with overlapping confidence intervals for all evaluated comparisons (Supplementary Figs. 3 & 4).

Treatment Failure

Bayesian NMA

All active treatments were significantly superior to Placebo for treatment failure, with 95% CrIs excluding 1 for all comparisons. Heller's Myotomy showed the highest probability of sustained treatment success (OR 0.00016, 95% CrI 0.0000019 to 0.0048), followed by Anterior POEM (OR 0.00031, 95% CrI 0.0000046 to 0.0073) and Heller's Myotomy + Dor Fundoplication (OR 0.00043, 95% CrI 0.0000061 to 0.0094). Botulinum Toxin showed the least favorable effect among active treatments (OR 0.013, 95% CrI 0.00027 to 0.23), followed by Pneumatic Dilation (OR 0.0022, 95% CrI 0.000036 to 0.044). Heller's Myotomy + Nissen Fundoplication produced an extreme estimate (OR 7.3×10^{-18}, 95% CrI 2.0×10^{-45} to 7.4×10^{-5}) attributable to a single study with zero events in one arm, and should be interpreted with caution (Fig. 3.1).

SUCRA Rankings

Treatment rankings for treatment failure were as follows: Heller's Myotomy + Nissen Fundoplication (SUCRA 87.7%, interpreted cautiously), Heller's Myotomy (79.6%), Anterior POEM (77.1%), Heller's Myotomy + Dor Fundoplication (63.2%), Heller's Myotomy + Toupet Fundoplication (57.8%), Posterior POEM (56.3%), Pneumatic Dilation + Botulinum Toxin (44.3%), Pneumatic Dilation (22.8%), Botulinum Toxin (11.1%), and Placebo (0%) (Fig. 3.2 & 3.3).

Frequentist Sensitivity Analysis

Results were consistent with the Bayesian primary analysis. All active treatments significantly outperformed Placebo, with the same directional treatment hierarchy observed. No material differences in treatment rankings were noted between the two analytical frameworks (Supplementary Fig. 5).

Mean Change in LES Pressure

Bayesian NMA

All active treatments produced significantly greater LES pressure reduction compared to Placebo, with 95% CrIs excluding zero for all comparisons. Pneumatic Dilation + Botulinum Toxin achieved the greatest reduction (MD − 28 mmHg, 95% CrI − 40 to − 15), followed by Anterior POEM (MD − 24 mmHg, 95% CrI − 37 to − 11) and Heller's Myotomy (MD − 23 mmHg, 95% CrI − 37 to − 9). Pneumatic Dilation showed the smallest reduction among active treatments (MD − 19 mmHg, 95% CrI − 31 to − 7) (Fig. 4.1). Most pairwise comparisons between active treatments did not reach statistical significance, reflecting the predominantly indirect nature of these estimates.

SUCRA Rankings

Treatment rankings for LES pressure reduction were as follows: Pneumatic Dilation + Botulinum Toxin (SUCRA 93.5%), Anterior POEM (77.1%), Heller's Myotomy (62.5%), Posterior POEM (57.7%), Heller's Myotomy + Toupet Fundoplication (54.4%), Botulinum Toxin (41.1%), Heller's Myotomy + Dor Fundoplication (40.1%), Pneumatic Dilation (23.3%), and Placebo (0.3%) (Fig. 4.2 & 4.3).

Frequentist Sensitivity Analysis

Frequentist estimates were consistent with Bayesian findings in both magnitude and direction. The league table confirmed that Pneumatic Dilation + Botulinum Toxin produced the greatest LES pressure reduction across all pairwise comparisons, and Placebo was significantly inferior to all active treatments. Treatment rankings were concordant between both analytical frameworks, strengthening confidence in the observed hierarchy (Supplementary Fig. 6).

Certainty Assessment

The overall confidence in NMA estimates was Low for the majority of comparisons in both outcomes, with one comparison rated as Very Low and one as Moderate. Across both outcomes, within-study bias was consistently rated as some concern, reflecting the predominantly open-label design of the

included trials. Reporting bias was similarly rated as some concern across most comparisons, given the preponderance of small trials and the possibility of selective publication within this literature. The most impactful source of downgrading was indirectness, since the majority of treatment-versus-Placebo estimates relied predominantly or entirely on indirect evidence. Imprecision was rated as some concern for most comparisons, reflecting wide credible intervals attributable to small sample sizes and sparse evidence for several treatment nodes. Notably, heterogeneity and incoherence were rated as no concern across all comparisons in both outcomes, consistent with the I^2 of 0% and the absence of statistically significant inconsistency on node-splitting analysis. The single Very Low rating in the treatment failure outcome corresponded to Heller's Myotomy + Nissen Fundoplication, which was additionally downgraded for imprecision due to the extreme odds ratio arising from a single zero-event study, and should be interpreted with particular caution. The Moderate confidence rating in the LES pressure outcome for Heller's Myotomy + Dor Fundoplication reflects the availability of partial direct evidence and relatively narrower credible intervals for this comparison. (Supplementary Tables 2 & 3)

Discussion

This systematic review and Bayesian NMA, encompassing 26 RCTs and 10 treatment modalities, provides the most comprehensive probabilistic synthesis of the evidence base for primary achalasia to date. The principal findings were consistent across Bayesian and frequentist analyses. First, all active treatments significantly outperformed placebo on both outcomes. Second, surgical and endoscopic approaches showed lower rate of treatment failure relative to botulinum toxin. Third, pneumatic dilation combined with botulinum toxin ranked the highest for LES pressure reduction by SUCRA, though this finding requires cautious interpretation given the limited supporting evidence.

The superiority of surgical and endoscopic approaches over Botulinum Toxin and Pneumatic Dilation monotherapy on the treatment failure outcome is consistent with the established mechanistic understanding of achalasia. Despite its relatively poor long-term efficacy, Botulinum toxin injection continues to play an important role in elderly patients with comorbidities and as salvage therapy. This aligns with our finding that Botulinum Toxin ranked second-to-last among active treatments for treatment failure (SUCRA 11.1%). The low ranking likely reflects its known pattern of symptom relapse: after 48 months, all patients treated by a single Botulinum Toxin injection had experienced symptomatic relapse, compared with 35% of patients treated by pneumatic dilation. Accordingly, current guidelines position Botulinum Toxin as a temporizing measure rather than definitive therapy for treatment-eligible patients [7].

