Endoscopic Dilatation versus Oesophageal Stent in Benign Oesophageal Stricture

Hadyanto Caputra, Iqbal I Awang*, Pringgodigdo Nugroho**, Ari Fahrial Syam****

*Faculty of Medicine, Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

**Division of Renal-hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia/ Dr. Cipto Mangunkusumo General National Hospital, Jakarta

***Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo General National Hospital, Jakarta

Corresponding author:

Ari Fahrial Syam. Division of Gastroenterology, Department of Internal Medicine, Dr. Cipto Mangunkusumo General National Hospital. Jl. Diponegoro No.71 Jakarta Indonesia. Phone: +62-21-3153957; Facsimile: +62-21-3142454. E-mail: ari_syam@hotmail.com

ABSTRACT

Aim: *Oesophageal stricture is one of the causes of dysphagia. It is a condition in which the lumen of oesophagus is narrowed by fibrotic tissue in the oesophageal wall. It is usually caused by inflammation or any other cause that leads to necrotizing of tissue. It is mainly differentiated into benign or malignant. The aim of this article is to answer the clinical question on the effectiveness of oesophageal stenting compared to endoscopic dilatation in patient with benign oesophageal stricture due to ingestion of corrosive substances, who had undergone several endoscopic dilatations.*

Method: *We conducted search of relevant articles using PubMed search engine to answer the clinical question. Keywords being used during the search process were: ("oesophageal stricture"[All Fields] OR "oesophageal stenosis"[All Fields] AND (("dilatation"[All Fields] AND ("stents"[MeSH Terms] OR "stents"[All Fields] OR "stent"[All Fields]). Results were further converged by adding specific filters, which were full text articles and clinical trial.*

Results: *The chosen article was further appraised in order to identify its validity and eligibility to answer the clinical question. We chose to use CONSORT (statement to improve the quality of reporting of RCTs) to facilitate the critical appraisal and interpretation of RCTs.*

Conclusion: *Stenting was associated with greater dysphagia, co-medication and adverse events. No randomized controlled trials which compared biodegradable stents with other stents or with balloon dilatation was identified. Lack of adequately robust evidence for effectiveness and cost-effectiveness formed the rationale of this trial.*

Keywords**:** *benign oesophageal stricture, endoscopic dilatation, stent*

ABSTRAK

Tujuan: *Striktur esofagus merupakan salah satu penyebab disfagia. Striktur esofagus adalah suatu kondisi di mana lumen esofagus menyempit karena adanya jaringan fibrosis pada dinding esofagus. Hal ini biasanya disebabkan oleh inflamasi atau penyebab lain yang selanjutnya dapat merangsang jaringan untuk mengalami nekrosis. Secara umum, striktur esofagus dibagi menjadi dua, yaitu jinak dan ganas. Tujuan artikel ini adalah untuk menjawab pertanyaan klinis tentang efektivitas sten esofagus dibandingan dengan dilatasi endoskopi pada pasien dengan striktur esofagus jinak akibat menelan zat korosif dan telah menjalani dilatasi endoskopi beberapa kali.*

Metode: *Kami melakukan pencarian artikel yang relevan dengan menggunakan alat pencarian PubMed untuk menjawab pertanyaan klinis tersebut. Kata kunci yang kami gunakan pada proses pencarian adalah: ("oesophageal stricture"[All Fields] OR "oesophageal stenosis"[All Fields] AND (("dilatation"[All Fields] AND ("stents"[MeSH Terms] OR "stents"[All Fields] OR "stent"[All Fields]). Kemudian, pada hasil pencarian, kami menambahkan filter full text articles dan clinical trial.*

Hasil: *Artikel yang terpilih selanjutnya ditelaah untuk mengevalusi validitas dan kesesuaiannya untuk menjawab pertanyaan klinis tersebut. Kami memilih metode CONSORT (pernyataan untuk meningkatkan kualitas pelaporan uji kontrol acak) untuk membantu menelaah dan menafsirkan uji kontrol acak secara kritis.*

