Received: 22 April 2024 | Accepted: 25 June 2024

DOI: 10.1002/jpn3.12323

JPGN

SHORT COMMUNICATION

Gastroenterology: Eosinophilic Gastrointestinal Disorders

# Utilization and impact of esophageal string testing in children with eosinophilic esophagitis: A 1 year experience

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**Funding information**

None

## Abstract

The 1-h esophageal string test (EST) is a minimally invasive test that can be used to monitor eosinophilic esophagitis (EoE) disease activity and guide treatment without endoscopy. We aimed to describe the real-world utilization and impact of EST on the care of children with EoE over the first year this was used at our center. Between 12/1/2022 and 11/30/2023, 39 ESTs were successful in 45 attempts (87% completion rate) in 31 patients. Five patients underwent multiple ESTs. Adverse events during the EST included vomiting. Reasons for failure to complete the EST (13%, $n = 6$) were patients could not swallow the capsule ($n = 5$) and vomiting ($n = 1$). EST was used to assess EoE without the need for endoscopy in 95% ($n = 37$) of cases. Treatment approach varied based on whether the EST indicated active (38.5%) or inactive (61.5%) EoE. The EST is a well-tolerated minimally invasive disease monitoring tool for patients with EoE.

**KEYWORDS**

disease activity, minimally invasive, nonendoscopic

## 1 | INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic condition driven by a dysregulated Th2 immune response that is characterized by clinical symptoms of esophageal dysfunction and esophageal mucosal eosinophilia. Disease activity is measured using a combination of both symptoms and esophageal inflammation.[1] Endoscopy with biopsy is the gold standard method of assessing esophageal inflammation but has limitations, including high cost, time away from work and school for patients and parents, invasive nature, and need for general anesthesia in pediatrics.

The 1-h esophageal string test (EST) is a nonendoscopic method that was designed to measure EoE disease activity.[2] The assay involves swallowing a weighted gelatin capsule containing a nylon string; the proximal end is taped to the cheek, and the distal end dwells in the esophagus for an hour. The string is then removed, and the levels of major basic protein (MBP-1) and Eotaxin-3 are quantified using an enzyme-linked immunosorbent assay from the esophageal segment of the string. These levels strongly correlate with those measured in esophageal biopsies and with peak eosinophil counts, and together they can distinguish active and inactive EoE with high specificity.[2,3]

While studies have shown that the EST can measure a variety of different biomarkers relevant to EoE and have characterized their relationship to different disease states, this assay has only recently been employed in clinical practice as a disease monitoring tool.[4,5] Our aim was to describe the real-world clinical utilization of EST in pediatric patients with EoE at our center during the first year of use and to determine how EST results affected clinical decision-making.

**What is Known**

- The esophageal string test (EST) is a non-endoscopic minimally invasive test developed to monitor disease activity in patients with eosinophilic esophagitis (EoE).
- Eosinophil-associated protein levels measured with the EST correlate with tissue biopsy peak eosinophil counts and can distinguish between active and inactive EoE.

**What is New**

- In the first year of utilizing the EST by a multidisciplinary EoE clinic, 31 patients with EoE ages 6–20 years old underwent EST with an 87% success rate.
- EST was safe, efficient, well-tolerated, and a lower cost alternative than conventional endoscopy.
- In a clinical setting, EST results led to management changes of EoE without the use of conventional endoscopy.

## 2 | METHODS

We queried the electronic medical record to identify all patients for whom an EST was ordered over a 12-month (12/1/2022–11/30/2023) period at Children's Hospital Colorado. This was the first year-long period during which providers from the multidisciplinary EoE clinic employed this test in routine clinical practice. We retrospectively reviewed medical records and recorded demographic data, insurance information, success rate, and the indication for the EST. We recorded the rationale for cancellation among the patients who ultimately did not undergo EST.

Patients were asked not to eat for 2 h and not to drink for 1 h before EST. In an outpatient clinic room, patients swallowed the EnteroTracker string test device (EnteroTrack LLC) which is a weighted gelatin capsule containing 90 cm of nylon string. One hour after swallowing the capsule, the string was removed. The esophageal segment was harvested and placed in EST elution buffer and sent to the lab as previously described.