Heller's Myotomy ranked highest for treatment failure (SUCRA 79.6%) and Anterior POEM second (SUCRA 77.1%), consistent with the mechanistic advantage of myotomy in permanently disrupting the hypertensive LES. POEM has improved efficacy compared to pneumatic dilation and shows comparable patient outcomes when compared to laparoscopic myotomy, supporting its role as a feasible first-line treatment. The comparable rankings of Heller's Myotomy, Anterior POEM, and Posterior POEM in the treatment failure hierarchy suggest that the route of myotomy, surgical versus endoscopic, anterior versus posterior, may be less determinative of overall failure rates than the principle of LES disruption itself, echoing findings from existing pairwise RCTs [36, 42].

Two randomized controlled trials comparing anterior and posterior POEM were identified during our systematic review, one of them could not be incorporated into the pooled network meta-analysis due to missing outcomes of interest. Ramchandani et al. [48] conducted a single-center randomized pilot study of 60 patients (30 per arm) and reported equivalent clinical efficacy at 6-month follow-up, with comparable Eckardt scores, LES pressure change, and esophageal emptying on timed barium swallow between both approaches. Notably, however, mucosotomy rates were significantly higher in the anterior group (20% vs. 3.3%, P = 0.02), and 24-hour pH monitoring at 3 months demonstrated significantly greater esophageal acid exposure in the posterior group (DeMeester score 35.3 vs. 9.56, P = 0.04), though this did not translate into clinically or endoscopically significant GERD differences between groups. Khashab et al. [51] subsequently conducted the largest multicenter randomized noninferiority trial to date, enrolling 150 patients across six international tertiary centers with 1-year follow-up. Clinical success was equivalent between anterior (90%) and posterior (89%) approaches, with no significant differences in adverse events, GERD rates by 24-hour pH monitoring, or quality of life measures. Closure was rated as technically easier with the posterior approach, which also required fewer clips. Together, these trials converge on a consistent conclusion that anterior and posterior POEM are clinically equivalent in terms of treatment success, with procedural nuances that do not appear to translate into meaningful differences in patient outcomes. These findings are broadly concordant with our NMA, in which Anterior POEM ranked marginally higher than Posterior POEM for both treatment failure and LES pressure reduction by SUCRA, but with substantially overlapping credible intervals that preclude any confident claim of superiority. The modest SUCRA difference observed in our analysis should therefore be interpreted in light of these RCT data, and technique selection should continue to be guided by operator familiarity, institutional experience, and individual patient anatomy rather than by probabilistic rankings alone.

Our analysis included three variants of Heller's Myotomy combined with fundoplication. Heller's Myotomy + Dor Fundoplication (SUCRA 63.2% for treatment failure) and + Toupet Fundoplication (SUCRA 57.8%) ranked closely, consistent with existing RCT evidence. Postoperative abnormal acid reflux and dysphagia were similar in the studies comparing Dor and Toupet fundoplication after Heller's Myotomy, suggesting that the choice of anti-reflux wrap does not materially affect treatment failure rates, and that surgeon experience and institutional preference appropriately guide this decision. The lone Nissen Fundoplication estimate was based on a single zero-event study and is too unreliable for clinical interpretation, as discussed previously.

Pneumatic Dilation combined with Botulinum Toxin ranked first for LES pressure reduction (SUCRA 93.5%; MD -28 mmHg, 95% CrI – 40 to -15 vs Placebo). This finding should be interpreted with caution given that this comparison is supported by only two studies with predominantly indirect evidence and a notably wide credible interval. The physiological rationale for the combination requires nuance. Botulinum Toxin only temporarily

inhibits acetylcholine-mediated cholinergic activity at the LES while pneumatic dilation mechanically disrupts sphincter fibers, evidence on its long-term durability remains limited. The discordance between this treatment's ranking for LES pressure (1st) and treatment failure (7th) highlights an important limitation of using manometric outcomes as surrogates for clinical efficacy: LES pressure reduction does not always translate proportionally into sustained symptom relief [54].

Several limitations warrant acknowledgment. First, Heller's Myotomy + Nissen Fundoplication is represented by a single trial with zero events in one arm (Falkenback 2003), producing an extreme and unreliable Bayesian OR. While we retained this treatment in the network to preserve the topology of indirect connections, its rankings and estimates should not be used to guide clinical decisions. Second, Placebo, the clinical reference, is a peripheral node in both networks, meaning most comparative estimates are derived from indirect evidence, which is reflected in the predominantly Low CINeMA ratings for indirectness. Third, the included trials span a wide publication period (1993–2023), during which diagnostic criteria, manometric methodology, and surgical technique have evolved considerably, introducing clinical heterogeneity that I^2 alone may not fully capture. Fourth, follow-up duration varied substantially across studies, and the NMA does not model time-to-failure trajectories, which are particularly relevant for Botulinum Toxin whose efficacy is explicitly time-dependent. Fifth, achalasia subtypes per the Chicago Classification were not consistently reported across included trials, precluding subgroup analysis by subtype, a recognized determinant of treatment response.

In conclusion, our systematic review and Bayesian NMA provides novel probabilistic ranking of all available treatment modalities for primary achalasia within a unified framework, identifying Anterior POEM as the highest-ranking endoscopic approach by NMA-derived SUCRA scores, though this ranking should be interpreted cautiously. In light of evidence by recent RCTs, these SUCRA rankings are best considered hypothesis-generating. The choice of POEM technique should continue to be guided by surgeon experience, institutional expertise, and individual patient anatomy. Botulinum Toxin and Pneumatic Dilation monotherapy appear most appropriate for patients who are not candidates for myotomy, or as a bridge to definitive therapy. The apparent superiority of the combined Pneumatic Dilation + Botulinum Toxin approach on LES pressure is based on only two studies with predominantly indirect evidence and should not be over-interpreted. Given the temporary nature of Botulinum Toxin and the discordance between this treatment's LES pressure ranking (1st) and treatment failure ranking (7th), adequately powered RCTs incorporating both manometric and long-term clinical endpoints are needed before this combination can be recommended in practice.

Declarations

Ethics Approval and Consent to Participate:

Not applicable

Consent for Publication:

Not applicable

Competing Interest:

Dr Daryl R. Ramai reports serving as a Consultant for Olympus America. All other authors declare no potential conflicts of interest.

Disclosures:

Drs. Hasnain Wajeeh Saqib, Mujtaba Moazzam, Muhammad Dawood, Abdul Rafay, Ali Raza, Mahad Ahmad, Muhammad Fakher Wali Wani, Muhammad Sahal Zakir, Talha Khan, Abdul Moeez, and Dr. Jorge D. Machicado have no potential conflicts of interest or financial ties to disclose. Dr. Daryl R. Ramai serves as a consultant for Olympus America.