Simpulan: *Pemasangan stent berhubungan dengan memberatnya gejala disfagia, penggunaan lebih dari satu obat, dan timbulnya efek samping. Tidak ditemukan adanya uji kontrol acak yang membandingkan stent dengan stent lain atau dilatasi balon. Kurangnya bukti kuat mengenai efektivitas dan kendali biaya merupakan dasar dilakukannya pencarian ini.*

Kata kunci: *striktur esofagus jinak, dilatasi endoskopik, stent*

INTRODUCTION

Esophageal stricture is one of the cause of dysphagia, which is a subjective sensation of organic abnormality during the process of food or liquid passing from the oral cavity to stomach. It varies from unable to swallow (oropharingeal dysphagia) to sensation of obstruction while food passing the oesphagus to stomach (esophageal dysphagia). Esophageal stricture is a condition which the lumen of esophagus narrowed by fibrotic in the esophageal wall. Usually due to inflamation and any other causes that lead to necrotizing of tissue.[1] Esophageal stricture is differentiated into benign or malignant. The later usually caused by malignancy or cancer in esophagus, could be intralumen or extralumen. And the first may caused by gastro esophageal reflux disease (GERD), corrosive substance, after anastomoses of esophagus, after radiotheraphy and chronic esophagitis.[2,3] Esophageal trauma caused by corrosive substance may lead to stricture. Stricture that caused by corrosive substance should be monitored periodically that recurrent of the sticture might happened. Ingestion of corrosive substances remain an important public health issue in Western countries despite education and regulatory efforts to reduce its occurrence. These injuries are still increasing in developing countries, related to the social, economic, and educational variables and mainly to a lack of prevention. The problem is largely unreported in these settings and its true prevalence simply cannot be extrapolated from the scarce papers or personal experience.[2,3,4]

Traditionally, ingested corrosive substances are either alkalis or acids. Alkaline material accounts for most caustic ingestions in Western countries whereas injuries from acid are more common in some developing countries, like India, where hydrochloric acid and sulfuric acid are easily accessible. Acids and alkalis produce different types of tissue damage. Acids cause coagulation necrosis, with eschar formation that may limit substance penetration and injury depth. Conversely, alkalis combine with tissue proteins and cause liquefactive necrosis and saponification, and penetrate deeper into tissues, helped by a higher viscosity and a longer contact time through the esophagus.[4,5] In 1994, Cipto Mangunkusumo hospital conducted endoscopic examination of upper gastrointestinal tract in 21 patients. It was found that 6 (28.57%) patients had esophageal stricture of any causes, 14.29% of them were found a solid tumor, 9.25% due to corrosive substance, and 4.76% in patients after sclerotherapy of esopahageal varices Several modalities to treat the stricture such as dilatation of esophagus, intra lession corticosteroid injection, placing stent, stricturoplasty, and resection of the stricture. Choosing treatment modality should consider several things and condition, and differ from one patient to another. The main goal is to recover the function of esophagus as a passage way and swallowing process.[6]

Benign oesophageal strictures (narrowing of the oesophagus) present with dysphagia of solid or liquid foods, which may result in malnutrition, aspiration, and weight loss. Strictures are conventionally treated by endoscopic dilatation using either a balloon (radially dilating the stricture) or a bougie (dilating the stricture by shearing longitudinal force).[6,7] The placement of self-expanding metallic stents is routinely used to maintain esophageal patency in patients with malignancy that either have non-resectable disease or are poor candidates

for surgery. Many reports have documented the clinical effectiveness of these tools, particularly covered metallic stents. However, the usefulness of metallic stents for benign stenosis is limited due to relatively little information regarding their long-term complications, including migration, the formation of new strictures, fistula formation and hyperplastic tissue reactions.[6,7] Since the cause of benign esophageal stenosis does not directly affect the patients' prognosis, it is more important to prevent the incidence of long-term complications. It is highly desirable to develop a stent that could be kept in the proper position during the repair process, and then be easily removed, thus avoiding re-stenosis. In other words, if a stent could be constructed from a biodegradable material, then a subsequent stent removal operation would not be necessary. The degradable nature of the stent would prevent serious long-term complications.[8] The question is, when a person had underwent dilatation for several times to treat the stricture, is it necessary to change the modality of mid or long term treatment such as placing stent in the stricture to prevent recurrent stenosis. Or, is dilatation still being a choice of treatment for the stenosis, although it would be done repeatedly in several months?

