HHS Public Access

Author manuscript

Gastrointest Endosc. Author manuscript; available in PMC 2018 October 01.

Published in final edited form as:

Gastrointest Endosc. 2017 October ; 86(4): 581–591.e3. doi:10.1016/j.gie.2017.04.028.

Esophageal dilation with either bougie or balloon technique as a treatment for eosinophilic esophagitis: a systematic review and meta-analysis

Michael Dougherty, MD, **Thomas M. Runge, MD MSCR**, **Swathi Eluri, MD MSCR**, and **Evan S. Dellon, MD MPH**

Center for Esophageal Disease and Swallowing and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine, Chapel Hill, NC

Abstract

Background and Aims—Esophageal dilation is a now recognized to be an important therapeutic modality in eosinophilic esophagitis (EoE). We aimed to evaluate the safety of esophageal dilation in EoE, especially regarding perforation risk, and to examine perforation risk by dilator type.

Methods—We conducted a systematic review of the published literature from January 1, 1950 to June 30, 2016 using Pubmed, EMBASE, and Web of Science. Studies were included if they described patients with EoE who underwent esophageal dilation and also reported the presence or absence of at least 1 adverse event (eg, perforation, bleeding, pain, or hospitalization). We used random-effects meta-analysis to estimate the frequency of each adverse event. Adverse event rates are listed as percentages with 95% CI throughout.

Results—Of 923 identified articles, 37 met inclusion criteria and represented 2034 dilations in 977 patients. On meta-analysis, post-procedure hospitalization occurred in 0.689% (0%–1.42%) of dilations, clinically significant GI hemorrhage in 0.028% (0%–0.217%), and clinically significant chest pain in 3.64% (1.73%–5.55%). Nine perforations were documented, a rate of 0.033% (0%–0.226%) per procedure after meta-analysis. None of the perforations resulted in surgical intervention or mortality. The majority (5/9) were reported before 2009 (rate of 0.41% [0%–2.75%]); from 2009 forward the rate was 0.030% (0%–0.225%). Dilation method was described in 30 studies (1957 dilations), in which 4 perforations were detected. The estimated perforation rate for bougies was 0.022% (0%–0.347%) and for balloons was 0.059% (0%–0.374%).

Conclusions—Perforation from esophageal dilation in EoE is rare, and there is no evidence of a significant difference in perforation risk related to dilator type. Esophageal dilation should be considered a safe procedure in EoE.

Corresponding Author: Evan S. Dellon, MD MPH, CB #7080, Room 4140 Bioinformatics Bldg 130 Mason Farm Rd Chapel Hill, NC 27599-7080, P: 919-966-2513; F: 919-843-2508, edellon@med.unc.edu.

Competing interests: None of the authors report any potential conflicts of interest with this study. Dr. Dellon is a consultant for Adare, Banner, Receptos, Regeneron, Roche, and Shire, receives research funding from Meritage, Miraca, Nutricia, Receptos, Regeneron, and Shire, and has received an educational grant from Banner.

Online Supplement. Sensitivity and subgroup random-effects meta-analyses.

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic inflammatory condition responsible for an increasingly large proportion of esophageal-related morbidity.[1, 2] Prominent presenting symptoms in adults and adolescents include dysphagia and food impaction,[3] and are often a consequence of esophageal strictures or narrowing.[4–7] Although medical and dietary therapies can decrease esophageal eosinophilia and microscopic evidence of fibrosis,[8] they may not resolve overt strictures or narrowing and therefore symptoms may not improve in the setting of a severe fibrostenotic phenotype.[7, 9, 10] In addition, a long duration of symptoms before diagnosis is associated with development of esophageal remodeling.[5, 11–15] In these cases esophageal dilation remains a mainstay of therapy, both with and without concomitant medical therapy.[16–18]

Early reports of dilation in EoE raised concerns that the inflamed and fragile esophageal tissue was particularly susceptible to dilation-related adverse events, including bleeding, severe chest pain, and most concerning, perforation.[19–22] More recently, however, there have been a number of studies reporting on large cohorts of EoE patients who have safely undergone esophageal dilation, bringing into question the perceived elevated risk in EoE.[12, 13, 23–28] Other publications have provided new data in pediatric populations.[28, 29] There remains significant uncertainty whether bougie or through-the-scope (TTS) balloon dilation should be preferred, or if one of these techniques has a better safety profile.[18, 23] The rapidly expanding literature on esophageal dilation in EoE may help to elucidate this issue as well as confirm the safety profile of this procedure.[12, 28, 30–32]

The current study aimed to evaluate the overall safety of esophageal dilation as a management option for fibrostenotic EoE, especially regarding esophageal perforation. We also sought to determine whether there were any differences in safety between bougie and balloon dilation in EoE.

METHODS

We performed a systematic review and meta-analysis to assess safety of esophageal dilation in EoE using methods consistent with the PRISMA guidelines.[33] Two authors (T.R. and S.E.) independently identified published reports of dilation in EoE, using Pubmed, EMBASE, and Web of Science. The search terms were “eosinophilic esophagitis” combined with “dilation” or “dilatation,” for example in Pubmed: ((*eosinophilic esophagitis) AND (dilation OR dilatation)) OR (*eosinophilic AND (dilation OR dilatation)). Additionally, the reference lists of all of the articles included in the final analysis, as well as previous reviews,[11, 23–25] were hand-searched to ensure identification of all relevant studies. All indexed publications in any language, from January 1, 1950 through June 30, 2016 were eligible for inclusion. Studies of any design were included if they described patients with EoE who underwent esophageal dilation and also reported the presence or absence of at least 1 adverse event (eg, perforation, bleeding, pain, hospitalization) occurring as a result of dilation. EoE was defined by esophageal eosinophilia in the presence of suggestive symptoms and endoscopic abnormalities (generally >15 per high-powered field in data collected after the publication of the 2007 guidelines).[20] Review articles, editorials, and

letters to the editor were excluded, as were studies that reported on patients described in a subsequent publication. The search authors independently reviewed article titles and abstracts for inclusion, with disagreements resulting in inclusion of the abstract for full text review. The search authors independently extracted the relevant data into evidence tables, which were checked by the first author (M.D.), with any discrepancies resolved by consensus and adjudicated by the senior author (E.S.D.).

Extracted data included the following: study type, the number of patients in the study with EoE, number of EoE patients undergoing dilation, total number of dilations, mean age of study population, percentage male, number of balloon versus bougie dilations (where available), any reported data on clinical efficacy, and mean follow-up duration (in months). Finally, we abstracted the numbers of post-dilation adverse events from 4 main categories: perforations, hospitalizations, significant GI bleeds, and chest pain, defined according to each study. We also assessed the subsequent clinical outcomes of any adverse event where reported, such as surgical intervention or mortality. Significant GI bleeds were those defined as needing additional clinical intervention, usually re-endoscopy, and did not include mucosal tears seen immediately after dilation. Chest pain was subdivided into “unspecified” and “clinically significant” categories, with the latter defined as either triggering an otherwise unplanned clinical action (such as opiate prescription, radiologic test order, healthcare visit, etc) or specifically referred to as “severe.”

We assessed risk of bias for each study using the NIH/NHLBI quality assessment tools (available at: https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools). The evaluation focused on the risk of a biased assessment of dilation safety, regardless of the quality of the study for assessing its primary outcome. In addition to the NIH tools, we also judged risk of bias to increase based on study design, on a continuum from randomized controlled trials (RCTs), to observational studies with comparison groups, to uncontrolled observational designs. We defined a cohort design on the basis of identification by exposure according to the method of Dekkers et al,[34] thus including uncontrolled designs. Case reports were automatically considered at high risk of bias.