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Author Contributions:

H.W.S. and M.M. contributed equally to study conceptualization, methodology, writing of initial draft, reviewing. H.W.S. performed the formal analysis. M.D. and A.R. contributed to literature screening and data extraction. A.R (2). and M.A. contributed to the quality assessment of the studies. M.F.W.W. and M.S.Z. contributed to the certainty assessment. T.K. created the tables and contributed to visualization. A.M. also contributed to writing of the initial manuscript draft. J.D.M. and D.R.R. supervised and reviewed the study and contributed to the final reviewing and editing of the manuscript.

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Attached as electronic supplementary table

References

1. Savarino E, Bhatia S, Roman S, Sifrim D, Tack J, Thompson SK et al (2022) Achalasia Nat Rev Dis Primers 8. https://doi.org/10.1038/S41572-022-00356-8
2. Lee K, Hong SP, Yoo IK, Yeniova AÖ, Hahn JW, Kim MS et al (2024) Global trends in incidence and prevalence of achalasia, 1925–2021: A systematic review and meta-analysis. United Eur Gastroenterol J 12:504. https://doi.org/10.1002/UEG2.12555
3. Yadlapati R, Kahrilas PJ, Fox MR, Bredenoord AJ, Prakash Gyawali C, Roman S et al Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. Neurogastroenterol Motil 2021;33. https://doi.org/10.1111/NMO.14058
4. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ (2008) Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology 135:1526–1533. https://doi.org/10.1053/J.GASTRO.2008.07.022
5. Rolland S, Paterson W, Bechara R, Achalasia (2023) Current therapeutic options. Neurogastroenterol Motil 35. https://doi.org/10.1111/NMO.14459
6. Dirks RC, Kohn GP, Slater B, Whiteside J, Rodriguez NA, Docimo S et al (2021) Is peroral endoscopic myotomy (POEM) more effective than pneumatic dilation and Heller myotomy? A systematic review and meta-analysis. Surg Endosc 35:1949–1962. https://doi.org/10.1007/S00464-021-08353-W
7. Vaezi MF, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT (2020) ACG Clinical Guidelines: Diagnosis and Management of Achalasia. Am J Gastroenterol 115:1393–1411. https://doi.org/10.14309/AJG.0000000000000731
8. North A, Tewari N (2024) Peroral endoscopic myotomy compared to laparoscopic Heller myotomy and pneumatic dilation in the treatment of achalasia: a systematic review. Dis Esophagus 37. https://doi.org/10.1093/DOTE/DOAD055
9. Aiolfi A, Bona D, Riva CG, Micheletto G, Rausa E, Campanelli G et al (2020) Systematic Review and Bayesian Network Meta-Analysis Comparing Laparoscopic Heller Myotomy, Pneumatic Dilatation, and Peroral Endoscopic Myotomy for Esophageal Achalasia. J Laparoendosc Adv Surg Tech A 30:1–9. https://doi.org/10.1089/LAP.2019.0432
10. Salanti G, Nikolakopoulou A, Efthimiou O, Mavridis D, Egger M, White IR (2022) Introducing the Treatment Hierarchy Question in Network Meta-Analysis. Am J Epidemiol 191:930–938. https://doi.org/10.1093/aje/kwab278
11. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C et al (2015) The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med 162:777–784. https://doi.org/10.7326/M14-2385
12. Grant R, Di Tanna GL (2025) Bayesian meta-analysis: A practical introduction. Bayesian Meta-Analysis: A Practical Introduction. :1–304. https://doi.org/10.1201/9781003375821/BAYESIAN-META-ANALYSIS-ROBERT-GRANT-GIAN-LUCA-DI-TANNA/RIGHTS-AND-PERMISSIONS
13. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I et al RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366. https://doi.org/10.1136/BMJ.L4898
14. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Giovane C, Del, Egger M et al (2020) CINeMA: An approach for assessing confidence in the results of a network meta-analysis. PLoS Med 17:e1003082. https://doi.org/10.1371/JOURNAL.PMED.1003082
15. van Valkenhoef G, Lu G, de Brock B, Hillege H, Ades AE, Welton NJ (2012) Automating network meta-analysis. Res Synth Methods 3:285–299. https://doi.org/10.1002/JRSM.1054;REQUESTEDJOURNAL:JOURNAL:17592887;PAGEGROUP:STRING:PUBLICATION
16. Warn DE, Thompson SG, Spiegelhalter DJ (2002) Bayesian random effects meta-analysis of trials with binary outcomes: Methods for the absolute risk difference and relative risk scales. Stat Med 21:1601–1623. https://doi.org/10.1002/SIM.1189;CSUBTYPE:STRING:SPECIAL;PAGE:STRING:ARTICLE/CHAPTER
17. Liu Y, Béliveau A, Wei Y, Chen MY, Record-Lemon R, Kuo PL et al (2023) A Gentle Introduction to Bayesian Network Meta-Analysis Using an Automated R Package. Multivar Behav Res 58:706–722. https://doi.org/10.1080/00273171.2022.2115965
18. Cochrane Handbook for Systematic Reviews of Interventions | (2026) Cochrane n.d. https://www.cochrane.org/authors/handbooks-and-manuals/handbook
19. van Ravenzwaaij D, Cassey P, Brown SD (2016) A simple introduction to Markov Chain Monte–Carlo sampling. Psychon Bull Rev 25:143. https://doi.org/10.3758/S13423-016-1015-8
20. Kwon S, Zhang S, Köhn HF, Zhang B (2024) MCMC stopping rules in latent variable modelling. Br J Math Stat Psychol 78:225. https://doi.org/10.1111/BMSP.12357
21. Higgins JPT, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21:1539–1558. https://doi.org/10.1002/sim.1186
22. van Valkenhoef G, Dias S, Ades AE, Welton NJ (2016) Automated generation of node-splitting models for assessment of inconsistency in network meta-analysis. Res Synth Methods 7:80–93. https://doi.org/10.1002/JRSM.1167;JOURNAL:JOURNAL:17592887;PAGE:STRING:ARTICLE/CHAPTER

