

Factors associated with complications during endoscopic esophageal dilation

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ABSTRACT

Background: endoscopic dilation is considered as the treatment of choice for esophageal strictures. However, there are no studies in our region that have assessed the safety of the procedure.

Objective: to assess the safety of esophageal dilation and the factors associated with the development of complications.

Materials and methods: a retrospective cohort was studied. All patients referred for esophageal dilation between January 2015 and June 2017 were included in the study. A complication rate was obtained and the association between nonadherence to the "rule of 3" and the development of complications was determined. Other predictive factors associated with complication development were also analyzed.

Results: a total of 164 patients that underwent 474 dilations were included in the study. Surgical anastomosis stricture was the most prevalent etiology. A total of six complications occurred, including three perforations (0.63%), two bleeding events (0.42%) and one episode of significant pain that required post-procedure observation (0.21%). Endoscopic esophageal dilation without adherence to the "rule of 3" was not associated with a higher risk of complications. Balloon dilation was the only predictive factor for complications.

Conclusions: esophageal dilation is a safe procedure. Non-adherence to the "rule of 3" does not appear to be associated with a higher risk of complications, including esophageal perforation.

Key words: Dilation. Esophageal stricture. Esophageal perforation.

INTRODUCTION

Esophageal stricture (ES) is a common finding in gastroenterology. ES often results in dysphagia and requires specific treatment, endoscopic esophageal dilation is the

most commonly used procedure. An ES may be categorized according to the benign or malignant nature and a simple or complex structure. Simple strictures are symmetrical and concentric, with a ≥ 12 mm diameter that allows the passage of a diagnostic endoscope. Complex strictures do not meet one or more of these characteristics, as they are asymmetrical with a diameter ≤ 12 mm and/or do not allow the passage of a diagnostic endoscope (1).

Endoscopic esophageal dilation is considered as the initial treatment of choice to relieve dysphagia in the case of benign strictures and as a bridge therapy to other procedures in the case of malignant strictures (stent placement or percutaneous endoscopic gastrostomy) (1). However, complications such as perforation, bleeding and lung aspiration may occur (1). Esophageal perforation is the most commonly feared complication and is reported in 0.1-2.6% of cases with a mortality rate of up to 20%. According to the currently available literature, factors associated with a higher risk of perforation include complex stricture (2-4), stricture from eosinophilic esophagitis, malignancy-associated stricture, radiation-induced stricture and limited experience of the practitioner performing the endoscopic procedure (2,5,6).

Whether the various modalities available for dilation are truly associated with efficacy or complication rates remains unclear, and their selection usually depends upon the preferences and experience of the practitioner. Modalities traditionally used include bougies (Maloney or Hurst), polyvinyl dilators with or without a guidewire (Savary-Gilliard or American) and TTS (through-the-scope) balloons (3). Maloney-type bougies are introduced blindly or under fluoroscopic control with a theoretical higher risk of complications when anatomic changes are present. Polyvinyl dilators may be introduced over a guidewire

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previously placed in the stomach and TTS balloons are passed through the working channel. An additional difference is that bougies exert both radial and longitudinal force, whereas balloons only exert radial force along the length of the stricture (1).

The extent of dilation that may be achieved in one session is controversial and clinical guidelines suggest the use of the "rule of 3" for esophageal dilations with bougies (7). This rule indicates that when encountering moderate resistance to the dilator, no more than three consecutive dilations with 1 mm increments should be performed in one session (1). However, this approach is not evidence-based and several studies currently suggest that wider dilations may be safe, particularly for simple strictures (8,9). This rule was originally made for bougie dilations as there was no strong evidence to allow recommendations for other dilator types. However, many endoscopists use this in all dilation procedures, even with other devices, in an attempt to minimize complications by controlling the diameter increments and avoiding aggressive dilations.