The main analysis used all studies. The primary outcome was percentage of dilations resulting in esophageal perforation. Secondary outcomes included other adverse events (eg chest pain, bleeding), perforations by dilator type, and perforations over time. We performed a random-effects meta-analysis for these outcomes (*metaprop* package for STATA version 14.2; StataCorp, College Station, Tex, USA), using a continuity correction of 0.5 in order to include studies with zero adverse events.[35] Heterogeneity was assessed with I^2, which represents the percentage of the variability in effect estimates due to heterogeneity rather than chance. We performed sensitivity analyses of subgroups by study size, study design, study quality, publication period, mean of the maximum dilator size, and pediatric versus adult studies. We also performed a sensitivity analysis using a logit transformation/back transformation instead of the continuity correction.[35] We evaluated for publication bias with the construction of a funnel plot of perforation rate versus number of dilations per study, and the Egger test for funnel plot asymmetry.

RESULTS

Search results

We initially identified 923 articles, of which 37 met inclusion criteria (Figure 1). These comprised 2034 dilations performed on 977 patients. There was one RCT, 1 prospective cohort, 24 retrospective cohorts, 1 case-control study, and 10 case series/reports. There were 31 articles and 6 meeting abstracts (Table 1). Three studies contributed the majority of dilation procedures (1232 dilations on 532 patients),[12, 13, 27] whereas 18 studies described single-digit numbers of dilated patients, totaling 86 dilation procedures (Table 1). Of the studies with more than one subject, three focused on pediatric patients,[28, 29, 36] 2 3 were restricted to adults, 2 had both adults and children,[12, 13] and in one, abstract age was not reported.[37] The follow-up periods of the individual studies ranged from 1 week to 14 years (median 14.7 months).

Study Quality

All but one study[30] were observational, and most did not evaluate adverse events as the primary outcome. Many of the studies with the largest samples and most comprehensive reporting of adverse events lacked a comparison group of either EoE patients who were not dilated or patients without EoE who were dilated.[13, 15, 27, 31, 39] Of the observational comparison studies, only 2[19, 28] were designed to evaluate the relationship of dilations to adverse events, and none used statistical methods to adjust for selection bias (for more severely affected patients) in those patients who underwent dilation. As such, there were no studies at low risk of bias, and 11 studies with only moderate risk of bias (Table 1).

Safety

“Hospitalization” was observed after 19 of 1814 dilations, excluding 2 pediatric studies where all patients were hospitalized overnight per protocol[29, 36] (Table 2). Significant GI bleeding postprocedure was extremely rare, after only 1 out of 1806 dilations. Clinically significant chest pain was reported in 49 of 924 dilations, with a range from 0% to 17% of procedures, depending on study. Incidence of chest pain of unspecified severity varied even more between studies, reported in anywhere from 0% to 74% of cases, with a median of 14.7% (Table 2).

Across all dilations, 9 total perforations were documented.[19, 22, 27, 40, 41] Six out of these 9 had data describing the clinical severity and management after the perforation.[22, 27, 40, 41] Five out of 6 were designated “contained” or “intramural” perforations (CT scan demonstrating extraluminal air only). Only one transmural perforation was described,[27] with contrast extravasation and pooling in the pleural space. All 6 perforations were managed without surgical intervention. No deaths attributable to dilation were described in the included studies.

Interestingly, most of the dilations (1831/2034, 90%) were from reports published in 2009 or later (Table 1), but the majority (5/9; 56%) of reported perforations were from publications before 2009. Reports published before 2009 described 5 perforations in 203 procedures; from 2009 forward, perforations occurred in 4 out of 1831 dilations. Across all time periods,

dilation method (balloon vs bougie) at the time of the procedure was noted in 30 studies. Perforations occurred in 2 out of 1120 procedures using bougies and 2 out of 837 procedures with balloon dilators.

Meta-analysis

The primary random-effects meta-analysis included all studies (Table 3). Meta-analytic point estimates of adverse event rates were generally much lower than unweighted pooled estimates. For example, perforation rate was 0.033% (95% CI, 0%–0.226%) per procedure. Forest plots of the risks of perforation, hospitalization, and chest pain, excluding case reports and case series, are shown in Figure 2 (A–D). The point estimates for frequency of perforation (both total and by dilator type), hospitalization, and GI hemorrhage were not statistically significantly different from zero. There was statistically significant between-study heterogeneity for the outcomes of hospitalization, clinically significant chest pain, and unspecified chest discomfort (Table 3). Figure 3 shows a funnel plot of perforation rate versus number of dilations per study, suggesting a possible bias of small studies toward greater perforation rates (Egger test p=0.074).

Sensitivity and subgroup analyses

Sensitivity analyses excluding studies of fewer than 10 patients, with high risk of bias, or with case report or case series designs did not reveal meaningfully different results from the primary meta-analysis (Supplemental Tables 1–3). For example, overall perforation risk was 0.029% (95% CI, 0% – 0.222%) for studies with 10 or more patients. Using a logit transformation, which avoids negative values for the lower limit of confidence intervals, also did not meaningfully alter point estimates, though the confidence intervals were wider (Supplemental Table 4). Subgroup analyses revealed possible trends toward different adverse event rates by publication period, maximum dilator size, and pediatric versus adult studies, although none of these differences reached statistical significance (Supplemental Tables 5–7). For instance, the point estimates of frequency of perforation (0.0%; 95% CI, 0%–1.88%), clinically significant chest pain (2.19%; 95% CI, 0%–5.65%), and any chest discomfort (10.2%; 95% CI, 0%–23.2%) were lower for pediatric than for adult studies, although only 2 to 3 studies contributed to each of these pediatric estimates[28, 29, 36] Perforation rate with larger dilators (>17 mm) was 1.35% (95% CI, 0%–8.43%) versus 0.03% (95% CI, 0%–0.226%) for smaller dilators, hospitalization 4.02% (95% CI, 0%–16.6%) versus 0.511% (95% CI, 0%–1.08%), and clinically significant chest pain 7.14% (95% CI, 0%–19.8%) versus 4.46% (95% CI, 1.41%–7.50%). Finally, the meta-analysis confirmed the direction of association between studies published before 2009 with higher perforation rates, estimating a 0.41% (95% CI, 0%–2.75%) rate before 2009 compared with 0.030% (95% CI, 0%–0.225%) in more recent studies.

DISCUSSION

Fibrostenotic adverse events of eosinophilic esophagitis include strictures and narrowing, and many patients may require esophageal dilation in addition to anti-inflammatory therapy. In the early 2000s, numerous reports emerged suggesting that dilation in EoE patients was fraught with risk, especially of esophageal perforation.[19, 22, 42, 43] In more recent years, a

much larger literature has emerged, suggesting that esophageal dilation can be performed safely. This systematic review and meta-analysis found that the cumulative published rate of perforation is quite low with dilation in EoE, occurring in 0.033% of procedures, and possibly even fewer in the modern era. Therefore, the risk of perforation approximates that of esophageal dilation for other benign indications.[18, 44–47] Although we identified no studies directly comparing bougie and balloon dilation, both techniques had similar safety profiles.