23. Mikaeli J, Bakhshipour A, Rabbani R, Shirani S, Soleimani HA (2010) ORIGINAL REPORT *Corresponding Author: Comparison of Pneumatic Dilation with Pneumatic Dilation Plus Botulinum Toxin for Treatment of Achalasia. vol. 48
24. Bansal R, Nostrant TT, Scheiman JM, Koshy S, Barnett JL, Elta GH et al (2003) Intrasphincteric Botulinum Toxin Versus Pneumatic Balloon Dilation For Treatment of Primary Achalasia. vol. 36
25. Chrystoja CC, Darling GE, Diamant NE, Kortan PP, Tomlinson GA, Deitel W et al (2016) Achalasia-specific quality of life after pneumatic dilation or laparoscopic heller myotomy with partial fundoplication: A multicenter, randomized clinical trial. Am J Gastroenterol 111:1536–1545. https://doi.org/10.1038/ajg.2016.402
26. Conte TM, Haddad LB, de Ribeiro P, de Moura IB, D'Albuquerque ETH, de Moura LAC (2020) Peroral endoscopic myotomy (POEM) is more cost-effective than laparoscopic Heller myotomy in the short term for achalasia: economic evaluation from a randomized controlled trial. Endosc Int Open 08:E1673–E1680. https://doi.org/10.1055/a-1261-3417
27. Falkenback D, Johansson J, Öberg S, Kjellin A, Wenner J, Zilling T et al (2003) Heller's esophagomyotomy with or without a 360° ° ° ° floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. 16
28. Hamdy E, El Nakeeb A, El Hanfy E, El Hemaly M, Salah T, Hamed H et al (2015) Comparative study between laparoscopic Heller Myotomy versus pneumatic dilatation for treatment of early Achalasia: A prospective randomized study. J Laparoendoscopic Adv Surg Techniques 25:460–464. https://doi.org/10.1089/lap.2014.0682
29. Ichkhanian Y, Abimansour JP, Pioche M, Vosoughi K, Eleftheriadis N, Chiu PWY et al (2021) Outcomes of anterior versus posterior peroral endoscopic myotomy 2 years post-procedure: Prospective follow-up results from a randomized clinical trial. Endoscopy 53:462–468. https://doi.org/10.1055/a-1204-4242
30. Kostic S, Johnsson E, Kjellin A, Ruth M, Lönroth H, Andersson M et al (2007) Health economic evaluation of therapeutic strategies in patients with idiopathic achalasia: Results of a randomized trial comparing pneumatic dilatation with laparoscopic cardiomyotomy. Surg Endoscopy Other Interventional Techniques 21:1184–1189. https://doi.org/10.1007/s00464-007-9310-0
31. Kumagai K, Kjellin A, Tsai JA, Thorell A, Granqvist S, Lundell L et al (2014) Toupet versus Dor as a procedure to prevent reflux after cardiomyotomy for achalasia: Results of a randomised clinical trial. Int J Surg 12:673–680. https://doi.org/10.1016/j.ijsu.2014.05.077
32. Mikaeli J, Bishehsari F, Montazeri G, Mahdavinia M, Yaghoobi M, Darvish-Moghadam S et al (2006) Injection of botulinum toxin before pneumatic dilatation in achalasia treatment: A randomized-controlled trial. Aliment Pharmacol Ther 24:983–989. https://doi.org/10.1111/j.1365-2036.2006.03083.x
33. Muehldorfer SM, Schneider TH, Hochberger J, Martus P, Hahn EG, Ell C Esophageal Achalasia: Intrasphincteric Injection of Botulinum Toxin A Versus Balloon Dilation. n.d
34. Pasricha PJ, Ravich WJ, Hendrix TR, Sostre S, Jones B, Kalloo AN (1995) Intrasphincteric botulinum toxin for the treatment of achalasia. N Engl J Med 332:774–778. https://doi.org/10.1056/NEJM199503233321203
35. Persson J, Johnsson E, Kostic S, Lundell L, Smedh U (2015) Treatment of achalasia with laparoscopic myotomy or pneumatic dilatation: Long-term results of a prospective, randomized study. World J Surg 39:713–720. https://doi.org/10.1007/s00268-014-2869-4
36. Ponds FA, Fockens P, Lei A, Neuhaus H, Beyna T, Kandler J et al (2019) Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation on Symptom Severity and Treatment Outcomes among Treatment-Naive Patients with Achalasia: A Randomized Clinical Trial. JAMA - J Am Med Association 322:134–144. https://doi.org/10.1001/jama.2019.8859
37. Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C et al (2012) Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: Results of a multicenter, prospective, randomized-controlled trial. Surg Endosc 26:18–26. https://doi.org/10.1007/s00464-011-1822-y
38. Richards WO, Torquati A, Holzman MD, Khaitan L, Byrne D, Lutfi R et al (2004) Heller myotomy versus heller myotomy with dor fundoplication for achalasia: A prospective randomized double-blind clinical trial. Ann Surg 240:405–415. https://doi.org/10.1097/01.sla.0000136940.32255.51
39. Saleh CMG, Familiari P, Bastiaansen BAJ, Fockens P, Tack J, Boeckxstaens G et al (2023) The Efficacy of Peroral Endoscopic Myotomy vs Pneumatic Dilation as Treatment for Patients With Achalasia Suffering From Persistent or Recurrent Symptoms After Laparoscopic Heller Myotomy: A Randomized Clinical Trial. Gastroenterology 164:1108–1118e3. https://doi.org/10.1053/j.gastro.2023.02.048
40. Tan Y, Lv L, Wang X, Zhu H, Chu Y, Luo M et al (2018) Efficacy of anterior versus posterior per-oral endoscopic myotomy for treating achalasia: a randomized, prospective study. Gastrointest Endosc 88:46–54. https://doi.org/10.1016/j.gie.2018.03.009
41. Torres-Villalobos G, Coss-Adame E, Furuzawa-Carballeda J, Romero-Hernández F, Blancas-Breña B, Torres-Landa S et al (2018) Dor Vs Toupet Fundoplication After Laparoscopic Heller Myotomy: Long-Term Randomized Controlled Trial Evaluated by High-Resolution Manometry. J Gastrointest Surg 22:13–22. https://doi.org/10.1007/s11605-017-3578-8
42. Werner YB, Hakanson B, Martinek J, Repici A, von Rahden BHA, Bredenoord AJ et al (2019) Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia. N Engl J Med 381:2219–2229. https://doi.org/10.1056/nejmoa1905380
43. Zaninotto G, Annese V, Costantini M, Del Genio A, Costantino M, Epifani M et al (2004) Randomized Controlled Trial of Botulinum Toxin Versus Laparoscopic Heller Myotomy for Esophageal Achalasia. Ann Surg 239:364–370. https://doi.org/10.1097/01.sla.0000114217.52941.c5
44. Zhu Q, Liu J, Yang C (2010) Clinical study on combined therapy of botulinum toxin injection and small balloon dilation in patients with esophageal achalasia. Dig Surg 26:493–498. https://doi.org/10.1159/000229784