The present study was performed due to all of the above and the lack of data with regard to complications associated with endoscopic esophageal dilation in our region. The overall objective was to assess the safety of esophageal dilation and to determine the factors associated with complications. The specific goals include the following: a) to determine the most common etiologies of esophageal stricture in a tertiary referral hospital; b) to estimate the rate of complications associated with esophageal dilation; c) to identify associations between nonadherence to the "rule of 3" and the development of complications; and d) to identify predictors of complications.

METHODS

Patients

This was a single-center retrospective cohort study performed in a tertiary institution in Lima, Peru, from January 2015 to June 2017. Patients with an esophageal stricture who underwent endoscopic esophageal dilation were included. The inclusion criteria were age above 18 years and esophageal stricture with associated dysphagia regardless of the etiology. Exclusion criteria included coagulopathy, underlying disease precluding the discontinuation of a previous therapy with anti-aggregants and/or anticoagulants and severe comorbidities that exclude sedation.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The protocol was assessed and approved by the Gastroenterology Department and the hospitals' Ethics Committee. Epidemiological and clinical data were recorded for all cases, as well as their prior endoscopic dilation history.

Endoscopic assessment of esophageal strictures

The following characteristics were assessed in all patients with ES: sex, age, stricture etiology, structural type (simple or complex according to the American Society for Gastrointestinal Endoscopy [ASGE] criteria [1]), dilator type (bal-

loon or bougie), dilation extent in mm according to dilator diameter and the number of increments in one session according to the "rule of 3". Furthermore, the application of the "rule of 3" was assessed not only for bougie dilations but also for balloon dilations, as many endoscopists use this during the latter procedure (9). Procedure-associated complications were defined according to the ASGE consensus criteria for endoscopic adverse events (10): a) instrumental complications: perforation (evidence of air or luminal contents outside the gastrointestinal tract) or bleeding (hematemesis and/or melena, or hemoglobin decrease > 2 g/dl); and b) post-procedure severe (cervical, thoracic, abdominal) pain requiring observation for longer than three hours. Complications were classified according to their time of onset as follows: intra-procedural (from procedure-related admission to leaving the endoscopy room), post-procedural (from leaving the endoscopy room to day 14 after the procedure), and late/delayed (more than 14 days after the procedure) (10).

Endoscopic dilation

All procedures were carried out under shallow or deep sedation with one or more of the following drugs: midazolam, propofol, pethidine and/or fentanyl. Drug selection was based on patient assessment and no cases required general anesthesia. Most procedures were carried out on an outpatient basis. Procedures were performed by two practitioners trained in advanced therapeutic endoscopy. One had a vast experience in esophageal dilation and the other endoscopist was properly trained but had performed fewer procedures. Hence, he was always accompanied by his more experienced colleague.

A contrast-enhanced esophageal scan was performed prior to the first dilation, only for suspected complex strictures. The instruments used included Savary-Gilliard® dilators (Wilson-Cook Medical, Inc., Winston-Salem, N.C., USA) or balloon dilators, either CRE® (Controlled Radial Expansion, Boston Scientific Cork Ltd., Cork, Ireland) or Hercules® (Wilson-Cook Medical, Inc., Winston-Salem, N.C., USA). The decision to use a specific dilator and a given number of increments in one session was left to the discretion of each endoscopist. The duration of dilation was approximately 60 seconds for each diameter.

Dilators were introduced with or without a previously positioned guidewire with the help of an endoscope (gastroscope EG-590WR and videoprocessor EPX-4400, Fujinon Co, Ltd., Tokyo, Japan). Usually, one to four progressively larger in diameter dilators were used per session, depending on patient tolerance and stricture type. No fluoroscopy was used for dilation procedures as the required equipment was not available in therapeutic endoscopy rooms. When more than one session was required, the procedures were scheduled every 2-4 weeks, until a diameter of at least 14-15 mm was reached. Subsequent sessions were planned for recurrent dysphagia. With regard to patients with peptic ES, the use of proton-pump inhibitors (PPIs) was advised with routine anti-reflux measures.