This study extends prior systematic reviews of dilation in EoE, published from 2007 to 2013[23–25,48] by including a meta-analysis. The current study also incorporates ten new, large cohort studies comprising 840 dilations compared with the most recent systematic review of the safety of dilation in EoE.[25] We included a broader range of study designs in order to capture the perforations in case reports, and demonstrated perforation rates consistent with the estimates of prior reviews of 0% to 0.3%.[23–25, 48] Even the unweighted pooled perforation rate of 0.44% (9/2034 dilations) in EoE-related strictures is comparable with the 0.4% cited for other benign causes of stricture,[45] also noting that refractory or other "difficult" benign strictures may result in higher rates of severe adverse events.[44] Furthermore, it is likely that the perforation rates from our study are conservatively high estimates, as higher-quality studies from the era of increased gastroenterologist awareness of EoE yielded a 13-fold decreased perforation rate (0.03% vs 0.41%, Supplemental Table 5), and there was only one confirmed transmural perforation in all of the dilations reviewed. Although there are likely many perforations and severe adverse events that occur in dilations for EoE and are not reported, the general bias of uncontrolled studies such as case series and case reports, included in this review, is toward selectively reporting adverse events rather than uneventful procedures. The funnel plot of published studies suggests such a tendency, though warrants cautious interpretation due to the impossibility of a completely symmetric funnel distribution when the point estimate approaches zero.

Additionally, this review included an experience with pediatric patients, and explored the safety profiles of different dilation methods (balloon and bougienage). In contrast to the caution regarding dilation recommended in recent guidelines,[49] the largest pediatric cohorts to date by Menard-Katcher et al and Al-Hussaini suggest that dilation can also be a safe and effective option for the appropriately selected pediatric patient. In fact, none of the reported perforations occurred in patients younger than 17 years of age,[41] which could reflect the inverse relationship of esophageal compliance with duration of uncontrolled disease activity.[7] Regarding dilator type, our review was limited by study heterogeneity and incomplete procedure-level data. The majority of balloon dilations in particular (681/837 procedures), were contributed by only 6 centers, and may not be generalizable to providers less experienced with this technique. In the absence of prospective data, we would agree with prior recommendations that dilator choice be tailored to the endoscopist's preference and experience, with consideration of stricture anatomy and procedural characteristics.[18, 45]

Though not definitive, our findings also support the straightforward notion that dilator size and aggressiveness are other risk factors for adverse events. Thus, we endorse the recommendations of others to "start low and go slow,"[18, 27] taking as many dilation sessions as necessary to achieve symptomatic relief in a controlled fashion. Perforation risk likely

depends more on the change in esophageal diameter in any one session than absolute dilator size, though few studies in our review reported the former metric. It may also be beneficial to pair dilation with a medical or dietary anti-inflammatory intervention, as dilation does not affect esophageal eosinophilia,[13, 50] and repeat dilations are needed more frequently if inflammation is not controlled.[12, 15, 36]

Limitations of this systematic review lie in the heterogeneity of types and definitions of outcomes reported across studies, as well as large variation in study methodology and quality. Only 2 out of 37 studies were prospective, and nearly half described single-digit numbers of patients in uncontrolled designs. All studies reported on perforations, but for each of the other included adverse events, less than 2/3 of the studies contributed to each total. As a result, our estimates may suffer from a lack of precision. Pain in particular is likely vastly underreported, and the studies reviewed showed tremendous variability in the definition, collection, and reporting of this symptom. Additionally, some “discomfort” may even be expected postprocedurally, so much so that patients can be forewarned about this symptom and reassured that it may represent an effective procedure.[18]

Another potential limitation is that we did not include all of the adverse events reported in some of the featured studies. For example, many earlier studies reported high incidences of “mucosal tears” or “rents.”[22, 26, 27, 36, 48, 51, 52] The EoE community has since come to a consensus that such findings are an expected and even desired result of successful dilation.[11, 21, 53] Last, our search strategy may have missed important reports of adverse events from the period before eosinophilic esophagitis was widely recognized. Several studies referred to patients with “ringed esophagus,” “stiff or slender esophagus,” or “congenital esophageal stenosis,” which probably described EoE.[42, 54–56] We did not include these in the formal review in order to preserve the systematic nature of the search strategy, limiting the inclusion of non-EoE diagnoses in an already heterogeneous group of studies and patients. The included group of studies still represents the overwhelming majority of experience with the disease entity now recognized as eosinophilic esophagitis.

This study also has a number of strengths. These include a rigorous systematic review and meta-analysis methodology in accordance with guidelines, comprehensive searching of both published and abstract data, multiple levels of checks on data extraction, and sub-analyses by dilator type and publication period. The result more than doubles the number of dilations analyzed in prior reviews,[23–25] lending greater confidence to the conclusion that dilation is a safe procedure in EoE.

In conclusion, this systematic review and meta-analysis found that esophageal dilation in EoE is safe, with an estimated perforation rate of 0.033% (95% CI, 0–0.226). Moreover, it appears that dilation with either a balloon or bougie technique has a similar safety profile. The finding that perforation rates are even lower in the last 6 to 7 years suggests that either there has been a degree of publication bias (reports of patients with a adverse event were preferentially published) or that gastroenterologists have learned from the early reports, become more aware of EoE, and subsequently adapted their dilation techniques to maximize the safety of the procedure. Dilation should be considered a safe, symptom-relieving procedural adjunct to dietary and medical interventions. Current knowledge gaps can be

addressed with prospective interventional studies comparing different combinations of anti-inflammatory and dilation treatments, to better establish the approach that optimally balances safety, efficacy, and patient preference in a cost-effective manner.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support: This research was funded by NIH Awards T32 DK007634 (MD, TMR, SE) and R01 DK101856(ESD)

ACRONYMS

EoE	Eosinophilic Esophagitis
RCT	randomized controlled trial
TTS	through the scope

References

1. Arias Á, Pérez-Martínez I, Tenías JM, et al. Systematic review with meta-analysis: the incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. Alimentary Pharmacology & Therapeutics. 2016; 43:3–15.
2. Jensen ET, Kappelman MD, Martin CF, et al. Health care utilization, costs, and the burden of disease related to eosinophilic esophagitis in the United States. The American journal of gastroenterology. 2015; 110:626–632. [PubMed: 25267327]
3. Dellon ES, Liacouras CA. Advances in Clinical Management of Eosinophilic Esophagitis. Gastroenterology. 2014; 147:1238–1254. [PubMed: 25109885]
4. Straumann A, Bussmann C, Zuber M, et al. Eosinophilic Esophagitis: Analysis of Food Impaction and Perforation in 251 Adolescent and Adult Patients. Clinical Gastroenterology and Hepatology. 2008; 6:598–600. [PubMed: 18407800]
5. Dellon ES, Kim HP, Sperry SLW, et al. A phenotypic analysis shows eosinophilic esophagitis is a progressive fibrostenotic disease. Gastrointestinal endoscopy. 2014; 79:577–85.e4. [PubMed: 24275329]
6. Hirano I, Aceves SS. Clinical Implications and Pathogenesis of Esophageal Remodeling in Eosinophilic Esophagitis. Gastroenterology clinics of North America. 2014; 43:297–316. [PubMed: 24813517]
7. Eluri S, Runge TM, Cotton CC, et al. The extremely narrow-caliber esophagus is a treatment-resistant subphenotype of eosinophilic esophagitis. Gastrointestinal Endoscopy. 2016; 83:1142–1148. [PubMed: 26608127]
8. Aceves SS, Newbury RO, Chen D, et al. Resolution of remodeling in eosinophilic esophagitis correlates with epithelial response to topical corticosteroids. Allergy. 2010; 65:109–116. [PubMed: 19796194]
9. Lucendo AJ, Arias Á, De Rezende LC, et al. Subepithelial collagen deposition, profibrogenic cytokine gene expression, and changes after prolonged fluticasone propionate treatment in adult eosinophilic esophagitis: A prospective study. Journal of Allergy and Clinical Immunology. 2011; 128:1037–1046. [PubMed: 21880354]
10. Straumann A, Conus S, Degen L, et al. Long-Term Budesonide Maintenance Treatment Is Partially Effective for Patients With Eosinophilic Esophagitis. Clinical Gastroenterology and Hepatology. 2011; 9:400–409.e1. [PubMed: 21277394]

