PROGRESSIVE ESOPHAGEAL DILATION FOR BENIGN STRICTURES: A RANDOMIZED CONTROLLED TRIAL

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal stenosis and obstruction
Study type	Interventional

Summary

ID

NL-OMON43360

Source
ToetsingOnline

Brief title
PROGRESSIVE ESOPHAGEAL DILATION FOR BENIGN STRICTURES

Condition

- Gastrointestinal stenosis and obstruction

Synonym
benign esophageal narrowing, benign esophageal stricture

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: benign, dilation, esophagus, stricture

Outcome measures

Primary outcome

The primary objective is to prospectively evaluate the efficacy of esophageal dilation according to the rule of 3 compared with the rule of > 3 in patients with severe benign esophageal strictures.

Efficacy:

- Total number of dilation sessions during dilation to 16-18mm and within 6 months of follow-up

Secondary outcome

- Number of patients remaining dysphagia free within 6 months after dilation to 16-18mm (measured with dysphagia diary)

- Time from first dilation session to dilation of 16-18mm

- Time to dilation of recurrent stricture after initial dilation to 16-18mm

- Safety: mortality, serious adverse event and adverse events

- Quality of Life (measured with EQ5D questionnaire)

- Direct medicals costs: procedures, secondary interventions

- Technical success

* Definition: defined as ease of dilation with multiple Savary bougie implantations of different sizes at the required location of stenosis.

Study description

Background summary

A benign esophageal stricture is a narrowing of the esophagus that causes difficulty to swallow, and endoscopically is defined by the inability to cross it with an endoscope of 9 mm of diameter. Clinical symptoms may be dysphagia, odynophagia, weight loss and regurgitation of food.

Benign esophageal strictures are relatively common in clinical practice. In the past, peptic stricture secondary to gastroesophageal reflux, were the most frequent, whereas at present are mainly secondary to caustic ingestion and radiotherapy (1). In recent years they have also been described as a result of advanced endoscopic therapy in the esophagus: endoscopic mucosal resection (EMR) and submucosal dissection (ESD).

Generally, most benign strictures respond well to endoscopic dilation, but in 25-35% of cases, multiple sessions of dilation are necessary.2 Postsurgical stenosis secondary to ingestion of caustic, and those caused by radiation treatments, have a low response rate to endoscopic treatment, where over 40% of cases tend to recur. Additionally, a hypopharyngeal location of a stenosis, regardless of the cause, is usually refractory to endoscopic dilation.

Endoscopic dilation therapy
The aims of dilation are to alleviate dysphagia, reduce the risk of pulmonary aspiration, maintain oral nutrition, and facilitate passage of endoscopes.3 Adverse events (AEs) of dilation include perforation, bleeding, pulmonary aspiration, and fistula formation. Perforation occurs in 0.1% to 2.6% of procedures and is the most feared AE with a mortality rate as high as 20%4,5. Risk factors for dilation-induced perforation include eosinophilic esophagitis, complex strictures, and malignant stenoses.4,6
Balloon and bougie dilators are used to perform dilation. As opposed to radial forces incurred by balloon dilators, bougie dilators also generate longitudinal forces. This difference has never been proven to have any effect on the rate of AEs or clinical outcome between Savary (bougie) and through-the-scope (TTS) balloon dilators.7-10 Theoretically, more dilation sessions are needed with bougie dilators because the rule of 3 may limit the number of sessions. The rule of 3 states that no more than 3 dilators of progressively increasing diameter should be passed after moderate resistance is encountered. This rule is applicable to bougienage alone and was intended to preclude overaggressive dilation and consequent perforation. Although the rule of 3 makes common sense, it is not evidence based. One study suggests that dilation using larger incremental diameters may be safe for simple strictures.11
One retrospective cohort study assesses a high volume of esophageal dilations and the association between the rule of 3 and non-adherence to the rule of 3 to AEs during esophageal bougienage and balloon dilation. Results demonstrate that adherence to the rule of 3 does not appear to reduce the risk of AEs, including esophageal perforation, after esophageal dilation with bougie or balloon

dilators. Malignant structures are associated with an increased risk of AEs and perforations.12

This clinical trial is designed to investigate prospectively, in a randomized controlled setting, the efficacy of non-adherence to the rule of 3 in benign esophageal strictures with the use of the Savary bougie dilator. The proposed alternative to the rule of 3 is the rule of > 3 esophageal dilation strategy. Advantages of this more progressive dilation strategy is less esophageal dilation sessions in total and thus less risks of AEs during esophageal dilation and lower costs. This is hypothesised to result in an accelerated response to dilation treatment for dysphagia due to severe benign esophageal strictures.

Study objective

The main objective is to compare the efficacy and safety of esophageal dilation with the balloon the Savary bougie dilator according to the rule-of-3 to rule-of > 3 strategy during 6 months in patients with a severe benign esophageal stricture.

Secondary objectives are to compare safety, quality of life and technical success of dilation with the Savary bougie dilator.