For the patients who successfully completed EST, results were recorded two ways: with EST EoE scores, algorithmic probability indices ranging from 0 to 1 which are calculated from combined levels of eosinophil-associated proteins Eotaxin-3 and MBP-1; and as either normal (EoE score < 0.53, corresponding with <15 eos/hpf on esophageal biopsy) or abnormal (EoE score ≥ 0.53, corresponding with ≥15 eos/hpf on esophageal biopsy).[2]

We recorded the time spent in the clinic on EST administration as the difference between the nurse procedure note time of filing and the patient arrival time in the clinic. We also calculated the difference between the time the specimen was received by the clinical laboratory and the patient arrival time in the clinic and used this measure of time spent on EST administration when the procedure notes were filed in a delayed fashion (>3 h after EST patient arrival time). We recorded the patient tolerance of EST administration as reported in the nurse's procedure note. Additionally, we recorded the type of EoE treatment the patient was using at the time of EST, and clinical changes made in response to EST testing.

We summarized baseline characteristics using descriptive statistics for parametric and nonparametric data as appropriate. We used *T* tests to compare EoE scores between patients with normal or abnormal results. We compared the proportion of ESTs that resulted in various management changes (i.e., escalation, de-escalation) using Fisher's Exact tests. This study was approved by the Colorado Multiple Institutional Review Board.

## 3 | RESULTS

During this first year, 31 patients underwent esophageal string testing. Fifty-four percent of the cohort were male ($n = 17$), and the average age was 12 years old (range: 6–20 years old). Insurance types included private 80.7% ($n = 25$), Medicaid 16.1% ($n = 5$), and TRICARE 3.2% ($n = 1$).

All patients who underwent EST had previously been diagnosed with an eosinophilic gastrointestinal disease. The majority (97%, $n = 30$) of patients had EoE and one patient had esophageal eosinophilia with eosinophilic gastritis. Patients had undergone a median of 3 endoscopies (range: 1–12) before EST. A minority (9.7%, $n = 3$) had previously undergone dilation of an esophageal stricture. Patients were on a variety of treatments before EST, including topical corticosteroid (TCS) monotherapy (38.8%, $n = 12$), proton pump inhibitor (PPI) monotherapy (9.7%, $n = 3$), diet elimination (16.1%, $n = 5$), dupilumab monotherapy (3.2%, $n = 1$), TCS and PPI (6.5%, $n = 1$), TCS and diet elimination (9.7%, $n = 3$), PPI and diet elimination (12.9%, $n = 4$), or no treatment (3.2%, $n = 1$).

A total of 51 ESTs were ordered by physicians in the multidisciplinary EoE clinic during the first year. Six patients did not proceed with scheduling the EST due to insurance denial ($n = 4$), prohibitive out-of-pocket cost ($n = 1$), or the family changed their mind to proceed with transnasal endoscopy ($n = 1$). Of 45 ESTs attempted, 39 ESTs were successful (87% successful completion rate) in 31 patients. Of these patients, 26 patients underwent one EST, 2 patients underwent 2 ESTs and 3 patients underwent 3 ESTs. Adverse events during the EST included vomiting ($n = 3$). One patient swallowed the EST whole including the string; these four patients were ultimately able to complete EST on a second attempt at the same visit. Patients who failed to complete the EST (13%, $n = 6$) were 7–12 years old and the reasons for failure were that patients were unable to swallow the pill ($n = 5$) and vomiting ($n = 1$). The average time spent in the clinic for EST was 129 min (range: 100–222 min).

The EST was used to assess EoE without the need for endoscopy in 95% ($n = 37$) of cases. The EoE score was normal in 61.5% of cases ($n = 24$) and was elevated or abnormal in 38.5% of cases ($n = 15$) (Table 1). For patients with normal EoE scores, physicians either continued current therapy (67%, $n = 16$) or de-escalated therapy (33%, $n = 8$). Patients with normal EoE scores were maintained on their current therapy more often than those with abnormal scores (67% vs. 7%, $p = 0.0002$), but the frequency with which EoE care was deescalated was not significantly different between these two groups (33% normal score vs. 7% abnormal score, $p = 0.115$). For patients with abnormal EoE scores, physicians either escalated therapy (73%), evaluated further with endoscopy (13%), continued current therapy (7%), or de-escalated therapy (7%). Patients with abnormal EoE scores were more likely to have their therapy escalated than those with normal scores (73% vs 0%, $p < 0.0001$). Table 1 depicts how EST results led to changes in subsequent management of EoE and the number of endoscopies, both transnasal endoscopy and conventional endoscopy under anesthesia, that these patients underwent during the same period. Representative examples of patients who underwent multiple ESTs with escalation and de-escalation of dietary, pharmacologic, and combination therapy in response to EST results are illustrated in Figure 1.