45. Annese V, Basciani M, Perri F, Lombardi G, Frusciante V, Simone P et al (1996) Controlled Trial of Botulinum Toxin Injection Versus Placebo and Pneumatic Dilation in Achalasia. 111
46. Moonen A, Annese V, Belmans A, Bredenoord AJ, Varannes SB, Des, Costantini M et al (2016) Long-term results of the European Achalasia trial: A multicentre randomised Controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. Gut 65:732–739. https://doi.org/10.1136/gutjnl-2015-310602
47. Novais PA, Lemme EMO (2010) 24-h pH monitoring patterns and clinical response after achalasia treatment with pneumatic dilation or laparoscopic Heller myotomy. Aliment Pharmacol Ther 32:1257–1265. https://doi.org/10.1111/j.1365-2036.2010.04461.x
48. Ramchandani M, Nabi Z, Reddy D, Talele R, Darisetty S, Kotla R et al (2018) Outcomes of anterior myotomy versus posterior myotomy during POEM: a randomized pilot study. Endosc Int Open 06:E190–E198. https://doi.org/10.1055/s-0043-121877
49. Torquati A, Lutfi R, Khaitan L, Sharp KW, Richards WO (2006) Heller myotomy vs Heller myotomy plus Dor fundoplication: Cost-utility analysis of a randomized trial. Surg Endoscopy Other Interventional Techniques 20:389–393. https://doi.org/10.1007/s00464-005-0116-7
50. Nabi Z, Ramchandani M, Sayyed M, Chavan R, Darisetty S, Goud R et al (2021) Comparison of short versus long esophageal myotomy in cases with idiopathic Achalasia: A randomized controlled trial. J Neurogastroenterol Motil 27:63–70. https://doi.org/10.5056/JNM20022
51. Khashab MA, Sanaei O, Rivory J, Eleftheriadis N, Chiu PWY, Shiwaku H et al (2020) Peroral endoscopic myotomy: anterior versus posterior approach: a randomized single-blinded clinical trial. Gastrointest Endosc 91:288–297e7. https://doi.org/10.1016/j.gie.2019.07.034
52. Borges AA, de Oliveira Lemme EM, Abrahao LJ, Madureira D, Andrade MS, Soldan M et al (2014) Pneumatic dilation versus laparoscopic Heller myotomy for the treatment of achalasia: Variables related to a good response. Dis Esophagus 27:18–23. https://doi.org/10.1111/dote.12064
53. Boeckxstaens GE, Annese V, Bruley Des Varannes S, Chaussade S, Costantini M, Cuttitta A et al (2011) Pneumatic Dilation versus Laparoscopic Heller's Myotomy for Idiopathic Achalasia A BS T R AC T. vol. 364
54. Pandolfino JE, Kwiatek MA, Kahrilas PJ (2008) The pathophysiologic basis for epidemiologic trends in gastroesophageal reflux disease. Gastroenterol Clin North Am 37:827–843. https://doi.org/10.1016/J.GTC.2008.09.009

