Risk factors and clinical outcomes of endoscopic dilation in benign esophageal strictures: a long-term follow-up study

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Background and Aims: Endoscopic dilation (ED) is still the mainstay of therapeutic management of benign esophageal strictures (BESs). This study aimed to establish risk factors for refractory BESs and assess long-term clinical outcomes of ED.

Methods: We performed a retrospective study in 891 patients who underwent ED from 2003 to 2018 for BESs. We searched electronic medical records in 6 tertiary care centers in the Netherlands for data on clinical outcome of ED. Median follow-up was 39 months. The primary endpoint was risk factors for refractory BESs, defined as factors associated with an increased number of ED sessions during follow-up. Secondary endpoints were time from first to last ED session and adverse events.

Results: Dilation up to 13 to 15 mm was associated with a higher number of ED sessions than dilation up to 16 to 18 mm (5.0 vs 4.1; hazard ratio [HR], 1.4; $P = .001$). Compared with peptic strictures, anastomotic (4.9 vs 3.6; HR, 2.1; $P < .001$), radiation (5.0 vs 3.6; HR, 3.0; $P < .001$), caustic (7.2 vs 3.6; HR, 2.7; $P < .001$), and postendotherapy (3.9 vs 3.6; HR, 1.8; $P = .005$) strictures were associated with a higher number of ED sessions. After 1 year of follow-up, the proportions of patients who remained free of ED was 75% in anastomotic, 71% in radiation, 70% in peptic, 83% in postendotherapy, and 62% in caustic strictures. Esophageal perforation occurred in 23 ED sessions (.4%) in 22 patients (2.4%).

Conclusions: More than 60% of patients with BESs remain free of ED after 1 year of follow-up. Because dilation up to 16 to 18 mm diameter was associated with fewer ED sessions during follow-up, we suggest that clinicians should consider dilation up to at least 16 mm to reduce the number of ED sessions in these patients. (Gastrointest Endosc 2020;91:1058-66.)

Abbreviations: BES, benign esophageal stricture; CI, confidence interval; CVD, cardiovascular disease; ED, endoscopic dilation; HR, hazard ratio; IQR, interquartile range; SD, standard deviation.

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A benign esophageal stricture (BES), characterized by fibrotic narrowing of the esophageal lumen causing dysphagia, is frequently encountered in daily endoscopic practice. Common causes of BES include GERD, or esophageal injury because of surgery (anastomotic), radiotherapy, ingestion of a caustic substance, or endoscopic resection or ablation.[1]

The mainstay in therapeutic management of BES is endoscopic dilation (ED), which is generally performed with a session of stepwise bougie or balloon dilations.[2] In approximately two-thirds of patients, adequate dilation is achieved with 3 to 5 ED sessions.[3] In the remaining one-third of patients a refractory BES develops, requiring more ED sessions to relieve dysphagia. Because ED is a demanding procedure for patients and adds to hospital and treatment costs, additional treatment options have become available to avoid ED or reduce the number of ED sessions during follow-up, including needle-knife stricture incision of anastomotic strictures, stricture injection with corticosteroids, or placement of a self-expandable metal or biodegradable stent.[1,4,5]

Previous studies have identified anastomotic, radiation, peptic, and severely narrowed strictures as risk factors for a higher number of ED sessions during follow-up of patients with BESs. However, these studies are likely to be biased by their single-center design, relatively small sample size, and varying definitions of refractory BES.[6-8] Therefore, we aimed to study a large multicenter cohort of patients with BESs to evaluate ED over a prolonged follow-up time and to establish risk factors for refractory BES development.

METHODS

This multicenter retrospective cohort study included patients who had been treated with ED for BESs. We performed a search through the electronic endoscopy databases of 6 endoscopy centers to identify patients between March 2003 and October 2018. The study protocol was approved by the Medical Ethics Committee and Institutional Review Board of all participating centers.

Endoscopy databases were searched by using procedure-specific codes linked to synonyms for "endoscopic dilation therapy" and "esophagus." Patients were included in the retrospective analysis when they underwent at least 1 endoscopic bougie or balloon dilation for BES. Patients were excluded when no esophageal ED was performed (ie, the endoscopic procedure was incorrectly coded); their age was <18 years; ED was performed for a motility disorder (eg, achalasia), a postlaryngectomy benign stricture, or a malignant stricture; or first or follow-up ED sessions for BESs were performed outside the participating centers.