11. Richter JE. Esophageal dilation in eosinophilic esophagitis. Best Practice & Research. 2015; 29:815–828.
12. Runge TM, Eluri S, Cotton CC, et al. Outcomes of Esophageal Dilation in Eosinophilic Esophagitis: Safety, Efficacy, and Persistence of the Fibrostenotic Phenotype. Am J Gastroenterol. 2016; 111:206–213. [PubMed: 26753894]
13. Schoepfer AM, Gonsalves N, Bussmann C, et al. Esophageal Dilation in Eosinophilic Esophagitis: Effectiveness, Safety, and Impact on the Underlying Inflammation. Am J Gastroenterol. 2010; 105:1062–1070. [PubMed: 19935783]
14. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in Diagnosis of Eosinophilic Esophagitis Increases Risk for Stricture Formation in a Time-Dependent Manner. Gastroenterology. 2013; 145:1230–1236.e2. [PubMed: 23954315]
15. Lipka S, Keshishian J, Boyce HW, et al. The natural history of steroid-naïve eosinophilic esophagitis in adults treated with endoscopic dilation and proton pump inhibitor therapy over a mean duration of nearly 14 years. Gastrointestinal Endoscopy. 2014; 80:592–598. [PubMed: 24703087]
16. Dellon ES, Gonsalves N, Hirano I, et al. ACG Clinical Guideline: Evidenced Based Approach to the Diagnosis and Management of Esophageal Eosinophilia and Eosinophilic Esophagitis (EoE). The American Journal of Gastroenterology. 2013; 108:679–692. [PubMed: 23567357]
17. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: Updated consensus recommendations for children and adults. Journal of Allergy and Clinical Immunology. 2011; 128:3–20.e6. [PubMed: 21477849]
18. Richter JE. Editorial: Eosinophilic Esophagitis Dilation in the Community–Try It, You will Like It–But Start Low and Go Slow. Am J Gastroenterol. 2016; 111:214–216. [PubMed: 26882944]
19. Cohen MS, Kaufman AB, Palazzo JP, et al. An Audit of Endoscopic Complications in Adult Eosinophilic Esophagitis. Clinical Gastroenterology and Hepatology. 2007; 5:1149–1153. [PubMed: 17683993]
20. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic Esophagitis in Children and Adults: A Systematic Review and Consensus Recommendations for Diagnosis and Treatment. Gastroenterology. 2007; 133:1342–1363. [PubMed: 17919504]
21. Hirano I. Dilation in eosinophilic esophagitis: to do or not to do? Gastrointestinal Endoscopy. 2010; 71:713–714. [PubMed: 20363413]
22. Kaplan M, Mutlu EA, Jakate S, et al. Endoscopy in eosinophilic esophagitis: “feline” esophagus and perforation risk. Clinical Gastroenterology and Hepatology. 2003; 1:433–437. [PubMed: 15017642]
23. Bohm ME, Richter JE. Review article: oesophageal dilation in adults with eosinophilic oesophagitis. Alimentary Pharmacology & Therapeutics. 2011; 33:748–757. [PubMed: 21320137]
24. Jacobs JW, Spechler SJ. A Systematic Review of the Risk of Perforation During Esophageal Dilation for Patients with Eosinophilic Esophagitis. Digestive diseases and sciences. 2010; 55:1512–1515. [PubMed: 20238250]
25. Moawad FJ, Cheatham JG, DeZee KJ. Meta-analysis: the safety and efficacy of dilation in eosinophilic oesophagitis. Alimentary Pharmacology & Therapeutics. 2013; 38:713–720. [PubMed: 23915046]
26. Dellon ES, Gibbs WB, Rubinas TC, et al. Esophageal dilation in eosinophilic esophagitis: safety and predictors of clinical response and complications. Gastrointestinal Endoscopy. 2010; 71:706–712. [PubMed: 20170913]
27. Jung KW, Gundersen N, Kopacova J, et al. Occurrence of and risk factors for complications after endoscopic dilation in eosinophilic esophagitis. Gastrointestinal Endoscopy. 2011; 73:15–21. [PubMed: 21067739]
28. Menard-Katcher C, Furuta GT, Kramer RE. Dilation of Pediatric Eosinophilic Esophagitis-Adverse Events and Short Term Outcomes. Journal of Pediatric Gastroenterology and Nutrition. 2017 [Epub ahead of print].
29. Al-Hussaini A. Savary Dilation is Safe and Effective Treatment for Esophageal Narrowing Related to Pediatric Eosinophilic Esophagitis. Journal of Pediatric Gastroenterology and Nutrition. 2016; 63:474–480. [PubMed: 27111342]

30. Kavitt RT, Ates F, Slaughter JC, et al. Randomized controlled trial comparing esophageal dilation to no dilation among adults with esophageal eosinophilia and dysphagia. Diseases of the Esophagus. 2015; 29:983–991. [PubMed: 26228516]
31. Saligram S, McGrath K. The safety of a strict wire-guided dilation protocol for eosinophilic esophagitis. European Journal of Gastroenterology & Hepatology. 2014; 26:699–703. [PubMed: 24901815]
32. Ukleja A, Shiroky J, Agarwal A, et al. Esophageal dilations in eosinophilic esophagitis: A single center experience. World Journal of Gastroenterology : WJG. 2014; 20:9549–9555. [PubMed: 25071351]
33. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of Clinical Epidemiology. 2009; 62:e1–e34. [PubMed: 19631507]
34. Dekkers OM, Egger M, Altman DG, et al. Distinguishing case series from cohort studies. Annals of internal medicine. 2012; 156:37–40. [PubMed: 22213493]
35. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives of Public Health. 2014; 72:39. [PubMed: 25810908]
36. Robles-Medranda C, Villard F, le Gall C, et al. Severe Dysphagia in Children With Eosinophilic Esophagitis and Esophageal Stricture: An Indication for Balloon Dilation? Journal of Pediatric Gastroenterology and Nutrition. 2010; 50:516–520. [PubMed: 19934772]
37. Simpson A, Wilson MSJ, Ellefson A, et al. PTU-164 The clinical utility of the endoscopic functional luminal imaging probe in eosinophilic oesophagitis: a case series. Gut. 2012; 61:A252–A253.
38. Dhalla S, D J, BS B, et al. Through-the-scope hydrostatic balloon dilation of strictures and rings is associated with low incidence of perforation in adults with eosinophilicesophagitis and dysphagia: The four-year experience of a single tertiary-care medical center. Gastroenterology (New York, NY 1943). 2012; 142:S439.
39. Lee GS-C, Craig PI, Freiman JS, et al. Intermittent Dysphagia for Solids Associated with a Multiringed Esophagus: Clinical Features and Response to Dilatation. Dysphagia. 2007; 22:55–62. [PubMed: 17216404]
40. Seeger K, Achem SR. Hepatic Portal Venous Gas: An Unusual Complication Following Upper Endoscopy and Dilation. ACG Case Reports Journal. 2014; 1:128–130. [PubMed: 26157850]
41. Eisenbach CC, Merle U, Schirmacher P, et al. Perforation of the esophagus after dilation treatment for dysphagia in a patient with eosinophilic esophagitis. Endoscopy. 2006; 38 (Suppl 2):E43–E44. [PubMed: 17123211]
42. Morrow JB, Vargo JJ, Goldblum JR, et al. The ringed esophagus: histological features of GERD. Am J Gastroenterol. 2001; 96:984–989. [PubMed: 11316216]
43. Straumann A, Rossi L, Simon H-U, et al. Fragility of the esophageal mucosa: A pathognomonic endoscopic sign of primary eosinophilic esophagitis? Gastrointestinal Endoscopy. 2003; 57:407–412. [PubMed: 12612531]
44. Repici A, Small AJ, Mendelson A, et al. Natural history and management of refractory benign esophageal strictures. Gastrointestinal Endoscopy. 2016; 84:222–228. [PubMed: 26828759]
45. Siersema PD, de Wijkerslooth LRH. Dilation of refractory benign esophageal strictures. Gastrointestinal Endoscopy. 2009; 70:1000–1012. [PubMed: 19879408]
46. Grooteman KV, Wong Kee, Song LM, Vleggaar FP, et al. Non-adherence to the rule of 3 does not increase the risk of adverse events in esophageal dilation. Gastrointestinal Endoscopy. 2016
47. Hagel AFAF, Naegel A, Dauth W, et al. Perforation during esophageal dilatation: a 10-year experience. Journal of gastrointestinal and liver diseases : JGLD. 2013; 22:385–389. [PubMed: 24369319]
48. Pasha SF, DiBaise JK, Kim HJ, et al. Patient characteristics, clinical, endoscopic, and histologic findings in adult eosinophilic esophagitis: a case series and systematic review of the medical literature. Diseases of the Esophagus. 2007; 20:311–319. [PubMed: 17617880]
49. Papadopoulou A, Koletzko S, Heuschkel R, et al. Management Guidelines of Eosinophilic Esophagitis in Childhood. Journal of Pediatric Gastroenterology and Nutrition. 2014; 58:107–118. [PubMed: 24378521]