CLINICAL QUESTION

Patient is a male, 25 years old, was hospitalized due to hematemesis and melena. It started when he had given a drink by his friend while working. He felt that the taste of carbonized drink very unusual, but he kept swallow it about half of bottle. About 2 hours later, while he was at home, all of sudden he had a projectile vomit which consist of blood, about 2 times. He felt that his throat like being burned. Than he fell out and administered to the hospital. He was diagnosed having a esophageal stricture due to corrosive substance. Before he drank the soda, he smelt some kind of chemical of floor cleaner.

He had underwent several endoscopic dilation with balloon, about 2-3 months due to repeated stricture that made him not be able to eat, even to drink. He should drink small amount of water to get it swallowed. He ask wether there is a way that he would not take dilation often. Other option is placing stent which can dilate the lumen for longer period, instead of short term repeated dilation. How effective is stent would replace endoscopic dilation?

In this paper of EBCR, we should find the answer of the question mentioned before, wether dilatation still being a choice for treating the stricture, or is it necessary to place a stent to prevent recurrent stenosis or stricture, instead of repeatedly dilating the stenosis through endoscopy in a benign oesophageal strictures.

METHOD

In order to answer the question, we conduct searching in PubMed for evidences in studies or clinical trials that has high correlation and answer the question. We used several keywords with bollean OR or/and AND. These are the keywords that being used for searching the articles: ("oesophageal stricture"[All Fields] OR "esophageal stenosis"[All Fields] AND (("dilatation"[All Fields] AND ("stents"[MeSH Terms] OR "stents"[All Fields] OR "stent"[All Fields]). The result shows 125 articles in any kind of studies. We filter the articles which are full text articles. Then the articles converge into 16 articles. We want to compare between modalities of therapy, so we should find articles that the type of study suitable to answer the question. The proper type of study should be a clinical trial. So then, we filterized the

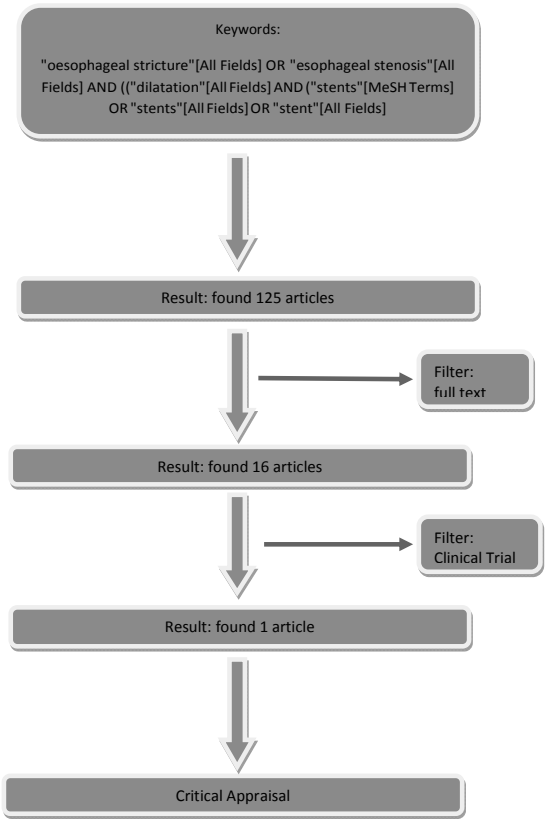

Figure 1. Framework and concept of searching articles

Figure 2. Checklist of item in reporting a randomized trial (CONSORT)[9]