Study design

A randomized controlled clinical trial, in a single center (Radboudumc), is designed to compare the efficacy of esophageal dilation with the Savary bougie dilator according to the rule-of-3 to rule-of > 3 strategy during 6 months in patients with a severe benign esophageal stricture.
After dilation to 16-18mm, the patient will be monitored for 6 months

Intervention

Dilation is carried out with the Savary bougie dilator in both groups. The stricture will be dilated to a diameter of 16-18mm, according to the preference of the endoscopist. As a general rule in daily practice (rule of 3) a minimum of 3 dilation sessions are required to reach a diameter of 16-18mm when a severe stricture is present. The maximum diameter should be reached within a maximum of 3 weeks time. A severe stricture is defined as a stricture with no patency for a standard endoscope (9-10mm diameter).
In the scenario where dilation is done progressively (rule of > 3) a minimum of 2 dilation sessions are required to reach a diameter of 16-18mm in severe strictures. The maximum diameter should be reached within a maximum of 2 weeks time. Endoscopy is performed immediately after the dilation session to check for potential complications and to confirm efficacy of the dilation.

Rule of 3 (standard of care)
One group consists of dilation according to the rule of 3. The rule of 3 is defined by the American Society for Gastrointestinal Endoscopy (ASGE) guideline13 on esophageal dilation: no more than 3 consecutive dilations in increments of 1 mm should be passed in a single dilation session.

Examples:
Patient presented with a severe stricture of 9mm diameter.
- first dilation session: 9 - 10 - 11mm
- second dilation session: (11) - 12 - 13 - 14mm
- third dilation session: (14) - 15 - 16 - 17mm

Patient presented with a severe stricture of 10mm diameter.
- first dilation session: 10 - 11 - 12mm
- second dilation session: (12) - 13 - 14 - 15mm
- third dilation session: (15) - 16 - 17 - 18mm

Rule of > 3 (intervention)
The rule of > 3 is defined as: no more than 6 consecutive dilations in increments of 1 mm should be passed in a single dilation session.

Example:
Patient presented with a severe stricture of 9mm diameter.
- first dilation session: 9 - 10 - 11 - 12 - 13mm
- second dilation session: (13) - 14 - 15 - 16 - 17mm

Patient presented with a severe stricture of 10mm diameter.
- first dilation session: 10 - 11 - 12 - 13mm
- second dilation session: (13) - 14 - 15 - 16 - 17 - 18mm

Study burden and risks

As of today no literature is available investigating the effect of a less conservative dilation strategy. In theory, the expected benefits for patients that are dilated according to the rule of > 3 are:
- A smaller number of sessions required to achieve response to treatment. The patient has to undergo less sessions of esophageal dilation to achieve relief of their dysphagia, resulting in less risk of AEs and less hospital visits.
- Response to treatment is reached at an earlier stage of treatment due to the extended effect of the dilation increments. Thus, the patient has relief of their dysphagia at an earlier stage of disease, resulting in a potential quality of life improvement.

In terms of safety, Grooteman et al12. reported that non-adherence to the rule of 3 was not associated with a higher risk of major AEs in patients with benign esophageal strictures. Non-adherence to the rule of 3 was defined as a esophageal dilation with increments higher than 1 mm per dilation and >= 3

dilations in a single session. In the non-adherence group 0.5% vs. 1.6% AEs in rule of 3-dilations was reported, with no significant difference (P = .18). For perforations, the most feared complication of dilation, 0% in the non-adherence group vs. 0.7% in rule of 3-dilations was reported, with no significant difference (P = .18)

Participation in the study does not cause any additional charge to patients. The esohpageal dilations and follow-up are not different from the usual in clinical practice.

The main advantage of esophageal dilation according to the rule of > 3 is that is possible less interventions required. Moreover, another advantage is that it can be more effective in solving the benign stricture at an earlier stage of disease.

The risk classification is determined as negligible based on the guideline of the *Nederlandse Federatie van Universitair Medische Centra*. The risks associated with the participation in the study are similar to the risks of treatment with conservative dilation, and not different from the complications arising from dilation according to the rule of 3.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Dysphagia due benign esophageal stricture requiring esophageal dilation (e.g. surgery, radiation therapy, caustic ingestion, peptic injury, photodynamic therapy)
- Requiring first esophageal dilation for dysphagia due to a severe benign esophageal stricture with no patency for standard upper endoscope (9-10mm diameter)
- No history of esophageal endoscopic dilations for benign strictures the past 6 months
- Dysphagia for solid, semisolid or liquid food (dysphagia score <= 2 [Ogilvie]16, and dysphagia score <= 21 [Dakkak and Bennett]19, see appendix)
- Written informed consent

Exclusion criteria

- Patient < 18 years old
- Patient is unwilling or unable to sign and date the informed consent
- Patient is unwilling or unable to comply with the follow-up schedule
- Patient is unable to understand informed consent and fill in the questionnaires due to a language barrier
- Patient is pregnant, breast-feeding, or planning to become pregnant in the next 12 month
- Patient is simultaneously participating in another drug or device study or the patient has completed the follow-up phase for the primary objective of any previous study less than 30 days prior to enrollment in this study
- Previous esophageal dilation for benign stricture within the past 6 months
- Patient with a life expectancy < 12 months
- Patient with a known eosinophilic esophagitis or motility disorder (such as achalasia)
- Patients with a known malignant esophageal stricture
- Patients with coagulopathy
- Patients with a benign stricture due to a previous performed laryngectomy

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-04-2017
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Savary-Gilliard bougie
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	19-04-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL60222.091.16