Figures

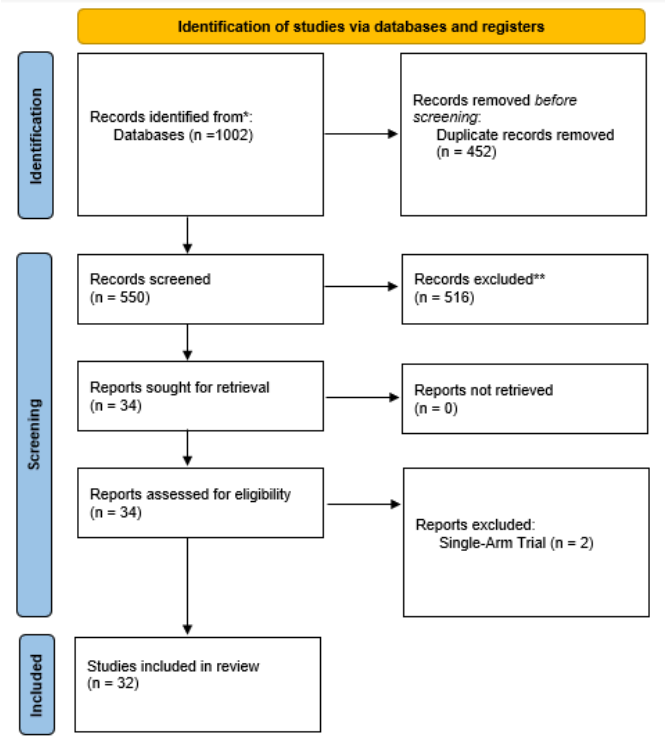


Figure 1

Figure 1: PRISMA Summary Flowchart for the Inclusion Process

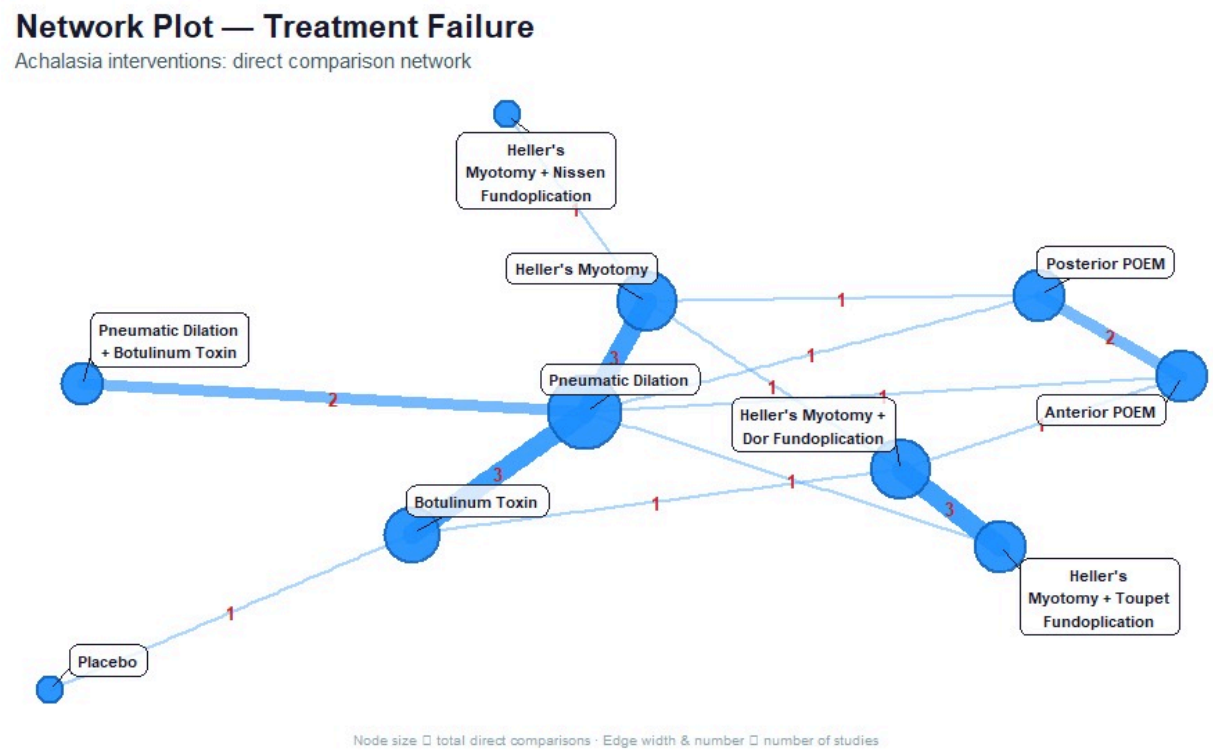


Figure 2

Figure 2.1: Network Plot for Treatment Failure

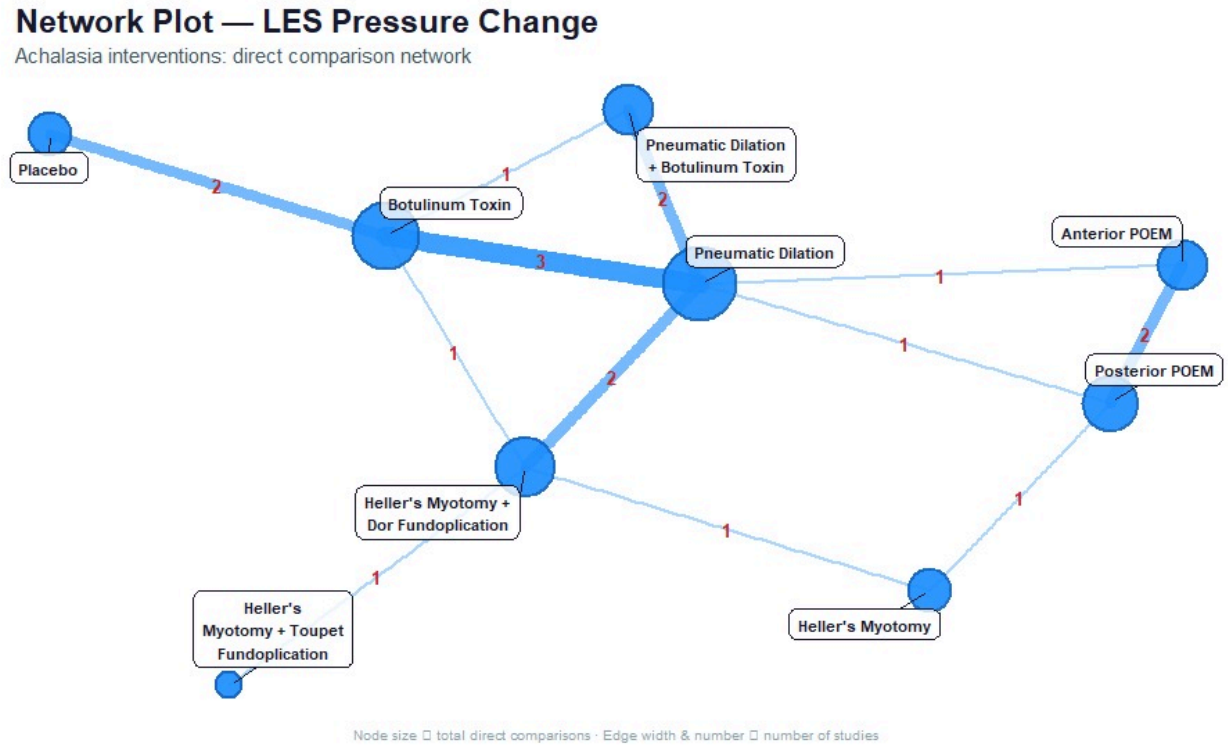


Figure 3

Figure 2.2: Network Plot for Mean Lower Esophageal Pressure Change