Paper section and topic	Item number	Descriptor	Reported on page number
Title and abstract	1	How participants were allocated to intervention (e.g., "random allocation," randomized, " or randomly assigned")	1
Introduction background	2	Scientific background and explanation of rationale	2
Methods			
participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	3
Interventions	4	Precise details of the interventions intended for each group and how and what they were actually administered.	3
Objectives	5	Specific objectives and hypotheses	3
Outcomes	6	Clearly defined primary and secondary outcome measure and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors)	3
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	3
Randomization			
Sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification).	3
	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	3
Allocation concealment	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	3
Implementation	11	Whether or not participants, those administering the interventions, and those assessing the outcome were blinded to group assignment. If done, how the success of blinding was evaluated.	3
Blinding (masking)	12	Statistical methods used to compare groups for primary outcome (s); method additional analyses, such as subgroup analyses and adjusted analyses.	3
Results			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	4
Recruitment	14	Dates defining the periods of recruitment and follow up.	4
Baseline data	15	Baseline demographic and clinical characteristics of each group	5
Numbers analyzed	16	Number of participants (denominator) in each group induded in each analysis and whether the analysis was by "intention to treat." State the results in absolute numbers when feasible (e.g., 10 of 20, not 50%).	4
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effects size and its precision (e.g., 95% confidence interval).	4
Anciliary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory	6
Adverse events	19	All important adverse events or side effects in each intervention group	7
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes	5
Generalizability	21	Generalizability (external validity) of the trial findings	7
Overall evidence	22	General interpretation of the results in the context of current evidence	7

search method by adding "clinical trial" in advance search. The result leads to one article that can answer the question, titled "Biodegradable stent or balloon dilatation for benign oesophageal stricture: Pilot randomised controlled trial" by Dhar A, et al, which published in World Journal of Gastroenterology in 28th December, 2014. The framework and concept of searching is illustrated in figure 1.

RESULTS

The choosen article should be appraised in order to see wether it has good validity and eligible to answer the question. A group of scientists and editors developed the CONSORT (statement to improve the quality of reporting of RCTs. The statement consists of a checklist and flow diagram that authors can use for

reporting an RCT. Many leading medical journals and major international editorial groups have adopted the CONSORT statement.[9]

The objective of CONSORT is to facilitate critical appraisal and interpretation of RCTs by providing guidance to authors about how to improve the reporting of their trials. Peer reviewers and editors can also use CONSORT to help them identify reports that are difficult to interpret and those with potentially biased results. However, CONSORT was not meant to be used as a quality assessment instrument.[9]

DISCUSSION

The study has been using CONSORT guideline in reporting the methods, from abstract to outcome. Also in flow diagram, it has already adapted The study used a pilot multicentre randomised controlled trial design. Blinding of clinicians and patients was not practicable; ecording of symptoms was performed by a single blinded observer at baseline, 3, 6 and 12 months.

The article state that balloon dilatation relieves dysphagia in about 80-90% of patients although associated with small risks of bleeding and perforation and, in around 30-40% of patients, the stricture recurs needing repeated endoscopic dilatation. Recurrence appears more common for complex strictures related to radiation therapy, corrosive injury or surgical anastomosis. Repeat dilatation is preferred for refractory strictures when compared to surgery, which is associated with high morbidity rates as well as high risk for patients with comorbidities.

This statement fits to the patient, which had underwent a corrosive injury and had several times of dilation. Dilation stretches the narrowed oesophagus by radial distension. Stretching is believed to disrupt the collagen and elastin fibres in the oesophageal wall, responsible for the fibrotic stricture, and open up the lumen. Most patients respond to the dilatation well and maintain luminal patency of the oesophagus for a reasonable period of time.

Patient is cathegorized as benign oesophageal strictures, due to injury by ingestion of acid or alkaline caustic agents (corrosive strictures). Other causes that cathegorized as benign oesophageal strictures are injury by acid reflux (peptic strictures); radiation induced inflammatory strictures; sequelae of therapeutic endoscopic interventions for early oesophageal cancer and Barrett's oesophagus (such as endoscopic mucosal resection or photodynamic therapy); post surgical anastomotic strictures; and eosinophilic oesophagitis.

Self-expanding plastic or metal stents have been used to dilate benign recurrent oesophageal strictures, as a means of reducing the need for repeated endoscopic balloon/bougie dilatation with mixed results and potential complications of stent migration, hyperplastic tissue ingrowth or overgrowth (metal stents), oesophageal obstruction due to collapsed stent, thoracic pain and disappointing longer-term symptom relief.

Biodegradable stents work to the same principle as removable metal/plastic stents without requiring endoscopic removal since the stent dissolves gradually in-situ, thus avoiding the need for it to be removed. The biodegradable stent is made from polydioxanone, a monocrystalline polymer that has been used in monofilament surgical suture materials, and has a 55% crystalline structure. It is degraded in living tissue by hydrolytic attack which breaks down the crystalline structure into smaller fragments.