50. Bohm M, Richter JE, Kelsen S, et al. Esophageal dilation: simple and effective treatment for adults with eosinophilic esophagitis and esophageal rings and narrowing. Diseases of the Esophagus. 2010; 23:377–385. [PubMed: 20353444]
51. Croese J, Fairley SK, Masson JW, et al. Clinical and Endoscopic Features of Eosinophilic Esophagitis in Adults. Gastrointestinal Endoscopy. 2003; 58:516–522. [PubMed: 14520283]
52. Potter JW, Saeian K, Staff D, et al. Eosinophilic esophagitis in adults: An emerging problem with unique esophageal features. Gastrointestinal Endoscopy. 2004; 59:355–361. [PubMed: 14997131]
53. Straumann A, Spichtin H-p, Grize L, et al. Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years. Gastroenterology. 2003; 125:1660–1669. [PubMed: 14724818]
54. Attwood SE, Smyrk TC, Demeester TR, et al. Esophageal eosinophilia with dysphagia. Digestive diseases and sciences. 1993; 38:109–116. [PubMed: 8420741]
55. Langdon D. Corrugated ringed esophagus. The American journal of gastroenterology. 1993; 88:1461–1461.
56. McKinley M, Eisner T, Fisher M, et al. Multiple rings of the esophagus associated with gastroesophageal reflux [case report]. The American journal of gastroenterology. 1996; 91:574–576. [PubMed: 8633512]
57. Ahn Y, Coomarasamy C, Ogra R. Efficacy of intralesional triamcinolone injections for benign refractory oesophageal strictures at Counties Manukau Health, New Zealand. The New Zealand Medical Journal (Online). 2015; 128:44–50.
58. Lenglinger J, Rieder E, Mesteri I, et al. Dilation of an esophageal stricture using a balloon with integrated impedance planimetry imaging. Diseases of the esophagus. 2014; 27:3A–168A.
59. Ally MR, Dias J, Veerappan GR, et al. Safety of dilation in adults with eosinophilic esophagitis. Diseases of the Esophagus. 2013; 26:241–245. [PubMed: 22676406]
60. Enns R, Kazemi P, Chung W, et al. Eosinophilic esophagitis: Clinical features, endoscopic findings and response to treatment. Canadian Journal of Gastroenterology. 2010; 24:547–551. [PubMed: 21152459]
61. Shepherd BD, Slaughter JC, Vaezi MF. S1869 Eosinophilic Esophagitis: Dilate or Medicate? Gastroenterology (New York, NY 1943). 2009; 136:A-281–A-282.
62. Jawa H, Chande N. Dilation treatment in eosinophilic esophagitis. Canadian journal of gastroenterology. 2009; 23(suppl)
63. Rajagopalan J, Triadafilopoulos G. Ring(s)-related esophageal meat bolus impaction: biopsy first, dilate later. Diseases of the Esophagus. 2009; 22:E14–E16. [PubMed: 19018847]
64. Zuber-Jerger II, Ratiu N, Kullman F. Long-lasting effect of endoscopic dilatation of an esophageal stenosis due to eosinophilic esophagitis. Journal of gastrointestinal and liver diseases : JGLD. 2006; 15:167–170. [PubMed: 16802012]
65. Cantù P, Velio P, Prada A, et al. Ringed oesophagus and idiopathic eosinophilic oesophagitis in adults: an association in two cases. Digestive and Liver Disease. 2005; 37:129–134. [PubMed: 15733527]
66. Kumar KS, Smith JW. Eosinophilic Esophagitis: The Ochsner Clinic experience. American Journal of Gastroenterology. 2005; 100:S41–S41.
67. Vasilopoulos S, Murphy P, Auerbach A, et al. The small-caliber esophagus: An unappreciated cause of dysphagia for solids in patients with eosinophilic esophagitis. Gastrointestinal Endoscopy. 2002; 55:99–106. [PubMed: 11756928]
68. Mahajan L, Wyllie R, Petras R, et al. Idiopathic eosinophilic esophagitis with stricture formation in a patient with long-standing eosinophilic gastroenteritis. Gastrointestinal Endoscopy. 1997; 46:557–560. [PubMed: 9434228]
69. Feczko PJP. Radiographic abnormalities in eosinophilic esophagitis. Gastrointestinal radiology. 1985; 10:321–324. [PubMed: 4054495]