Data collection and definitions

We reviewed the electronic medical records of included patients and collected data regarding baseline patient characteristics (eg, age, gender, body mass index), stricture characteristics (eg, etiology, luminal diameter), ED characteristics (eg, procedure date, number and size of dilations), adverse events related to ED, and follow-up duration. BES was defined as fibrotic narrowing of the esophageal lumen, causing symptoms of dysphagia and requiring treatment.

In this study, we exclusively assessed patients treated with ED for BES. ED was defined as a session of stepwise dilations with bougies or balloons within a single endoscopic procedure. Stricture diameter was determined by the diameter of the first bougie or balloon used in an ED session. Size of dilation was determined from the first to the last bougie or balloon used in 1 ED session. The "rule of 3" was defined as bougie dilation with no more than 3 consecutive dilators of 1 mm after resistance is encountered with a bougie dilator in 1 ED session. Because this rule requires tactile resistance during dilation of the stricture, it does not apply to balloon dilation.[9]

Anastomotic strictures were defined as benign luminal narrowing after esophagectomy or gastrectomy, located at the esophagogastric or esophagojejunal anastomosis, respectively. Postendotherapy strictures were defined as benign luminal narrowing as a result of EMR, endoscopic submucosal dissection, or radiofrequency ablation. Cardiovascular disease (CVD) was defined as a history of myocardial infarction, angina pectoris, stroke, peripheral arterial disease, or heart failure.[10]

Procedures

Because this study assessed retrospectively collected data, endoscopic procedures were not standardized. Nonetheless, all participating centers complied with the guidelines for ED in clinical practice.[2] During the endoscopic procedure, patients received conscious sedation, deep sedation, or general anesthesia with an endotracheal tube, depending on the treating physician's discretion. ED was performed using wire-guided bougies (mainly Savary-Gilliard bougies, Cook Medical, Bloomington, Ind, USA) or balloon dilators, with or without fluoroscopic guidance.

Primary and secondary endpoints

The primary endpoint was risk factors for refractory BES. The mean number of ED sessions during follow-up was used to define a stricture as refractory. Risk factors for refractory BES were defined as factors associated with an increased number of ED sessions during follow-up. We assessed potential and previously identified risk factors for refractory BES, including stricture etiology, severely narrowed stricture diameter (<10 mm), and maximum stricture diameter achieved during the first 3 ED sessions during follow-up.[6-8] In addition, we separately assessed potential and previously identified risk factors for refractory postesophagectomy anastomotic strictures, including previous anastomotic leakage, preoperative CVD, early (≤90 days) stricture formation after surgery, location of the

TABLE 1. Baseline characteristics of patients treated with endoscopic dilation for benign esophageal strictures

Characteristics	All patients (n = 891)	Risk factor analysis (n = 751)					
		Anastomotic (n = 416)	Radiation (n = 132)	Peptic (n = 86)	Postendotherapy (n = 59)	Schatzki (n = 37)	Caustic (n = 21)
Age at diagnosis, y	63 ± 13	63 ± 11	66 ± 11	66 ± 15	67 ± 10	56 ± 18	48 ± 13
Gender, male	588 (66.0)	296 (71.2)	69 (52.3)	60 (69.8)	39 (66.1)	23 (62.2)	10 (47.6)
BMI, kg/m^2	20.8 ± 4.0	21.3 ± 3.8	19.2 ± 4.2	20.6 ± 3.9	22.1 ± 4.0	22.6 ± 3.5	20.7 ± 4.7
Cardiovascular disease	277 (31.1)	123 (29.6)	45 (34.1)	25 (29.1)	20 (33.9)	12 (32.4)	2 (9.5)
Diabetes	111 (12.5)	51 (12.3)	13 (9.8)	13 (15.1)	9 (15.3)	5 (13.5)	3 (14.3)
GERD	217 (24.4)	65 (15.6)	19 (14.4)	45 (52.3)	36 (61.0)	19 (51.4)	1 (4.8)
Stricture diameter <10 mm	424 (47.6)	205 (49.3)	76 (57.6)	37 (43.0)	25 (42.4)	14 (37.8)	8 (38.1)

Values are mean ± standard deviation or n (%).
BMI, Body mass index.