Two patients with abnormal EoE scores underwent endoscopic evaluation in the 2-month period following EST without an interim treatment change. One patient with a history of EoE and an EoE score of 0.831 was unsure about escalating treatment given minimal symptoms; their endoscopy showed active EoE (distal esophagus 15 eos/hpf, proximal esophagus 45 eos/hpf). The second patient had a history of eosinophilic gastritis with esophageal eosinophilia and had an EoE score of 0.670 but no symptoms, and subsequent esophageal biopsies were normal.

**TABLE 1** Esophageal string test results and management decisions.

| | Abnormal EST results, $n = 15$ | Normal EST results, $n = 24$ | $p$ Value[a] |
|---|---|---|---|
| Average EoE score: mean (SD) | 0.80 (0.13) | 0.37 (0.08) | < 0.0001 |
| Treatment changes: *n* (%) | | | |
| Escalations | 4 (27%) | | |
| Increased medication dose | 4 (27%) | 0 | 0.016 |
| Started new medication | 5 (33%) | 0 | 0.005 |
| Removed food | 2 (13%) | 0 | |
| Further evaluation with endoscopy | 2 (13%) | 0 | ns |
| Continued current therapy | 1 (7%) | 16 (67%) | 0.0002 |
| De-escalations | | | |
| Added food | 1 (7%) | 6 (25%) | ns |
| Decreased medication dose | 0 | 2 (8%) | ns |
| Total number of endoscopies these patients underwent during this period: *n* | | | |
| EGD | 6 | 5 | ns |
| TNE | 0 | 5 | ns |

Abbreviations: EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; EST, esophageal string test; ns: not significant; SD, standard deviation; TNE, transnasal endoscopy.

[a]EoE Scores compared using *t*-test, treatment changes compared using Fisher's Exact test.