Patients were observed for potential complications following each session. Complications were managed by a multidisciplinary team using endoscopic techniques when

feasible or surgery. When required, partially-covered, self-expandable metal stents were used (Niti-S[®], TaeWong Medical, Seoul, Korea).

Statistical analysis

All continuous-variable results were summarized using average, standard deviation and range values, according to their distribution. Categorical variables were reported as a number and percentage. Relationships between categorical variables were analyzed using the Chi-squared test and Fisher's exact test when necessary. A bivariate and multivariate logistic regression analysis was used to estimate odds ratios for each predictor and the occurrence of a complication. A p-value < 0.05 was considered as statistically significant for all analyses. The analysis was performed using the Stata 10 statistical system.

RESULTS

A total of 164 patients were included in the study from January 2015 to June 2017, 54 were male (33%) and 110 female (67%). The average age at the first dilation was 60.88 years (range: 19-92 years). The most prevalent etiology was stricture at the surgical anastomosis in 43 patients (26.22%) and only eight patients underwent treatment for malignant stenosis (4.88%). A total of 474 dilations were performed and each patient underwent an average of 2.87 dilations during the study (range: 1-28 dilations). A stricture at the surgical anastomosis required a larger number of dilations per patient. Two patients had a pharyngocolonic anastomosis and were intervened following caustic esophagitis that required 28 and eleven sessions, respectively. Table 1 shows the characteristics of patients included in the study and their endoscopic esophageal dilations. The dilation extent varied according to etiology, and increments from 1 mm to 7 mm were applied, the latter for a patient with a stricture at the surgical anastomosis.

Complications associated with endoscopic dilation occurred in six cases (1.27%). There were three perforations (0.63%), two post-dilation bleeding events (0.42%) and one episode of significant pain that required observation after the procedure (0.21%) (Table 2). All complications were intra-procedural and no significant association was found between stricture etiology and the occurrence of a complication. Four of the six complications occurred during the first dilation session. The remaining two complications developed during the sixth and twelfth session, respectively, both in the setting of a stricture at the surgical anastomosis. One perforation occurred during the sixth dilation session. Two of the three perforations developed during dilation for a complex stricture. All perforations were treated satisfactorily with self-expandable metal stents. One perforation unusually occurred in a patient with a stricture of an unknown origin that was later found to be malignant. Bleeding episodes were resolved with endoscopic therapy. The painful event required no specific therapy and none of the complications required surgery.

Table 3 shows the association between complications related to esophageal dilation and five potential risk fac-

Table 1. Characteristics of the patients and the endoscopic dilation procedure

Characteristics	n (%)
Age (years)	60.88
Male sex	54 (32.93%)
Number of dilations (n)	474
Average no. of dilations per patient	2.87
<i>Etiology (n, %)</i>	
Anastomosis stricture	166 (35.02%)
Cricopharyngeal membrane	69 (14.56%)
Caustic stricture	47 (9.92%)
Cricopharyngeal bar	43 (9.07%)
Achalasia	39 (8.23%)
Malignant stricture	30 (6.33%)
Unspecified etiology	28 (5.91%)
Peptic stricture	21 (4.43%)
Actinic stricture	12 (2.53%)
Schatzki ring	7 (1.48%)
Epidermolysis bullosa	6 (1.27%)
Extrinsic compression	3 (0.63%)
Upper esophageal ring	3 (0.63%)
<i>Location (n, %)</i>	
Proximal	59 (35.98%)
Distal	62 (37.80%)
Anastomosis	43 (26.22%)
<i>Stricture complexity (n, %)</i>	
Simple	293 (61.81%)
Complex	181 (38.19%)
<i>Dilatador</i>	
Savary-Gilliard	315 (66.46%)
Balloon	159 (33.54%)
<i>Adherence to the "rule of 3"</i> *	
Yes	325 (68.57%)
No	149 (31.43%)
<i>Dilation above 3 mm</i>	
Yes	86 (18.14%)
No	388 (81.86%)

*Dilations below 3 mm may be performed without adhering to the "rule of 3" when increments of over 1 mm are used.

tors. No complications occurred after dilations of over 3 mm or dilations for achalasia. In the multivariate analysis, only balloon dilation was found to be significantly associated with the development of complications. Predictive factors for a perforation after esophageal dilation are also listed in table 3. All perforations occurred after esophageal dilation using a balloon dilator. None of the factors assessed were related to perforation development following dilation.