anastomotic stricture (cervical vs intrathoracic), severely narrowed stricture diameter (<10 mm), and maximum stricture diameter reached during the first 3 ED sessions during follow-up.[11-15]

Secondary endpoints comprised clinical outcomes of ED. We assessed time from first to last ED session (ie, clinical course) and adverse events. Time from first to last ED session was defined as the time between initial and last dilation after which no further ED treatment was required. Adverse events were defined as events related to ED that required repeated endoscopy or hospitalization.[16,17]

Additional endpoints included the rule of 3 as a potential risk factor for esophageal perforation in a subgroup of patients treated with bougie dilators in which stricture resistance for at least 1 bougie was reported by the endoscopist[16,17] and clinical success of stent placement as a second-line treatment for BES, defined as an ED-free period of 6 months after stent placement. Because this study assessed retrospectively collected data, various types of esophageal stents were used during the study period.

Statistical analysis

For the analysis of the primary endpoint, we used a mixed-effects model with a random intercept to account for clustering of patients within participating centers. Because we anticipated extra dispersion of the outcome repeated measures (ED sessions), we performed multilevel negative binomial regression analysis. Because this analysis results in a multivariate proportional hazard model, we tested whether risk factors were associated with differences in mean number of ED sessions while correcting for follow-up duration and confounding. For this model, we first used univariate analysis to select risk factors based on $P \leq .2$. Using backward stepwise elimination until all remaining variables reached $P < .05$, we determined whether factors were associated with differences in mean number of ED sessions. Results were expressed as means (± standard deviations [SD]), medians (interquartile range [IQR] or 95% confidence intervals [CIs], when appropriate), and hazard ratios (HRs) with 95% CIs and significance levels. We used geometric means and SDs to correct for extreme outliers. The mean number of ED sessions was calculated and plotted over a follow-up of 2 years, stratified by etiology.

Time from first to last ED session during follow-up was calculated and shown with Kaplan Meier curves and stratified by etiology. Patients treated with 1 ED session were censored at 0 months. Adverse events were expressed as percentages. To assess whether the rule of 3 was associated with esophageal perforation, we used a univariate logistic regression model. Results were expressed as percentages, odds ratio with 95% CI, and significance levels.

A 2-tailed $P < .05$ was considered significant in all statistical analyses. SPSS version 25.0 (IBM SPSS Statistics for Windows; IBM Corp, Armonk, NY, USA) was used for all study analyses.

RESULTS

The search through the endoscopy databases yielded a total of 1501 eligible patients, of whom 891 met the inclusion criteria. Median follow-up of all patients was 39 months (IQR, 19-75). The baseline characteristics of all included patients are shown in Table 1. Patients had a mean age of 63 (SD, ±13) years, and two-thirds (66.0%) were men. Figure 1 shows the study flow diagram of patient inclusion for the analysis of risk factors.

Risk factors for refractory BESs

In total, 751 patients with BESs (anastomotic, 416; radiation, 132; peptic, 86; postendotherapy, 59; Schatzki ring, 37; caustic, 21) were included in the risk factor analysis (Table 1). The mean (± SD) number of ED sessions was 4.9 (± 2.3) in anastomotic, 5.0 (± 2.6) in radiation, 3.6 (± 2.4) in peptic, 3.8 (± 2.7) in postendotherapy, 7.2 (±