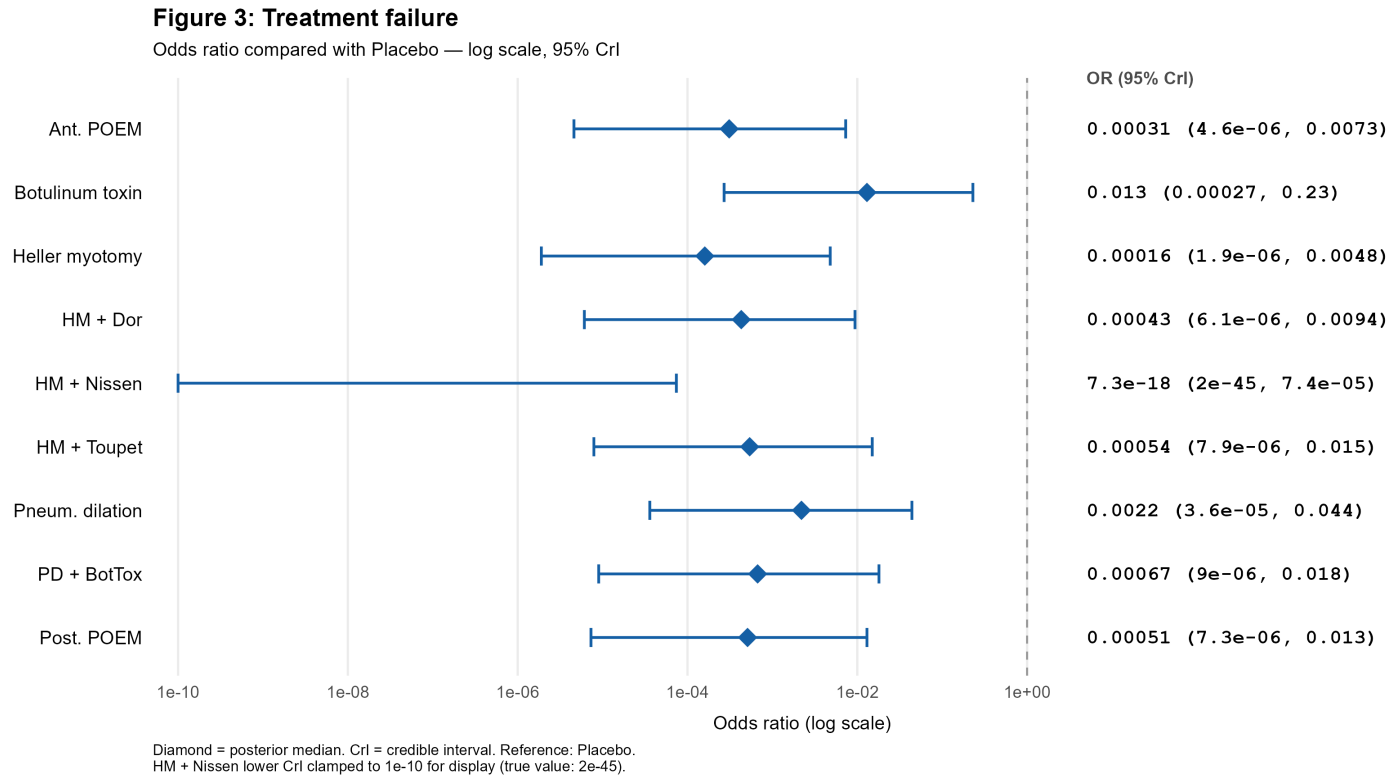


Figure 4

Figure 3.1: Bayesian Forest Plot for Treatment Failure

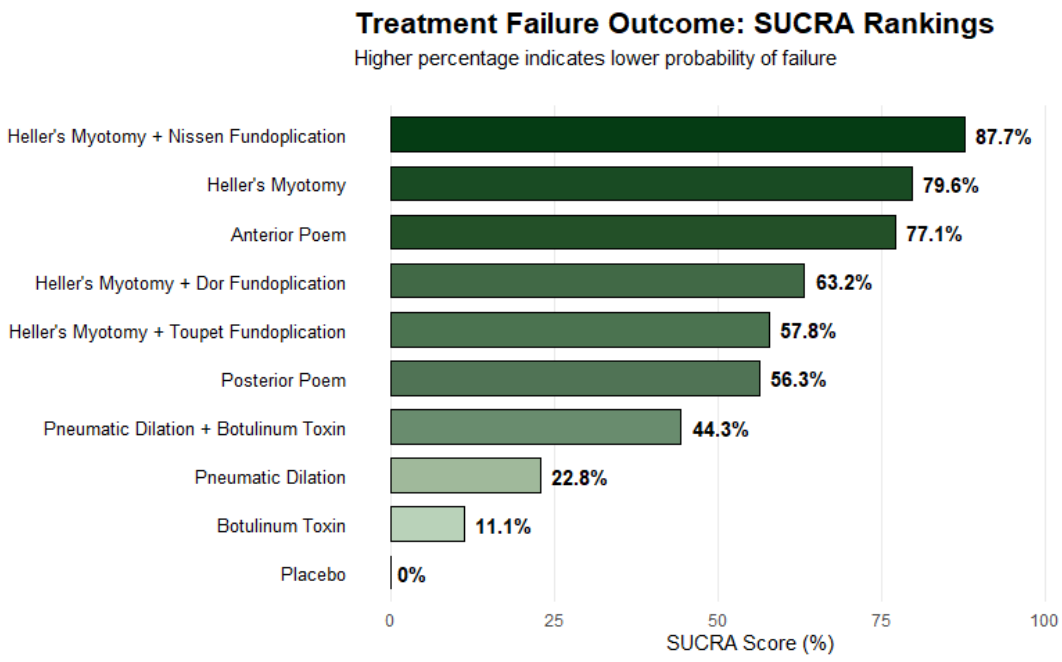


Figure 5

Figure 3.2: SUCRA Bar Rankings for Treatment Failure

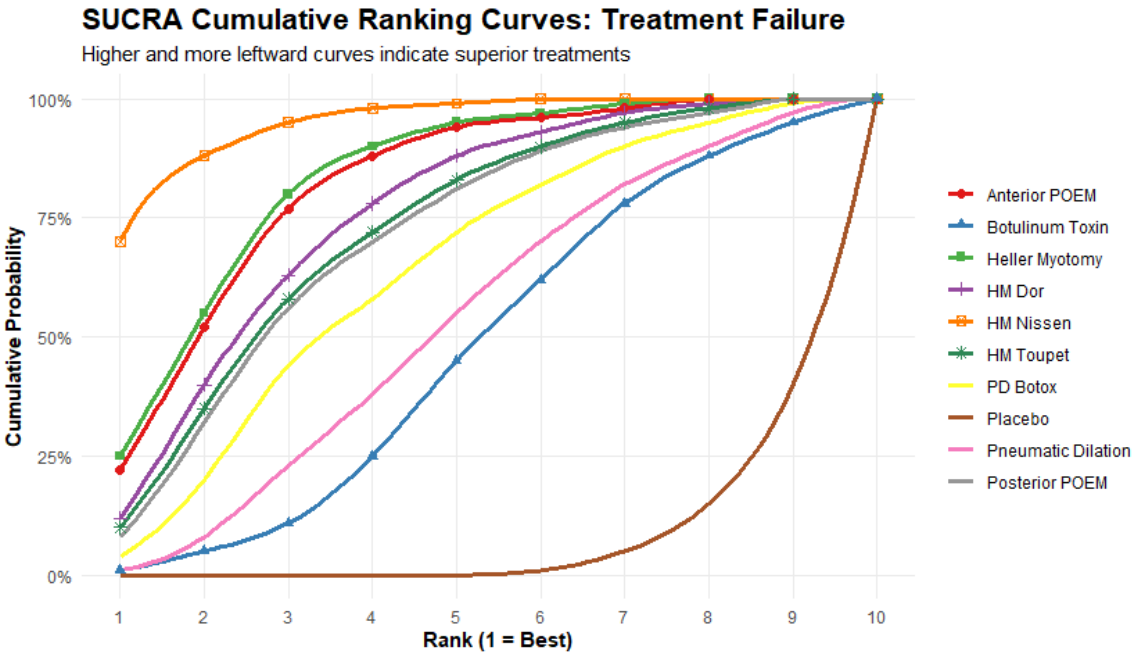


Figure 6

Figure 3.3: SUCRA for Treatment Failure

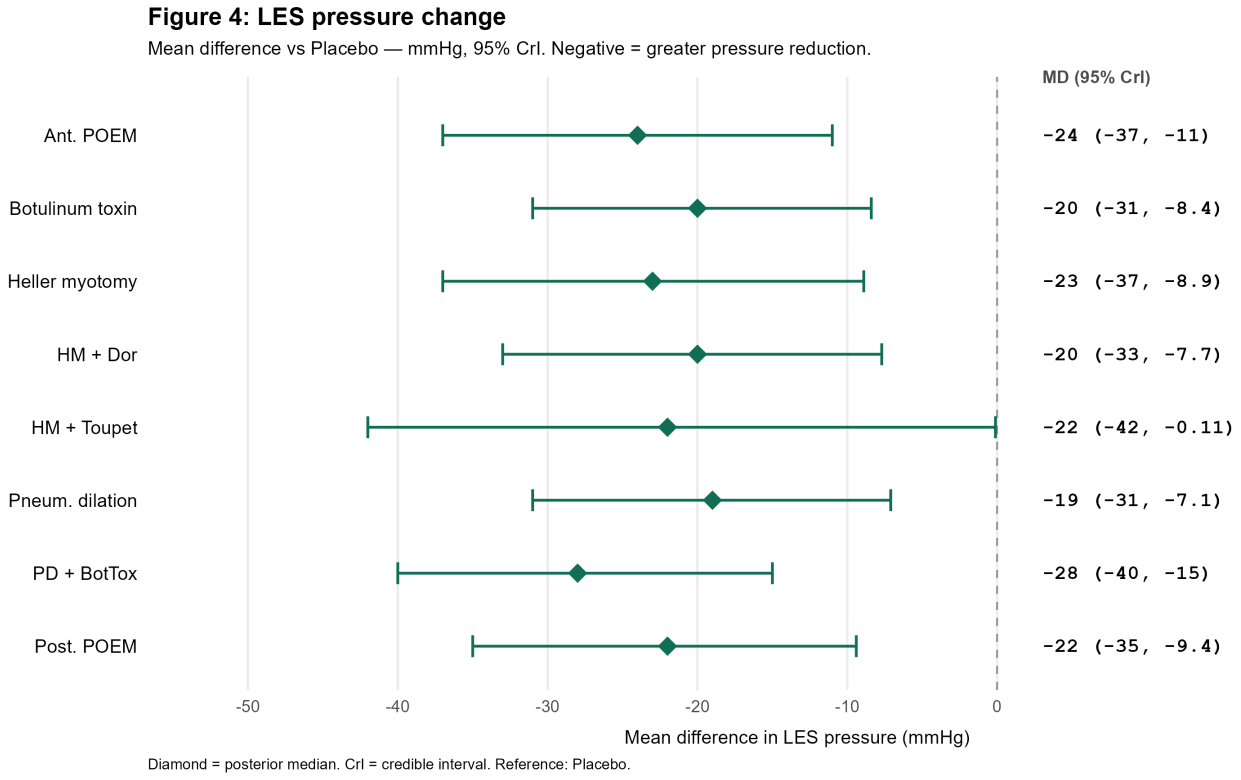