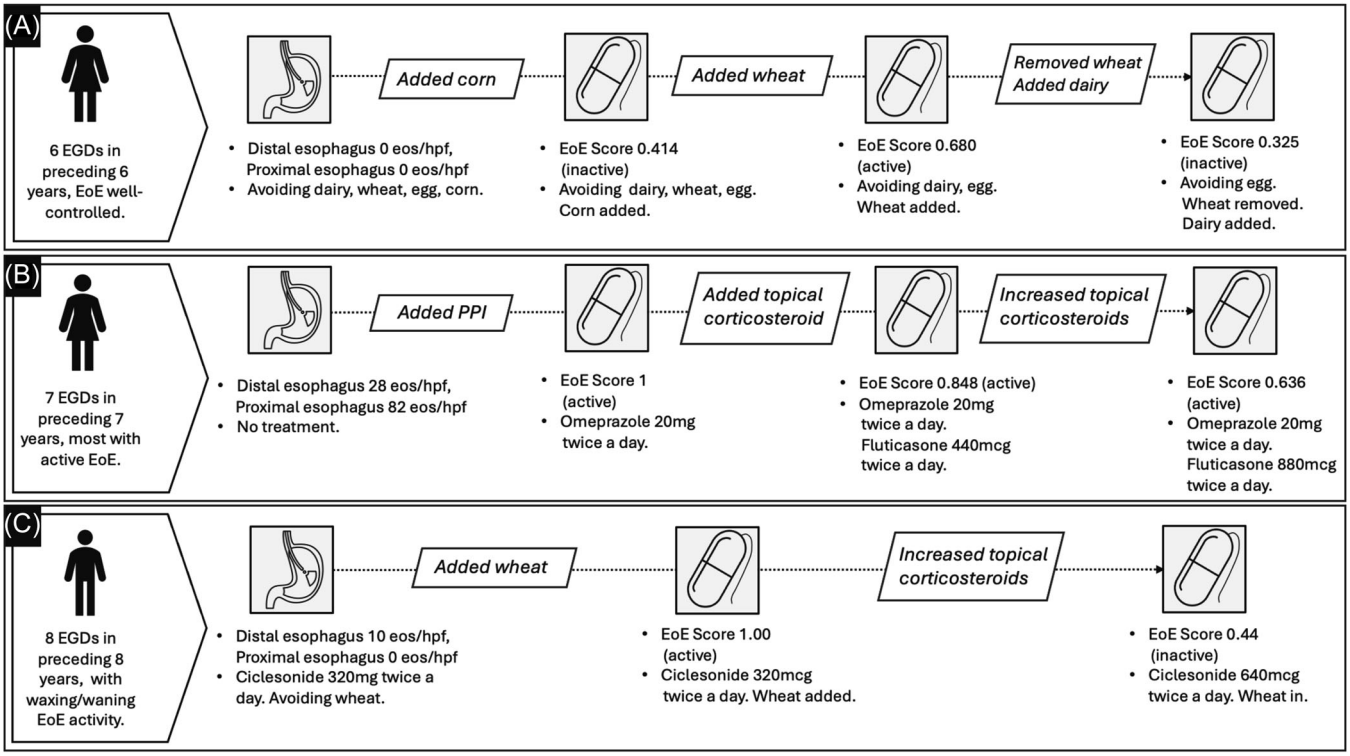


**FIGURE 1** Examples of management changes based on esophageal string testing. (A) Timeline of dietary therapy guided by EST results. (B) Timeline of pharmacologic therapy guided by EST results. (C) Timeline of combination dietary and pharmacologic therapy guided by EST results. EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; EST, esophageal string testing; PPI, proton pump inhibitor.

## 4 | DISCUSSION

We made a number of meaningful observations over our first year of experience using the EST in clinical practice. First, EST results were impactful and led to management changes without utilization of conventional endoscopy in most cases. In a subset of patients who underwent serial ESTs, multiple treatment changes were made. Second, EST offered a number of pragmatic benefits over conventional endoscopy under anesthesia including lower cost as well as less time spent preparing for, undergoing, and recovering from the endoscopy. Lastly, EST was safe and well-tolerated by pediatric patients.

EoE disease activity is a combined measure of symptoms and histologic measures of esophageal inflammation, but it is well-recognized that EoE symptoms wax and wane and only modestly correlate with histologic activity.[6,7] Given the invasive nature and cost of endoscopy as well as concerns around neurodevelopmental impacts of repeated anesthesia in young children, limiting the frequency of endoscopic evaluation in children with EoE is a priority.[8] Here, we show that the EST replaced follow-up endoscopic evaluation in a cohort of children with EoE, leading to changes in management.

When it comes to monitoring EoE, EST has advantages to endoscopy in a number of ways. For one, the EST is much less expensive than conventional endoscopy: 85% lower based on precoverage cost estimates at our center. The EST procedure does not require advanced providers and was administered by trained nurses at our center. Additionally, insurance covered EST in most cases. Second, patients spent an hour less in the hospital clinic compared to conventional endoscopy.[9] Third, the fasting time before EST is only 2 h which is 4–6 h less than the cut-offs used for conventional endoscopy under anesthesia. Fourth, the EST carries none of the risks associated with anesthesia or conventional endoscopy and requires no recovery time.

EST has a number of limitations compared to endoscopy. It cannot differentiate between EoE and other causes of esophageal eosinophilia like gastroesophageal reflux disease. It does not differentiate distal and proximal esophageal inflammation because biomarkers are eluted from the entire esophageal portion of the string. The stomach and the duodenum are not assessed using the EST. Additionally, while eosinophils are the primary source of MBP-1 and Eotaxin-3, other cells such as basophils, mast cells, neutrophils, and T lymphocytes can sequester or express low levels of these proteins and potentially cause false positive or false negative results. Patients with other allergic conditions may swallow secretions from the nasopharynx which could alter eosinophil-associated protein measurements from the esophageal portion of the string. Lastly, a unique strength of

endoscopy is the ability to perform interventions that provide immediate therapeutic benefit to patients with EoE like esophageal dilation.