Table 2. Complications according to their origin

Complications	n (% per origin)	p
<i>Per etiology</i>		
Anastomosis stricture	4 (2.41%)	0.908
Cricopharyngeal bar	1 (2.33%)	
Malignant stricture	1 (3.33%)	
<i>Per location</i>		
Anastomosis stricture	4 (2.41%)	0.876
Proximal	1 (2.33%)	
Distal	1 (3.33%)	
<i>Per complication type</i>		
<i>Perforation</i>		
Anastomosis stricture	2 (1.20%)	0.910
Malignant stricture	1 (3.33%)	
<i>Bleeding</i>		
Anastomosis stricture	1 (0.60%)	0.959
Cricopharyngeal bar	1 (2.33%)	
<i>Post-dilation pain</i>		
Anastomosis stricture	1 (0.60%)	

DISCUSSION

Endoscopic dilation is the initial approach for the management of esophageal dilation. However, the optimum technique or ideal type of dilator for this procedure has not yet been determined. The ASGE esophageal dilation guidelines recommend a conservative approach using the "rule of 3", particularly for complex strictures in order to avert the risk of perforation (1). However, several studies currently highlight the safety of esophageal dilation without using the "rule of 3" as well as dilation over 3 mm in one session (8,9).

The literature reports a complication rate of 1% for endoscopic esophageal stricture dilation, regardless of the etiology (9). Six complications developed in our cohort: three perforations, two post-dilation bleeding events and one episode of significant pain that required post-procedural observation. The complication rate was 1.27%, similar to that reported by Grooteman et al. (9). The perforation rate

was 0.63%, which was also similar to previous reports of many studies that described a perforation rate ranging from 0.1% to 2.6% (2,3,9,11,12). The "rule of 3" was used during most of the procedures in our study. However, dilation without this rule was not predictive of complications or perforation in our cohort.

ASGE guidelines for esophageal dilation indicate that the presence of a complex stricture represents a risk factor for the development of perforation after dilation (1). However, stricture complexity was not associated with the subsequent development of complications or perforation in our study. The evidence underlying this claim derives primarily from retrospective studies where Maloney dilators were used (3). Hence, the significance of this factor might be an overestimation, as suggested by Grooteman et al. (9).

As highlighted in several studies, there is insufficient available evidence to determine whether Savary-Gilliard® or balloon dilators is superior with regard to safety (3,13-15). In our study, all three perforations occurred during procedures that used balloon dilators. Furthermore, balloon dilation was associated with complication development in the univariate and multivariate analysis. Due to our experience, we decided to use Savary-Gilliard® dilators for most procedures because of their user-friendly nature and the fact that they provide a greater "feeling" of the stricture at the time of dilation. It is possible that this benefit was decisive in order to prevent complications, as this feature is not shared by balloon dilators.

Other factors reported to be associated with a higher risk of perforation include malignant stricture (3,16), caustic stricture (17) and radiation stricture (6). Jethwa and Grooteman reported a perforation rate of 3.3% and 4.1%, respectively, after malignant stricture dilation (9,16). In our study, eight patients had malignant strictures and underwent a total of 30 dilation sessions. A perforation rate of 3.3% (one perforation) was observed in this group, similar to that reported by Jethwa and Grooteman. However, stricture etiology was not associated with complication development following endoscopic dilation. Nevertheless, the role of this etiology in complication development cannot be ruled out due to the low frequency of dilations for malignant strictures in our cohort. No esophageal perforations occurred in our cohort following dilations for caustic or radiation-related strictures.

