

Outcomes of Esophageal Self Dilation for  
Benign Refractory Esophageal Stricture  
Management: Randomized Controlled Trial

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**Version 5****Date: 3/14/2019 5/6/2019 11/19/2021****Title:** Outcomes of Esophageal Self Dilation for Benign Refractory Esophageal Stricture Management: Randomized Controlled Trial**Principal Investigator:** Jeffrey Alexander, MD

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**Co- Investigators:** David A Katzka MD, Tarek Sawas, MD Yi Qin, MD, Allon Kahn, Mike, Michael Crowell**Study Coordinators:** Crystal Lavey, CCRP, Alyssa Johnson, CRC**Background:**

Benign esophageal strictures can be a challenging condition to treat. The mainstay of treatment is endoscopic dilations. However, 30 to 40% of these strictures recur despite rigorous dilations<sup>1</sup>. Although a consensus definition does not exist, a stricture is typically termed as a refractory benign esophageal stricture (RBES), when there is a failure to maintain luminal patency after at least 5 endoscopic dilations<sup>2</sup>. These strictures are fibrotic and cicatricial, and are most commonly the sequelae of radiation, surgery, caustic agent ingestion, peptic injury, photodynamic therapy, or endoscopic mucosal resection<sup>3</sup>. Hypertrophy of scar tissue is the underlying mechanism leading to re-stenosis<sup>4</sup>.

Patients with RBES are extremely difficult to manage and the current armamentarium includes repeated endoscopic dilations, corticosteroid or mitomycin C injections, incisional therapy, and/ or temporary stent placement<sup>5-10</sup>. These procedures are costly, their efficacy can be short-lived, and are associated with great burden both for the patient and clinician. Despite intensive interventions, patients often still fail and go on to require enteral nutrition support. The largest study on the natural history of RBES found that the mean dysphagia free interval was 3 months, and only 2.4 months for patients treated with endoscopic stenting. The clinical success rate for patients treated with stenting was only 12.5%.<sup>11</sup>

Esophageal self-dilation therapy (ESDT), where the patient learns to pass a polyvinyl dilator orally on a routine basis, has been in practice since at least the 1970s, however, no prospective studies have evaluated the outcomes of ESDT. The largest study to date on ESDT retrospectively studied 30 patients<sup>12</sup>, and all the published studies on this topic consist of less than 50 patients in total<sup>12-19</sup>. In these retrospective and observational studies, ESDT appears to be effective for RBES, reducing the number of endoscopic dilations from an average of 21.7 to an average of 1<sup>12</sup>. However, many questions with regards to ESDT remain unanswered. Firstly, in the absence of any prospective data it is uncertain how effective ESDT is. Moreover, currently patients are offered ESDT when standard therapies fail.

**Hypotheses:**

Among patients with refractory benign esophageal stricture who were treated endoscopically, we hypothesized the following:

1. Compared to an endoscopy as needed approach, esophageal self -dilation therapy decreases the number of endoscopic dilations and prolongs dysphagia free intervals
2. Esophageal self -dilation therapy is a safe and well tolerated therapy
3. ESDT significantly lowers health cost in managing refractory esophageal stricture

### **Primary Aims:**

1. Assess the clinical efficacy of ESDT for patients with RBES defined as number of endoscopic interventions 6 months following serial dilation

### **Secondary Aims:**

1. Length of intervention free interval and dysphagia score
2. Evaluate factors which could influence clinical success of ESDT including etiology and location of the stricture
3. Assess the safety of ESDT by identifying clinically significant adverse events including perforation, bleeding and pain.
4. Assess acceptance of ESDT by measuring the number of patients who accepts the procedure and are able to complete it over the total number of patients offered ESDT
5. The cost saving in ESDT compared to the current standard of care (repetitive endoscopic dilation)
6. Evaluate long term outcomes of self-dilatation at 3, 6, 9 and 12 months following participation in the 6 month randomized or prospective observational trial

### **Methods:**

#### Study Design:

This is a prospective randomized controlled trial evaluating the outcomes of self-dilation. Patients who present to the esophageal clinic in Rochester MN and Mayo [Clinic Phoenix](#), AZ with refractory benign esophageal strictures who undergo standard clinical care of serial endoscopic dilation to achieve an esophageal diameter of at least 10-12 mm will be randomized to either continuing standard clinical care consisting of endoscopic dilation as needed vs self-dilation therapy.

#### Inclusion Criteria for Patients:

1. 18 years of age or older
2. Refractory benign esophageal stricture defined as an esophageal stricture with persistent dysphagia despite undergoing 5 endoscopic dilations within a 1 year period. Persistent dysphagia will be considered if patients has solid food dysphagia at least once a week

#### Exclusion Criteria

1. Patient with malignant esophageal stricture
2. Angulated stricture which prevents safe passage of Maloney dilator in office setting
3. In ability to achieve an esophageal diameter of 10 mm with endoscopic dilatation
4. Known significant esophageal motor disorder (i.e. achalasia, aperistalsis, functional obstruction, jackhammer, distal esophageal spasm)\*

5. The presence of esophageal stent
6. Inability to learn self-dilation secondary to blindness or cognitive dysfunction
7. Use of chronic anticoagulants