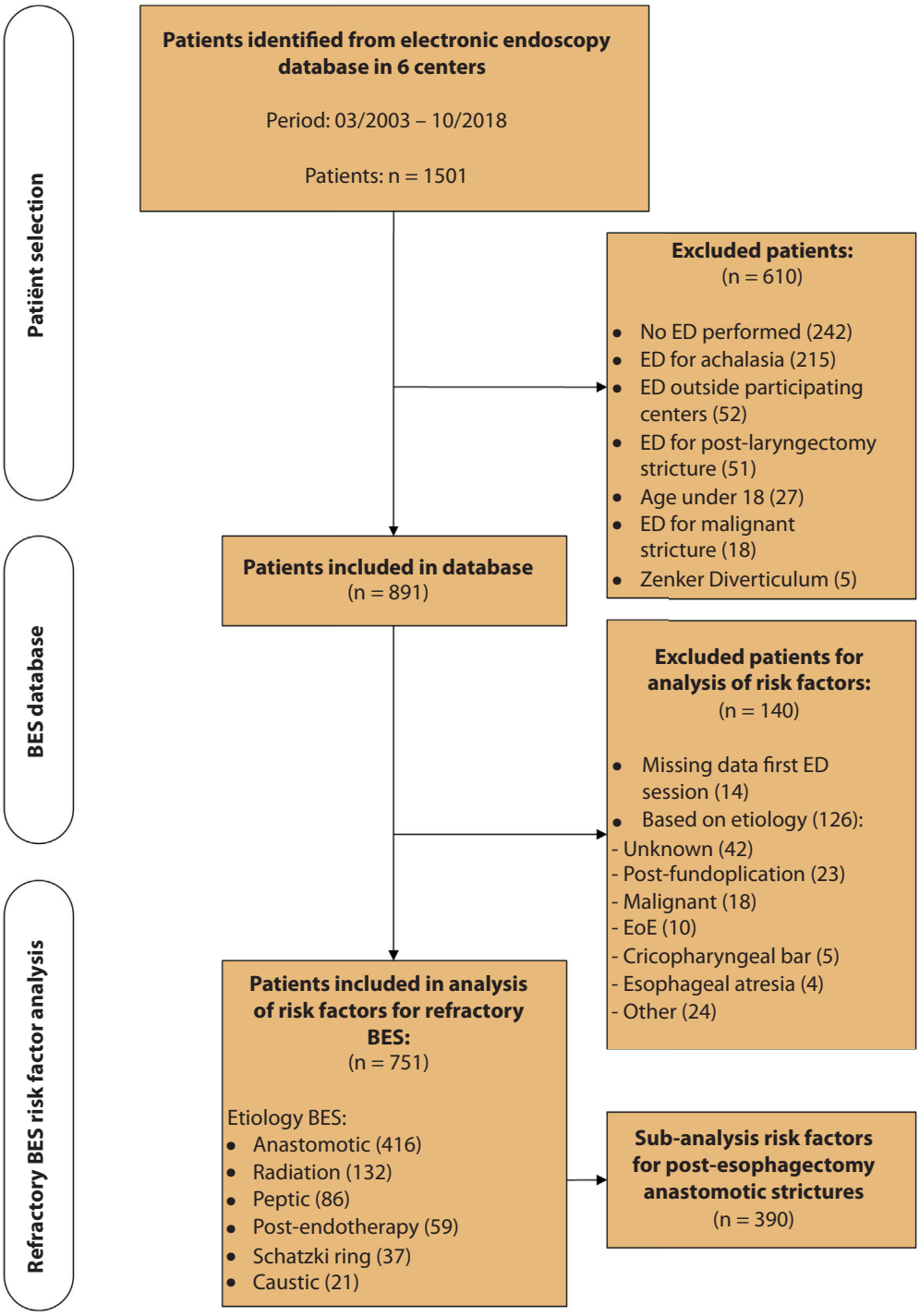

Figure 1. Study flow diagram of patient selection for risk factor analysis. *ED*, Endoscopic dilation; *BES*, benign esophageal stricture; *EoE*, eosinophilic esophagitis.

2.2) in caustic strictures, and 1.8 (± 1.9) in Schatzki rings. Figure 2 shows the mean number of ED sessions during a follow-up period of 2 years after the first ED session, stratified by etiology.

Table 2 shows the associations between potential risk factors and differences in the mean number of ED sessions during follow-up of patients with BESs. A higher number of ED sessions were observed during follow-up of patients in whom a maximum luminal esophageal diameter of 13 to 15 mm was reached during the first 3 ED sessions (mean ED sessions, 5.0 vs 4.1; HR, 1.4; 95% CI, 1.2-1.7; $P = .001$) when compared with patients in whom 16 to 18 mm was reached. No association was found between mean number of ED sessions and stricture diameter of <10 mm versus ≥10 mm at diagnosis (mean ED sessions, 4.6 vs 4.5; $P = .147$).