The most common indication for endoscopic dilation in our cohort was stricture at the surgical anastomosis, consistent with other studies (12,18). These strictures tend to be more refractory to treatment and require more dilation

Table 3. Variables associated with complications and perforations

	Multivariate analysis (factors associated with complications)			Multivariate analysis (factors associated with perforation)		
	OR	CI	p	OR	CI	p
Complex stricture	1.36	0.18-9.99	0.763	2.94	0.22-38.72	0.411
Malignant stricture	1.66	0.90-3.08	0.105	1.50	0.80-2.80	0.204
Balloon dilator	17.88	1.52-210.89	0.022			
No "rule of 3"	1.90	0.16-22.49	0.612	1.47	0.80-19.45	0.769

sessions compared to other etiologies (18). A perforation rate of 1.2% was observed in this group, which is higher than that reported by Grooteman et al. (0.3%) (9). However, such a high prevalence of strictures at surgical anastomoses may not occur in other sites with more experienced surgical teams.

Eosinophilic esophagitis may present with symptoms such as dysphagia and may be ultimately associated with presence of rings and/or strictures (19). Strictures associated with eosinophilic esophagitis were not included as such in our cohort, although this etiology may be included in the unspecified stricture group. Biopsy samples were obtained for all unspecified stricture cases (28 patients) but were inconclusive for a definitive diagnosis. Interestingly, there are no publications that highlight eosinophilic esophagitis as a relevant etiology for esophageal stricture in our population.

The present study demonstrated that nonadherence to the “rule of 3” is not associated with a higher rate of complications or perforations following esophageal dilation. Furthermore, there were no complications during dilations over 3 mm. The “rule of 3” was devised to avoid aggressive dilation and has never been methodologically validated, despite its ubiquitous presence in clinical guidelines and expert recommendations. However, these results do not mean that the “rule of 3” should be completely disregarded, as it might be useful for endoscopists less experienced in the field of esophageal dilation (9). In our experience, dilation aggressiveness should be adjusted according to stricture severity, while always bearing in mind the maximum dilation obtained in prior sessions.

It is important to note that our cohort were treated by two expert endoscopists from a high-volume reference center. These results may not be replicated by less experienced teams or in centers lacking endoscopic dilation equipment available in our center. Due to our experience, we chose to use Savary-Gilliard® dilators on most occasions. Therefore, the results obtained may differ in units with different equipment. It should also be highlighted that our institution does not have fluoroscopy equipment available during endoscopic dilation sessions. However, despite this difficulty, the complication rate obtained is consistent with international reports. Our complication rate would likely be even lower if this equipment was available.

Our study is relevant as it is the first one in our region that includes a high number of cases to assess dilation safety. Furthermore, it is the first in our country to assess complication predictors associated with esophageal dilation. The study also describes dilation results and complications in our institution, with rates comparable to those suggested by the ASGE and reported by other studies worldwide. The limitations of the study stem from its retrospective nature. Hence, this report should encourage further prospective studies that assess esophageal dilation safety.

Hopefully this article will represent a first step in our region and will lead to further studies to assess the various approaches to esophageal dilation. This is important, not only to compare our results with other studies but also to develop an evidence-based protocol that leads to an improved patient care. While the goal of this study was not a validation of the “rule of 3” when using balloon

or Savary-Gilliard® dilators, this report shows that many endoscopists would rather use this rule, despite the weak supporting evidence. We encourage the design of further studies to assess the “rule of 3” with other dilators, as this is the only recommendation provided by clinical guidelines to perform a safe dilation with better controlled risks.

To conclude, esophageal dilation is a safe procedure for the management of esophageal stricture. Nonadherence to the “rule of 3” does not seem to be associated with a higher risk of complications, including esophageal perforation. Balloon dilation is associated with a higher rate of complications in our population.

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