### Study Flow and Recruitment

1. Patients referred to the esophageal clinic with dysphagia secondary to RBES will be asked to complete the Mayo Dysphagia Questionnaire (MDQ-30). The MDQ will be completed before obtaining informed consent. Quality of life will also be measured at the beginning at end of the 6 months using Short form-36
2. First, patients will undergo the standard of care which is serial endoscopic therapy with esophageal dilation. Patients will be dilated 1-3 times a week with the aim to achieve a post-dilation luminal diameter of at least 10-12 mm
3. After informed consent, participants will be randomized to one of two groups using a block randomization approach; Group 1) self-dilation, group 2) observation with repeat endoscopy and dilations as needed at symptoms recurrence.
4. Patients randomized to self-dilation who refuse self-dilation will be assigned to the observation group and will be counted in the ESDT failure
5. Patients randomized to ESDT will be taught ESDT immediately following the last endoscopic dilation. ESDT teaching will take over 1-3 training sessions by one of two esophageal physicians and a nurse. Patients will be instructed to start ESDT twice a day. If dysphagia is adequately controlled, and there was no resistance with passing the dilator, patients will be asked to decrease the frequency of ESDT to daily, weekly, and monthly over an average period of 6 months as directed by the esophageal care team.
6. Patients randomized to the observation group will undergo repeat endoscopy and dilation as needed if their dysphagia relapse which is the current standard of care. A relapse will be considered if a patient developed solid food dysphagia at least once a week.
7. Patients in the observation group who requires 2 endoscopic dilation within 3 months will be offered to cross over to the self dilation group
8. Patients in the self dilation group who can not tolerate self dilation but require more treatment will be offered to crossover to the standard clinical care group endoscopic dilation as needed after 3 months from the entry point
9. At the end of the six months, the standard clinical care group will be offered self-dilation.
10. At any point of the study if patients decide to crossover to the other group, this will be allowed but counted as treatment failure
11. Close supervision and follow up will be performed via weekly phone calls from a member of the study personnellPatients will be asked to complete the MDQ-30 monthly and at the end of the study.
12. Patients who decline participation in the randomized study will be offered both treatments clinically then will be followed prospectively and their data will be collected. These patients will be asked to fill the dysphagia score to assess symptoms regardless of the method of treatment.
13. At the conclusion of the 6 months randomized or observational study duration patients will be offered the following:
  1. All patients who participated in the randomized or observational study will be offered to continue prospective follow up with phone calls to obtain the MDQ-30 score and

need for endoscopy at 3, 6, 9, and 12 months after conclusion of the initial 6 month duration of the study

**Remuneration:**

1. Patients in the randomized self-dilation group will be provided with the self-dilator free of charge.
2. Patients in the randomized observation group will receive endoscopic dilation as needed with charges to the patients and their health insurance as appropriate since this is the standard of care
3. Patients in both groups will receive stipend of \$25 for each questionnaire for the time spent in completing the dysphagia questionnaire during the randomized 6 month study duration
4. Patients who participate in the prospective observational study, and who either chose self-dilation or observation will receive stipend of \$25 for each questionnaire for the time spent in completing the dysphagia questionnaire

Patients who agree to the prospective extension study will receive a stipend of \$25 for each of [the 4 monthly](#) MDQ phone calls to collect questionnaires.

**Statistical Analysis:**Sample Size Estimation:

Based on the current knowledge from our prior experience, the clinical success of ESDT appears to be 80%. The clinical success of repetitive endoscopic dilation is reported in the literature to be 30%. Assuming a 50% improvement in clinical success with ESDT and using 1:1 randomizing, the estimated minimum number of patients needed is 30 patients (15 in each group). Given the extreme paucity of data on self dilation and ambiguity about the potential improvement we intend to recruit 40 patients across the two sites (Rochester and Phoenix). This estimated number will provide at least 80% power of finding a significant difference at a P value of 0.05

Up to 40 patients who chose not to participate in the randomized trial, but who agree to be followed in the prospective observational group will be recruited.

The following table summarizes the key questions and corresponding approaches to be addressed by this study.

Primary Endpoint:

1. Compare the number of endoscopies required in a 6 month interval in patients who achieved at least a 10-12 mm esophageal diameter during serial dilation for RBES and were subsequently treated with ESDT versus standard clinical care.

Secondary Endpoints:

1. Determine the length of intervention free interval
2. Dysphagia score
3. Number of clinically significant adverse events including perforation, bleeding and pain
4. Cost of ESDT compared to the current standard of care (repetitive endoscopic dilation)

Definition:

Perforation will be defined as Evidence of air or luminal contents outside the GI tract.

Bleeding will be defined as hematemesis and/or melena or hemoglobin drop >2 g/L

Question	Approach	Statistical Test
Clinical success	Compare the number of patients who remained free of endoscopic therapy between the two groups	Logistic regression in a univariate and multivariate analysis
Time to the next endoscopy	Compare time endoscopic therapy. Patients who requires endoscopic dilation will be considered failure	Cox regression and Kaplan Meier
Adverse events	Compare the number of patients who developed adverse events between the two groups	Logistic regression in a univariate and multivariate analysis
The cost	Compare the cost of treatment including endoscopic therapy, hospitalization from complications	Linear regression
Factors affecting clinical success in ESDT	Investigating factors which could determine clinical success including age, gender, etiology, length of the stricture and location of the stricture	Multivariate logistic regression

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