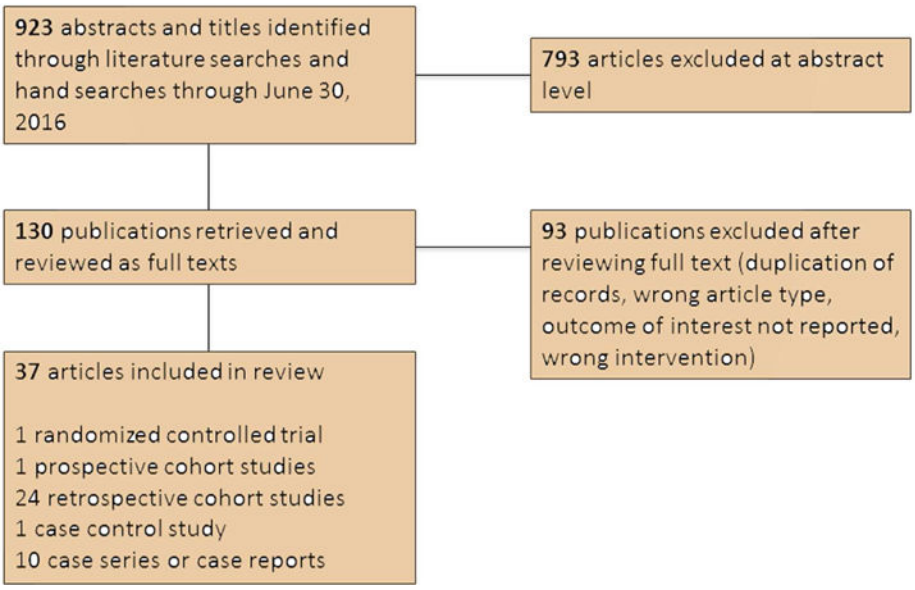
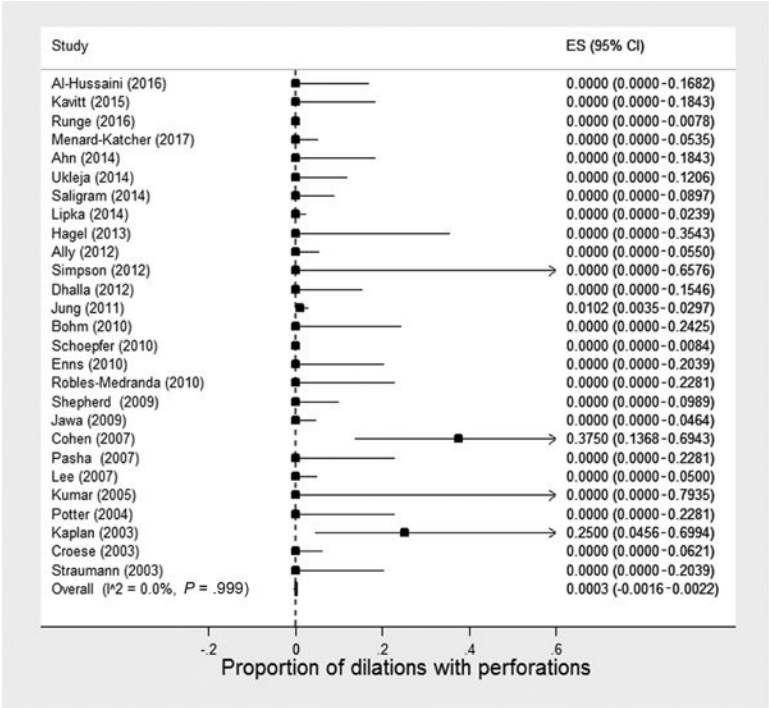
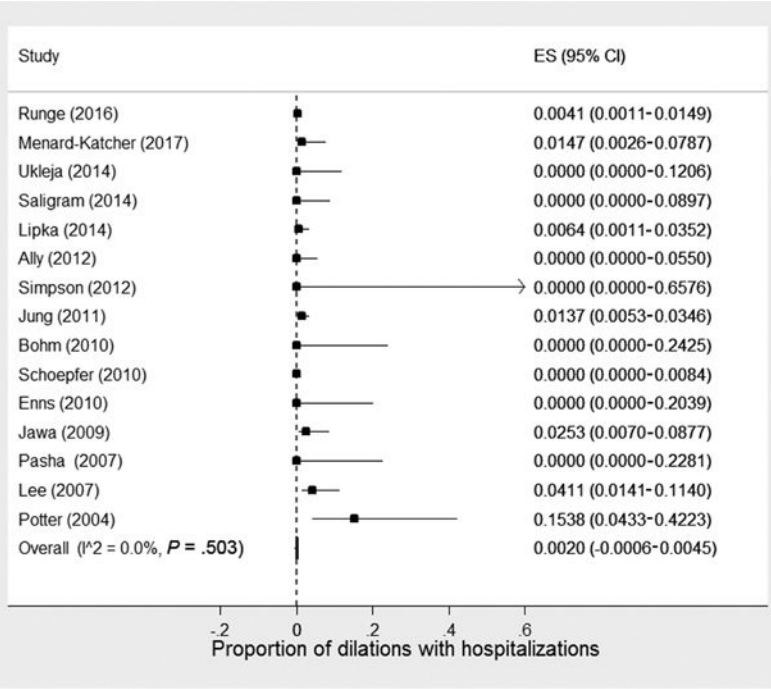
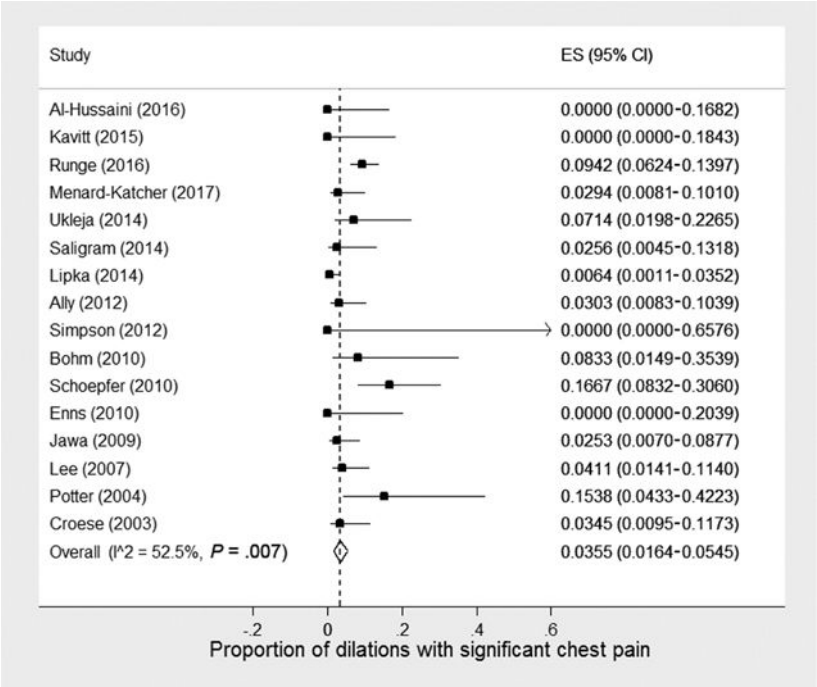


Figure 1.
Results of search strategy.







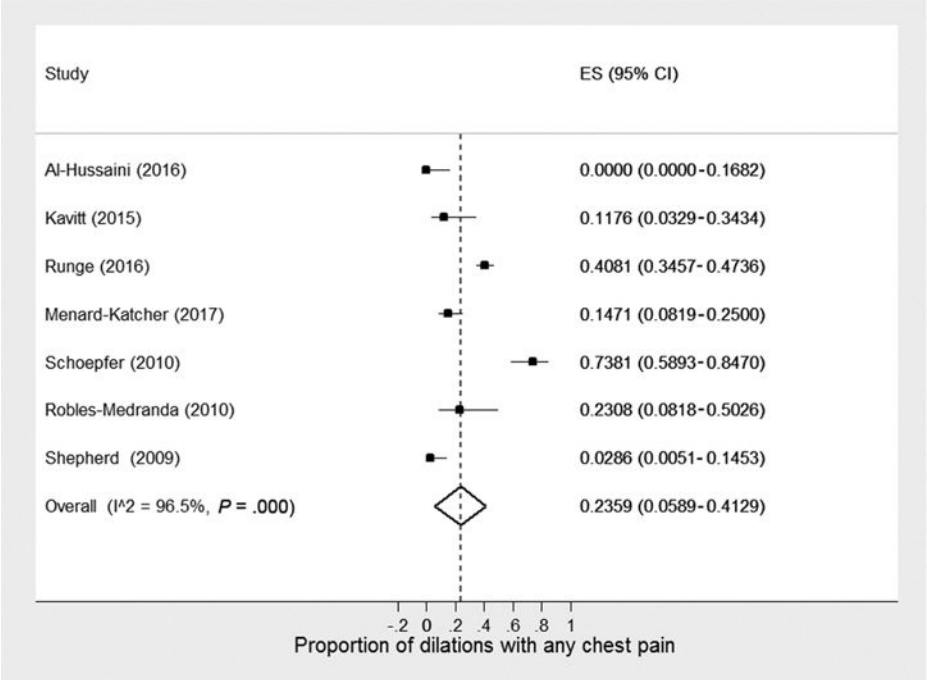


Figure 2.