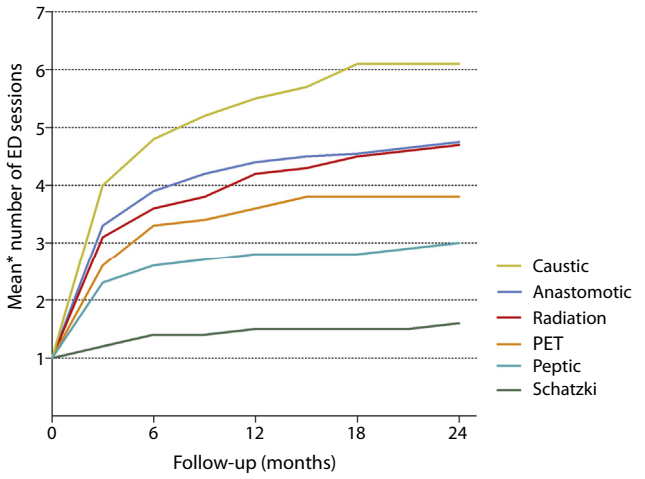

Figure 2. Mean number of endoscopic dilation sessions during 2 years of follow-up after first session for benign esophageal stricture, stratified by etiology. *ED*, Endoscopic dilation; *PET*, postendotherapy. *Means represent geometric means, calculated per 3-month time period.

Furthermore, when compared with peptic strictures, a higher number of ED sessions were observed during follow-up of patients with anastomotic (mean ED sessions, 4.9 vs 3.6; HR, 2.1; 95% CI, 1.6-2.8; $P < .001$), radiation (mean ED sessions, 5.0 vs 3.6; HR, 3.0; 95% CI, 2.2-4.1; $P < .001$), postendotherapy (mean ED sessions, 3.9 vs 3.6; HR, 1.8; 95% CI, 1.2-2.6; $P = .005$), and caustic strictures (mean ED sessions, 7.2 vs 3.6; HR, 2.7; 95% CI, 1.6-4.5; $P < .001$). In contrast, a lower number of ED sessions were observed in patients with a Schatzki ring (mean ED sessions, 1.8 vs 3.6; HR, .5; 95% CI, .3-.8; $P = .002$), when compared with peptic strictures.

Risk factors for refractory postesophagectomy anastomotic strictures

Three hundred ninety patients with postesophagectomy anastomotic strictures were included in the analysis of potential risk factors for refractory strictures. Median follow-up was 39 months (IQR, 17-80). The median time to the first ED session after esophagectomy was 91 days (IQR, 56-182).

Table 2 shows the associations between potential risk factors in postesophagectomy anastomotic strictures and differences in mean number of ED sessions during total follow-up. Risk factors associated with a higher number of ED sessions included first ED session within 90 days compared with >90 days after esophagectomy (mean ED sessions, 6.6 vs 3.7; HR, 1.8; 95% CI, 1.5-2.3; $P < .001$); preoperative CVD (mean ED sessions, 5.3 vs 4.9; HR, 1.5; 95% CI, 1.2-1.9; $P = .002$); previous anastomotic leakage (mean ED sessions, 6.1 vs 4.7; HR, 1.3; 95%, CI, 1.0-1.7; $P = .037$); and maximum luminal esophageal diameter reached in the first 3 ED sessions of 13 to 15 mm compared with 16 to 18 mm (mean ED sessions, 5.6 vs 4.7; HR, 1.4; 95% CI, 1.0-1.8; $P = .024$). No associations were found between the mean number of ED sessions and stricture diameter at diagnosis when comparing <10 mm versus ≥10 mm (mean ED sessions, 5.0 vs 5.1; $P = .297$) or cervical versus intrathoracic location of anastomosis (mean ED sessions, 5.5 vs 3.7; $P = .243$).

Time to last ED session

We assessed the time between first and last ED sessions during long-term follow-up of patients included in the risk factor analysis (n = 751). Median time between first and last ED session was 121 days (95% CI, 89-153) in anastomotic strictures, 103 days (95% CI, 55-151) in radiation strictures, 60 days (95% CI, 17-103) in peptic strictures, 87 days (95% CI, 47-127) in postendotherapy strictures, 259 days (95% CI, 32-486) in caustic strictures, and 34 days (1-148) in Schatzki rings.

Figure 3 shows Kaplan-Meier curves of time from the first to last ED sessions in patients with BESs associated with a higher number of ED sessions, stratified by etiology. After 1 year of follow-up, 75.2% of patients (313/416) with anastomotic strictures remained free of ED, whereas this was 71.2% (94/132) in radiation strictures, 69.8% (60/86) in peptic strictures, 83.1% (49/59) postendotherapy strictures, 61.9% (13/21) in caustic strictures, and 73.0% (27/37) in Schatzki rings.