This study adds to a growing body of evidence suggesting that EST is safe and well-tolerated by pediatric patients with EoE. While the majority of children were able to complete the test and none had serious adverse events, non-completion occurred 13% of the time. The percentage of children unable to swallow the EST in this real-world cohort was similar to the 14% reported by Ackerman et al in a cohort of 134 children and adults with EoE undergoing EST.[2]

These incompletion rates are higher than those reported with the Cytosponge cell collection device, a minimally invasive method of esophageal sampling used in adult patients to collect esophageal epithelial samples. The Cytosponge is administered in a similar fashion: a 20 mm pill attached to a tether is swallowed then removed.[10] Among adult patients with EoE and other esophageal disorders, incompletion rates for Cytosponge range from 7% to 9%.[11,12] Previous studies involving Cytosponge have been performed in adults greater than 18 years old, therefore the lower completion rate with EST may be due to patient age and comfort with swallowing capsules. Previous studies with EST include children down to age 7 years.[2,3] Identifying predictors of successful EST completion should be a focus of future studies.

In summary, the EST led to EoE management changes and was safe, well-tolerated, approved by insurance and was both quicker and more affordable than endoscopy. Further studies are needed to understand the advantages and disadvantages of EST, including patient tolerance, acceptability, cost-effectiveness, and impact on time to remission. The EST is a promising minimally invasive technique that has the potential to advance both EoE clinical care in addition to research.

## CONFLICTS OF INTEREST STATEMENT

Maureen Bauer has served as a consultant for Sanofi and DynaMed. Nathalie Nguyen has served as a consultant for Regeneron and EvoEndo. The remaining authors declare no conflict of interest.

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## REFERENCES

1. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: proceedings of the AGREE conference. Gastroenterology. 2018;155:1022-1033.
2. Ackerman SJ, Kagalwalla AF, Hirano I, et al. One-hour esophageal string test: a nonendoscopic minimally invasive test that accurately detects disease activity in eosinophilic esophagitis. *Am J Gastroenterol*. 2019;114:1614-1625.
3. Furuta GT, Kagalwalla AF, Lee JJ, et al. The oesophageal string test: a novel, minimally invasive method measures mucosal inflammation in eosinophilic oesophagitis. *Gut*. 2013;62:1395-1405.
4. Fillon SA, Harris JK, Wagner BD, et al. Novel device to sample the esophageal microbiome--the esophageal string test. *PLoS One*. 2012;7:e42938.
5. Muir AB, Ackerman SJ, Pan Z, et al. Esophageal remodeling in eosinophilic esophagitis: relationships to luminal captured biomarkers of inflammation and periostin. *J Allergy Clin Immunol*. 2022;150:649-656.
6. Safroneeva E, Straumann A, Coslovsky M, et al. Symptoms have modest accuracy in detecting endoscopic and histologic remission in adults with eosinophilic esophagitis. *Gastroenterology*. 2016;150:581-590.
7. Chang JW, Chen VL, Rubenstein JH, Dellon ES, Wallner LP, De Vries R. What patients with eosinophilic esophagitis May not share with their providers: a qualitative assessment of online health communities. *Dis Esophagus*. 2022;35(6):doab073. doi:10.1093/dote/doab073
8. Reighard C, Junaid S, Jackson WM, et al. Anesthetic exposure during childhood and neurodevelopmental outcomes: a systematic review and meta-analysis. *JAMA Network Open*. 2022;5:e2217427.
9. Friedlander JA, DeBoer EM, Soden JS, et al. Unsedated transnasal esophagoscopy for monitoring therapy in pediatric eosinophilic esophagitis. *Gastrointest Endosc*. 2016;83:299-306.
10. Katzka DA, Geno DM, Ravi A, et al. Accuracy, safety, and tolerability of tissue collection by cytosponge vs endoscopy for evaluation of eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2015;13:77-83.
11. Januszewicz W, Tan WK, Lehovsky K, et al. Safety and acceptability of esophageal cytosponge cell collection device in a pooled analysis of data from individual patients. *Clin Gastroenterol Hepatol*. 2019;17:647-656.
12. Katzka DA, Smyrk TC, Alexander JA, et al. Accuracy and safety of the cytosponge for assessing histologic activity in eosinophilic esophagitis: a two-center study. *Am J Gastroenterol*. 2017;112:1538-1544.

**How to cite this article:** Quinn LA, Andrews R, Bauer M, Nguyen N. Utilization and impact of esophageal string testing in children with eosinophilic esophagitis: a 1 year experience. *J Pediatr Gastroenterol Nutr*. 2024;1-5. doi:10.1002/jpn3.12323