Forest plots of random-effects meta-analysis for (A) perforation, (B) hospitalization, (C) clinically significant chest pain, and (D) unspecified chest pain. Case series and case reports not displayed. The boxes represent the point estimate, and the bars represent the 95% confidence intervals which are left-truncated as it is not possible to have a proportion less than zero in this meta-analysis (ES, effect size. CI, confidence interval. I^2, the percentage of total variation across studies that is due to heterogeneity rather than chance.)

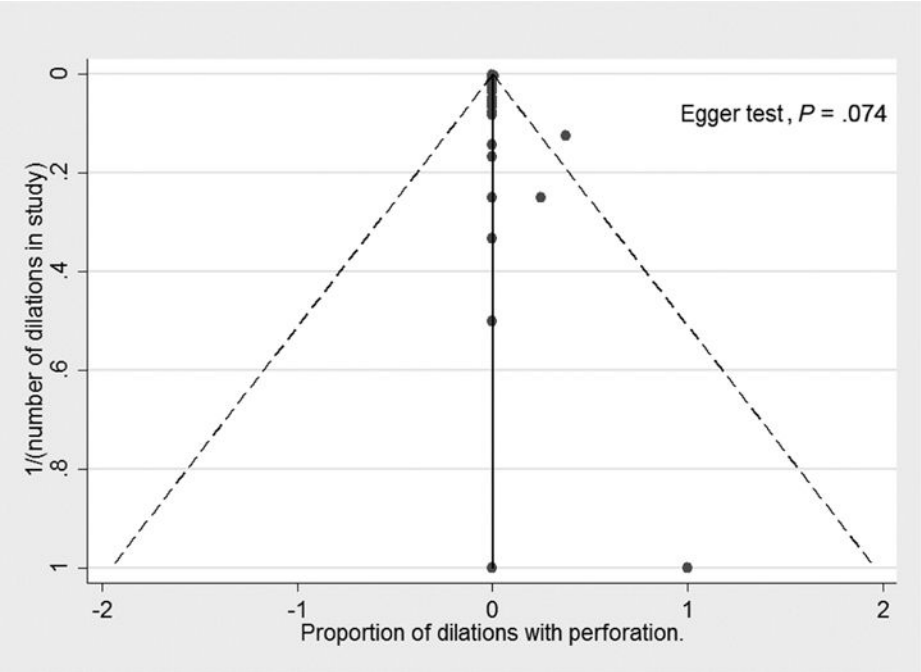


Figure 3.

Funnel plot of perforation rate by study size (1/number of dilations), with 95% pseudo-confidence limits.

Table 1

Characteristics of original publications of esophageal dilation in eosinophilic esophagitis.

Author	Year	Study Type	Risk of Bias	EoE patients	EoE pts dilated	Total Dilations	Mean age, SD/ Range	Male	Balloon dilators, n (%)	Bougie dilators, n (%)
Menard-Katcher[28]	2017	Retrospective cohort	Moderate	781	40	68	13.8 (+/−3.3)	73%	11 (28)	36 (72)
Al-Hussaini[29]	2016	Retrospective Cohort	High	50	10	19	8.2 (+/−3.8)	78%	0	19 (100)
Runge[12]	2016	Retrospective cohort	Moderate	509	164	486	39 (+/−15)	71%	395 (81)	91 (19)
Kavitt[30]	2015	RCT	Moderate	31	17	17	35 (IQR 23–39)	65%	0	17 (100)
Ahn[57]	2014	Retrospective cohort	High	3	3	17	76 (+/−12)	0%	NR	NR
Ukleja[32]	2014	Retrospective cohort	Moderate	61	22	28	38 (18–61)	72%	24 (86)	4 (14)
Sahgram[31]	2014	Retrospective Cohort	High	30	30	39	33 (NR)	90%	0	39 (100)
Lipka[31]	2014	Retrospective Cohort	High	13	13	157	30 (15–57)	77%	4 (3)	153 (97)
Lenglinger[58]	2014	Case report†	High	1	1	1	19 (NA)	100%	1 (100)	0
Seeger[40]	2014	Case report	High	1	1	1	34 (NA)	100%	1 (100)	0
Hagel[47]	2013	Retrospective cohort	Moderate	4	4	7	NR	NR	2 (29)	5 (71)
Ally[59]	2012	Retrospective cohort	Moderate	196	54	66	41 (+/−12)	85%	13 (19)	53 (80)
Simpson[37]	2012	Retrospective Cohort†	High	5	2	2	NR	NR	2 (100)	0
Dhalla[38]	2012	Retrospective Cohort†	High	19	19	21	38 (+/−15)	71%	21 (100)	0
Jung[27]	2011	Retrospective cohort	Moderate	161	161	293	44 (+/−15)	70%	216 (74)	77 (26)
Bohm[50]	2010	Retrospective Cohort	High	16	9	12	41 (+/−11)	75%	0	11 (100)
Schoepfer[13]	2010	Retrospective cohort	Moderate	681	207	453	43 (+/−13)	80%	NR (22)	NR (78)
Enns[60]	2010	Retrospective cohort	High	54	15	15	44 (+/−14)	76%	NR	NR
Robles-Medranda[36]	2010	Retrospective cohort	Moderate	13	4	13	13 (+/−4.4)	77%	13 (100)	0
Shepherd[61]	2009	Retrospective cohort†	High	58	35	35	36 (+/−11)	71%	NR	NR
Jawa[62]	2009	Retrospective Cohort†	High	58	51	79	35 (NR)	85%	NR (10)	NR (90–98)
Rajagopalan[63]	2009	Case report	High	1	1	2	30 (NA)	0%	0	2 (100)
Cohen[19]	2007	Case-control	Moderate	36	8	8	34 (+/−2.0)	78%	5 (63)	2 (25)‡
Pasha[48]	2007	Retrospective cohort	High	42	13	13	44 (+/−16)	74%	12 (92)	1 (8)

Author	Year	Study Type	Risk of Bias	EoE patients	EoE pts dilated	Total Dilations	Mean age, SD/ Range	Male	Balloon dilators, n (%)	Bougie dilators, n (%)
Lee[39]	2007	Retrospective Cohort	High	32	32	73	37 (IQ R21–49)	75%	0	73 (100)
Eisenbach[41]	2006	Case report	High	1	1	1	17 (NA)	0%	NR	NR
Zuber-Jerger[64]	2006	Case report	High	1	1	1	26 (NA)	100%	0	1 (100)
Cantu	2005	Case Series	High	2	2	3	34 (+/−A2.8)	100%	0	(3 (100)
Kumar[66]	2005	Retrospective cohort †	High	8	1	1	35 (26–50)	75%	NR	NR
Potter[52]	2004	Retrospective cohort	High	29	13	13	35 (19–65)	72%	1(8)	12 (92)
Kaplan[22]	2003	Retrospective cohort	High	8	4	4	27 (+/−A6.3)	75%	NR	NR‡
Croese[51]	2003	Retrospective cohort	High	31	17	58	34 (14–77)	78%	0	58 (100)
Straumann[43]	2003	Case series	High	5	4	4	38 (+/−11)	100%	0	4(100)
Straumann[53]	2003	Prospective cohort	Moderate	30	11	15	33 (6–65)	73%	0	11 (100)
Vasilopolous[67]	2002	Case series	High	4	4	6	25 (+/−5.6)	100%	0	7 (100)
Mahajan[68]	1997	Case report	High	1	1	1	27 (NA)	100%	0	1 (100)
Feczko[69]	1985	Case series	High	3	2	2	37 (+/−17)	66%	NR	NR

SD, standard deviation (where available); IQR, interquartile range; NR, not reported; NA, not applicable; pts, patients.