The longer persistence of the PDX stent is thought to allow adequate time for oesophageal remodelling to take place. Typically the stent maintains integrity and radial distensile force for 6-8 weeks, and disintegrates in 11-12 weeks following implantation.

Randomisation was web-based, stratified by hospital site with a block size of four, allocating patients in a 1:1 ratio to biodegradable oesophageal stent (BS) or standard endoscopic balloon dilatation (ED) When the study had recruited 17 patients (10 BS and 7 ED). One patient from each group was subsequently withdrawn before treatment due to ineligibility (BS: mental incapacity; ED prior cancer), leaving 9 BS and 6 ED patients for analysis.

The primary outcome was the average dysphagia score during the first 6 months, where dysphagia was patient assessed on a five-point scale. Secondary endpoints assessed were: the number of repeat endoscopic procedures (therapeutic and diagnostic); adverse events (including hospital admissions); quality of life assessed physically using the surrogate markers of weight; generic quality of life assessment.

Although both groups improved, average dysphagia score for patients receiving stents remained significantly higher after 6 months: BS-ED 1.17 (95% CI: 0.63-1.78; $p = 0.029$). Estimation of dysphagia by AUC method was similar (noting the

0.5 weighting for a 6 months average. Stenting was associated with greater dysphagia, co-medication and adverse events. This may have occurred in part because of chance atypical low dysphagia follow-up scores in the balloon dilatation group.

CONCLUSION

Stenting was associated with greater dysphagia, co-medication and adverse events. This may have occurred in part because of chance atypical low dysphagia follow-up scores in the balloon dilatation group. No randomized controlled trials comparing biodegradable stents with other stents or with balloon dilatation have been identified. Lack of adequately robust evidence for effectiveness and cost-effectiveness formed the rationale of this trial.

REFERENCES

1. Contini S, Scarpignato C. Caustic injury of the upper gastrointestinal tract: a comprehensive review. World J Gastroenterol 2013;19;3918-30.
2. Kobayashi S, Kanai N, Ohki T, Takagi R, Yamaguchi N, Isomoto H, et al. Prevention of esophageal strictures after endoscopic submucosal dissection. World J Gastroenterol 2014;20:15098-109.
3. Broor SL, Kumar A, Chari ST, Singal A, Misra SP, Kumar N, et al. Corrosive oesophageal strictures following acid ingestion: clinical profile and results of endoscopicdilatation. J Gastroenterol Hepatol 1989;4:55-61.
4. Gumaste VV, Dave PB. Ingestion of corrosive substances by adults. Am J Gastroenterol 1992;87:1-5.
5. Haller JA, Andrews HG, White JJ, Tamer MA, Cleveland WW. Pathophysiology and management of acute corrosive burns of the esophagus: results of treatment in 285 children. J Pediatr Surg 1971;6:578-84.
6. Ackroyd R, Watson DI, Devitt PG, Jamieson GG. Expandable metallic stents should not be used in the treatment of benign esophageal strictures. J Gastroenterol Hepatol 2001;16:484-7.
7. Song HY, Park SI, Do YS, Yoon HK, Sung KB, Sohn KH, et al. Expandable metallic stent placement in patients with benign esophageal strictures: results of long-term follow-up. Radiology 1997;203:131-6.
8. Saito Y, Tanaka T, Andoh A, Minematsu H, Hata K, Tsujikawa T, et al. Usefulness of biodegradable stents constructed of poly-I-lactic acid monofilaments in patients with benign esophageal stenosis. World J Gastroenterol 2007;13:3977-80.
9. Altman DG, Schulz KF, Moher D. The riveised CONSORT Statement for Reporting Randomized Trial: Explanation and Elaboration. Ann Intern Med 2001;134:663-94.
10. Dhar A, Close H, Viswanath YK, Rees CJ, Hancock HC, Dwarakanath AD, et al. Biodegradable stent or baloon dilatation for beningn oesophageal stricture: Pilot randomised controlled trial. World J Gastroenterol 2014;20:18199-20