Figure 7

Figure 4.1: Bayesian Forest Plot for Mean Lower Esophageal Pressure Change

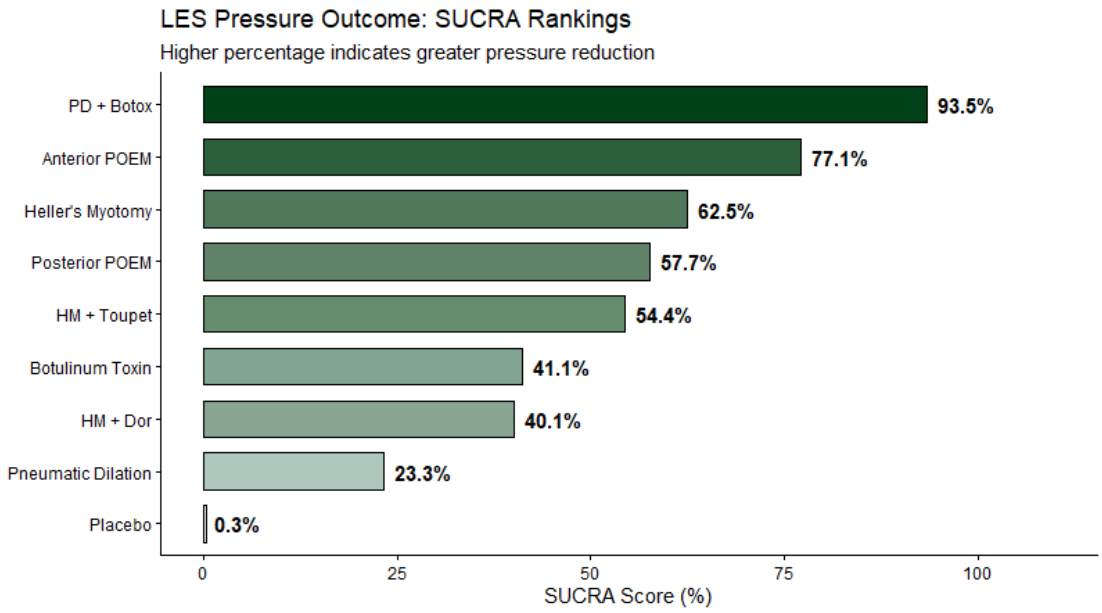


Figure 8

Figure 4.2: SUCRA Bar Rankings for Mean Lower Esophageal Pressure Change

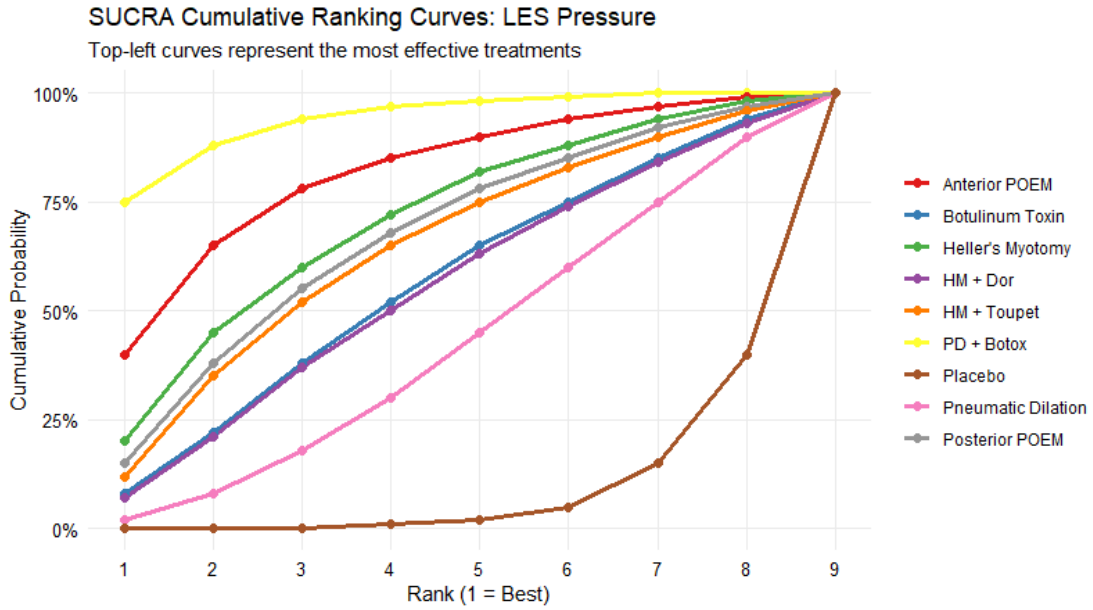


Figure 9

Figure 4.3: SUCRA for Mean Lower Esophageal Pressure Change