† Meeting abstract

‡ One patient in each of these series was dilated using the endoscope as a dilator.

Table 2

Outcomes and adverse events of esophageal dilation in eosinophilic esophagitis.

Author	Year	Balloon dilators, n (%)	Bougie dilators, n (%)	Clinical improvement	Mean follow-up (months), SD/ Range	Perforations, n	Hospitalizations, n	GI Bleed, n	Significant chest pain, %	Any chest pain, %
Menard-Katcher[28]	2017	11 (28)	36 (72)	86%	17.6 (+/−18.4)	0	1	0	2.9%	14.7%
Al-Hussaini[29]	2016	0	19 (100)	100%	30 (12–108)	0	NA*	0	0%	0%
Runge[12]	2016	395 (81)	91 (19)	87%	15(IQR 5–48)	0	2	0	9.4%	40.8%‡
Kavitt[30]	2015	0	17 (100)	92%	2 (+/−0)	0	NR	0	0%	11.8%
Ahn[57]	2014	NR	NR	NR	NR	0	NR	NR	NR	NR
Ukleja[32]	2014	24 (86)	4 (14)	NR	59 (+/−18)	0	0	0	7.1%	NR
Saligram[31]	2014	0	39 (100)	100%	48 (NR)	0	0	0	2.6%	NR
Lipka[31]	2014	4 (3)	153 (97)	85%	168 (60–288)	0	1	0	0.64%	NR
Lenglinger[†58]	2014	1 (100)	0	100%	0.25 (NA)	0	0	0	NR	NR
Seeger[†40]	2014	1 (100)	0	NR	6 (NA)	1	1	0	NR§	NR§
Hagel[47]	2013	2 (29)	5 (71)	NR	NR	0	NR	NR	NR	NR
Ally[59]	2012	13 (19)	53 (80)	NR	NR	0	0	0	3.0%	NR
Simpson[†37]	2012	2 (100)	0	100%	NR	0	0	0	0%	NR
Dhalla[†38]	2012	21 (100)	0	NR	NR	0	NR	NR	NR	NR
Jung[27]	2011	216 (74)	77 (26)	NR	NR	3	4	1	NR	NR
Bohm[50]	2010	0	11 (100)	89%	22 (+/−9.9)	0	0	0	8.3%	NR
Schoepfer[13]	2010	NR (22)	NR (78)	93%	25 (+/−19)	0	0	0	16.7%	73.8%‡
Enns[60]	2010	NR	NR	80%	6 (NR)	0	0	0	0%	NR
Robles-Medranda[36]	2010	13 (100)	0	100%	36 (+/−10)	0	NA*	NR	NR	23.1%
Shepherd[†61]	2009	NR	NR	97%	5 (1–12)	0	NR	NR	NR	2.9%
Jawa[†62]	2009	NR (10)	NR (90–98)	79%	NR	0	2	NR	2.5%	NR
Rajagopalan[63]	2009	0	2 (100)	100%	6 (NA)	0	NR	NR	50%	NR
Cohen[19]	2007	5 (63)	2 (25)	NR	NR	3	NR	NR	NR	NR
Pasha[48]	2007	12 (92)	1 (8)	85%	NR	0	0	NR	NR	NR

Author	Year	Balloon dilators, n (%)	Bougie dilators, n (%)	Clinical improvement	Mean follow-up (months), SD/ Range	Perforations, n	Hospitalizations, n	GI Bleed, n	Significant chest pain, %	Any chest pain, %
Lee[39]	2007	0	73 (100)	75%	6 (NR)	0	3	0	4.1%	NR
Eisenbach[41]	2006	NR	NR	NR	1 (NA)	1	1	0	NR	NR
Zuber-Jerger[64]	2006	0	1 (100)	100%	36 (NA)	0	0	0	0%	NR
Cantu[65]	2005	0	3 (100)	100%	14.7 (+/−6.4)	0	0	NR	NR	NR
Kumar[66]	2005	NR	NR	NR	NR	0	NR	NR	NR	NR
Potter[52]	2004	1 (8)	12 (92)	54%	NR	0	2	NR	15.4%	NR
Kaplan[22]	2003	NR	NR¶	NR	NR	1	NR	NR	NR	NR
Croese[51]	2003	0	58 (100)	94%	NR	0	NR	0	3.4%	NR
Straumann[43]	2003	0	4 (100)	100%	14 (+/−8.2)	0	0	0	0%	NR
Straumann[53]	2003	0	11 (100)	91%	86 (17–138)	0	NR	NR	NR	NR
Vasilopolous[67]	2002	0	7 (100)	100%	12 (NR)	0	2	NR	33.3%	NR
Mahajan[68]	1997	0	1 (100)	100%	6 (NA)	0	0	NR	NR	NR
Feczko[69]	1985	NR	NR	100%	NR	0	NR	NR	NR	NR

SD, standard deviation (where available); IQR, interquartile range; NR, not reported; NA, not applicable

*AII patients in these pediatric studies were hospitalized for 24 hours post-procedure, per protocol.

†Meeting abstract

‡Information on post-dilation discomfort was only available for a portion of these cohorts, N=223 for Runge et al, and N=42 for Schoepfer et al.

§This patient experienced epigastric but not chest pain.

The cases of perforation reported pain, but for the rest of the cohort the authors were “unable to access information concerning the frequency of postdilation pain.”

¶One patient in each of these series was dilated using the endoscope as a dilator. Cohen et al did not report dilator type used in cases of perforation, and the endoscope caused the perforation in Kaplan.

Table 3

Random-effects meta-analysis of adverse events from dilations in eosinophilic esophagitis.

Adverse event (number of studies contributing data)	Point estimate, % of procedures	95% CI*, % of procedures	Heterogeneity (I^2)12, *P* value
Perforation (37)	0.033	0 – 0.226	0%, P=0.73
Bougie (23)	0.022	0 – 0.347	0%, P=1.0
Balloon (16)	0.059	0 – 0.374	0%, P=0.71
Hospitalization (22)	0.689	0 – 1.42	44.0%, P= 0.015
GI hemorrhage (20)	0.028	0 – 0.217	0%, P=1.0
Clinically significant chest pain (20)	3.64	1.73 – 5.55	47.3%, P = 0.010
Any chest discomfort (7)	23.6	5.89–41.3	96.5%, P<0.0001

*CI, Confidence Interval. All lower limits truncated at zero. Meta-analysis conducted with a continuity correction of 0.5. For those adverse events with 0% heterogeneity, estimates are identical to those of fixed-effects meta-analysis.

†I-squared, defined as the percentage of total variation across studies that is due to heterogeneity rather than chance.