ED-related adverse events

Table 3 shows characteristics of 5453 ED sessions performed in 891 patients. Patients were treated under conscious sedation in 4594 ED sessions (84.2%), propofol sedation in 689 ED sessions (12.6%). and general anesthesia with an endotracheal tube in 28 ED sessions (.5%). ED was assisted by fluoroscopy in 1085 sessions (19.9%). Savary bougies were used in 4909 (90.0%), balloon dilators in 462 (8.5%), and Eder-Puestow Olives in 33 sessions (.6%). Reinspection of the esophagus after ED was reported in 2066 sessions (37.9%).

In all 5453 ED sessions, 70 adverse events (1.3%) requiring repeat endoscopy and/or hospitalization occurred in 63 patients (7.1%) (Table 4). The most common adverse events were retrosternal pain after 27 ED sessions (.5%) in 24 patients (2.7%) and esophageal perforation after 23 ED sessions (.4%) in 22 patients (2.4%). Furthermore, esophageal hemorrhage occurred in 9 ED sessions (.2%) in 9 patients (1.0%), fever occurred after 6 ED sessions (.1%) in 6 patients (0.7%), and fistulas developed after 5 ED sessions (.1%) in 5 patients (.6%). No patient died from an ED-related cause.

Table 5 shows the association between the rule of 3 and esophageal perforation. For this analysis we used the subgroup of 2716 ED sessions in which the endoscopists reported bougie resistance for at least 1 bougie dilator. In these patients, 10 esophageal perforations (.4%) occurred in 10 patients. We found no association between noncompliance versus compliance with the rule of 3 and esophageal perforation (4 perforations [.6%] vs

TABLE 2. Multivariate analysis of factors associated with a higher number of ED sessions during follow-up of patients with benign esophageal strictures

	Mean* ED sessions	Hazard ratio	95% Confidence interval	*P* value
Benign esophageal strictures (n = 751)				
Risk factors†				
Etiology of benign esophageal strictures				
Peptic	3.6	Reference	—	—
Anastomotic	4.9	2.1	1.6-2.8	<.001
Radiation	5.0	3.0	2.2-4.1	<.001
Schatzki ring	1.8	.5	.3-.8	.002
Postendotherapy	3.9	1.8	1.2-2.6	.005
Caustic	7.2	2.7	1.6-4.5	<.001
Stricture diameter <10 mm				
Yes	4.5	Reference	—	—
No	4.6	.9	.7-1.1	.147
Maximum dilation size first 3 ED sessions				
16-18 mm	4.1	Reference	—	—
13-15 mm	5.0	1.4	1.2-1.7	.001
Postesophagectomy anastomotic strictures (n = 390)				
Risk factors‡				
Stricture <90 days postoperative				
No	3.7	Reference	—	—
Yes	6.6	1.8	1.5-2.3	<.001
Preoperative cardiovascular disease				
No	4.9	Reference	—	—
Yes	5.3	1.5	1.2-1.9	.002
Anastomotic leakage				
No	4.7	Reference	—	—
Yes	6.1	1.3	1.0-1.7	.037
Anastomotic location				
Cervical	5.5	Reference	—	—
Intrathoracic	3.7	.8	.6-1.1	.243
Stricture diameter <10 mm				
Yes	5.0	Reference	—	—
No	5.1	1.2	.9-1.5	.297
Maximum dilation size first 3 EDs				
16-18 mm	4.7	Reference	—	—
13-15 mm	5.6	1.4	1.0-1.8	.024

ED, Endoscopic dilation; —, no value.
*Means represent geometric means to correct for extreme outliers.
†Analysis is adjusted for stricture etiology, stricture diameter at baseline (<10 mm), maximum dilation size during first 3 ED sessions, and center of treatment.
‡Analysis is adjusted for moment of stricture development (<90 days), preoperative cardiovascular disease, anastomotic leakage, anastomotic location, stricture diameter at baseline (<10 mm), maximum dilation size during first 3 ED sessions, and center of treatment.

6 perforations [.3%], respectively; odds ratio, 2.4 [95% CI, .7-9.1]; $P = .185$).

Clinical success of esophageal stent placement

Of 751 patients, 78 (10%) were treated with stent placement. Before stent placement, patients had undergone a median of 4 ED sessions (IQR, 1-6; range, 1-25). After stent placement, patients were treated with a median of 4 ED sessions (IQR, 1-6; range, 0-30). The median ED-free follow-up was 82 days (95% CI, 64-100). Clinical success of stent placement was achieved in 21 patients (27%).

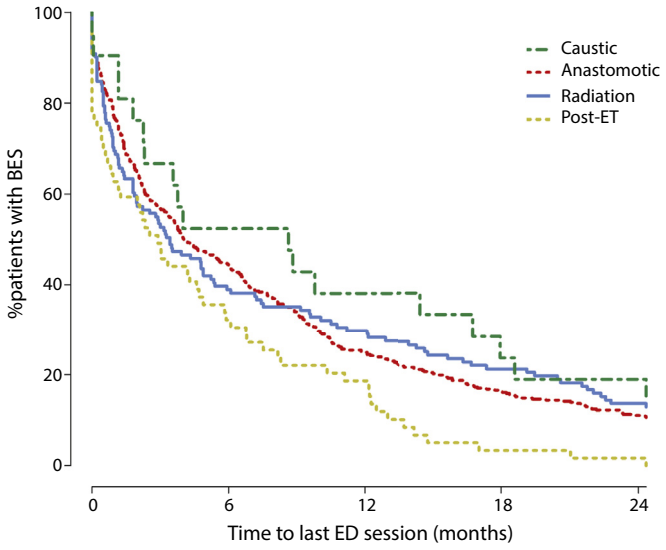

Figure 3. Time from first to last endoscopic dilation (ED) session during 2 years of follow-up of patients with benign esophageal strictures associated with a higher number of ED sessions, stratified by etiology. Event was defined as the last ED session during follow-up. Patients treated with 1 ED session were censored at 0 months. *BES*, Benign esophageal stricture; *post-ET*, postendotherapy.

DISCUSSION

In this multicenter cohort study, we evaluated ED during long-term follow-up of patients with BESs and identified risk factors for refractory BESs. We found that dilation up to 16 to 18 mm diameter after the first 3 ED sessions was associated with fewer ED sessions during follow-up when compared with dilation up to 13 to 15 mm diameter. In addition, anastomotic, radiation, caustic, and post-endotherapy strictures were associated with a higher number of ED sessions when compared with peptic strictures. Furthermore, we found that more than 60% of patients with BESs remained free of ED after 1 year of follow-up.

Previous retrospective studies that investigated risk factors for refractory BES so far have shown varying results.[3,6-8,18,19] This may be explained by 2 factors. First, most studies used different definitions for refractory BES. In 2005, Kochman et al[20] proposed a refractory BES definition to achieve uniformity among clinical studies. Since then, this definition has only been used in 1 study that investigated risk factors for refractory BES[6] but not in other studies.[7,21] Second, the varying results may also be related to the relatively small sample size of previous studies (range, 63-87 patients), which may have resulted in poor adjustment for confounding (eg, type of BES) in the multivariate analysis.[6-8]

The proposed Kochman definition (ie, the inability to successfully maintain a stricture to a diameter of 14 mm over 5 sessions at 2-week intervals) may not always be suitable for observational studies because this outcome measure is difficult to assess retrospectively. Moreover, a recent study has suggested that ED to 16 mm or more and not to 14 mm has a longer-lasting effect in postesophagectomy anastomotic strictures.[14] In an effort to find a more reliable clinical outcome measure for this retrospective analysis, we selected mean number of ED sessions during follow-up to assess treatment success of benign strictures.

Besides risk factors for refractory BESs in the entire group of BESs, we separately identified risk factors for refractory postesophagectomy anastomotic strictures because we found that this type of BES is currently the most common type of (refractory) BES in clinical practice. In accordance with previous literature, we established anastomotic leakage, early stricture formation postsurgery, and preoperative CVD as risk factors for a higher number of ED sessions.[13] Interestingly, cervical anastomosis was not associated with a higher number of ED sessions, despite being associated with a higher rate of stricture formation after surgery when compared with intrathoracic anastomosis.[15]

Findings from this study may have several implications for clinical practice. First, because we found that dilation up to 16 to 18 mm was associated with fewer ED sessions, we suggest that clinicians should consider ED to at least 16 mm in BES.

Second, because endoscopic treatment of superficial esophageal dysplasia and carcinoma is generally accepted, postendotherapy strictures have become a common cause of BES in endoscopic practice.[22,23] Because we found postendotherapy strictures to be associated with a higher number of ED sessions, we suggest that clinicians should consider using already known additive treatment options that could prevent postendotherapy strictures, such as oral administration or local injection of corticosteroids after endoscopic esophageal resection.[24-26]

Third, we demonstrated that most types of BESs frequently require repeated ED sessions within the first year of follow-up (Fig. 2). In addition to ED, alternative endoscopic treatment options are available for BESs.[1] Previous studies have shown that esophageal biodegradable stent placement, needle-knife stricture incision, and, as mentioned above, stricture injection with corticosteroids reduced the number of ED sessions in patients with refractory BESs when compared with ED alone and therefore should be considered in daily clinical practice.[5,27-31] Nonetheless, with regard to esophageal stent placement, our study shows that stent placement was successful in only a limited number of patients (27%). Most patients still needed ED within 6 months after stent placement.[1]

Another approach to reduce the number of ED sessions could be to increase dilation diameter per session (not following the rule of 3).[17] Accordingly, when dilating over 3 mm per ED session, a sufficient esophageal diameter was achieved with fewer ED sessions required to relieve dysphagia. Importantly, because our study shows that noncompliance with the rule of 3 was not associated with esophageal perforation (Table 5), we confirm

TABLE 3. Characteristics of endoscopic dilation in patients with benign esophageal strictures

Characteristics	No. of ED sessions (%) (n = 5453 in 891 patients)
Patient sedation or anesthesia	
Conscious sedation	4594 (84.2)
Deep sedation	689 (12.6)
General anesthesia with an endotracheal tube	28 (.5)
None	51 (.9)
Missing	91 (1.7)
Fluoroscopic assistance	1085 (19.9)
Type of endoscopic dilator	
Savary	4909 (90.0)
Balloons	462 (8.5)
Eder-Puestow	33 (.6)
Missing	49 (.9)
Reinspection after ED session	2066 (37.9)
Bougie resistance reported in Savary subgroup (n = 4909)	
Yes	2716 (55.3)
No	2193 (44.7)
Rule of 3 in resistance to Savary dilation subgroup (n = 2716)	
Compliance	2033 (74.9)
Noncompliance	670 (24.7)
Missing	13 (.4)

ED, Endoscopic dilation.

TABLE 4. Adverse events of endoscopic dilation in patients with benign esophageal strictures

Adverse event	Events in patients n (%)
Total adverse events	70 (1.3) in 63 (7.1)
Perforation	23 (.4) in 22 (2.4)
Hemorrhage	9 (.2) in 9 (1.0)
Fever	6 (.1) in 6 (.7)
Retrosternal pain	27 (.5) in 24 (2.7)
Fistula	5 (.1) in 5 (.6)

findings from a study that suggested dilation over 3 mm per session can be safely performed without an increased risk of esophageal perforation.[16]

Finally, the present study may help clinicians to manage patients' expectations of treatment with ED. The presence of risk factors may be used to inform patients about the risk of repeated ED sessions to completely relieve dysphagia. Furthermore, this study provides an estimation of time required to relieve dysphagia without the further need of ED in most patients (Fig. 3).

TABLE 5. Rule of 3 and risk of esophageal perforation in patients treated with endoscopic dilation for an esophageal stricture

Rule of 3	Perforation, n (%)	Odds ratio	95% Confidence interval	*P* value
Compliance	6 (.3)	Reference	—	—
Noncompliance	4 (.6)	2.4	.7-9.1	.185

—, No value.

The main strength of this study is the long-term follow-up (median of 39 months) of patients with the most common etiologies of BES in daily clinical practice. The large multicenter data set provided the opportunity to perform multilevel multivariate regression analysis, which allowed adjustment for potential confounders, differences in follow-up duration, and treatment center (ie, clustering of data). Furthermore, performed ED sessions during follow-up were well documented in the endoscopy databases and patients' medical records, which resulted in no missing data on the primary endpoint. Nonetheless, the retrospective study design should still be recognized as a limitation.

In conclusion, dilation up to 16 to 18 mm diameter was found to be associated with fewer ED sessions during follow-up when compared with dilation up to 13 to 15 mm. Therefore, our findings suggest that clinicians should consider dilation to at least a 16-mm esophageal diameter. This may reduce the number of ED sessions required to relieve dysphagia in patients with BESs.

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