Oesophageal stents for the treatment of radiation and anastomotic oesophageal strictures

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Abstract

Benign oesophageal strictures can arise in the treatment of oesophageal cancer as a result of radiation therapy, or at anastomotic sites, post-oesophagectomy. Data on the benefit of stenting of these types of stricture is limited. We analyzed the effects of oesophageal stents on such benign esophageal strictures. In this retrospective study, data was obtained from consecutive patients, 18 years and above from January 2000 to May 2016. Inclusion criteria comprised of oesophageal stenting in post-radiation strictures and anastomotic strictures, without any malignant residual disease.
17 patients had 22 stents inserted. 11 of these were female. 17 stents were self-expanding metallic stents (SEMS) and five were biodegradable (BDS). 12 strictures occurred post-radiation, while five were anastomotic strictures. Technical and clinical success rates were 100% and 86.4% respectively. Overall long-term clinical success was 45.5% (47% for BDS, 40% for SEMS). Minor, short-term complications, including pain and/or vomiting, were observed in 54.6% (n=12). The overall mean dysphagia score pre- and post-stenting was 2.95 and 1.36 *(p=0.0001)*. Comparison of the dysphagia free survival for anastomotic and post-radiation strictures was statistically similar *(p=0.22)*, as was the dysphagia free survival comparison between BDS and SEMS *(p=0.055)*.
BDS and SEMS are a safe and effective treatment modality for oesophageal strictures arising post-radiation or at the site of anastomoses. Retrospective study design and a low number of patients remain limiting factors of the study. (Acta Gastroenterol. belg., **2018**, 81, **361-365**).

Key words : Oesophageal strictures, oesophageal stent, dysphagia, anastomotic stricture, radiation stricture.

Oesophageal strictures may be either benign or malignant. Benign oesophageal strictures can arise as a result of various conditions, including gastro-oesophageal reflux, radiation therapy, ablative therapy or the ingestion of a corrosive substance (1, 2). Benign strictures can also form at the site of anastomosis, after an oesophagectomy and gastric tube formation, in 5-46 % of patients undergoing this procedure (3). The majority of benign oesophageal strictures can be treated by conventional methods of endoscopic dilatation including bougienage and balloon dilatation. Strictures arising in the context of radiation and at the site of an operative anastomosis are often complex and may require multiple sessions of dilatation (1). Over the past several years, fully-covered metallic oesophageal stents have come to be used for treating such strictures, although their use is not standardized, and data on outcomes remains scarce (4). We aimed to study the utility of stents in complex benign oesophageal strictures developing after treatment of oesophageal cancer. Thus, we have looked primarily at post-radiation and anastomotic strictures.

Methods

This was a retrospective study conducted at Shaukat Khanum Memorial Cancer Hospital & Research Centre in Lahore, Pakistan. Approval from the hospital's institutional review board was obtained and data was collected on consecutive patients, from Jan 2000 to Jan 2016, aged 18 years and above. Patients included were those who had undergone oesophageal stent placement for dysphagia secondary to post-radiation oesophageal strictures, with no residual malignant disease, as well as those who developed anastomotic site strictures following oesophagectomy for primary oesophageal or gastro-oesophageal malignancy. This included those patients who underwent prior dilatation of strictures with the use of bougienage with no clinical benefit. The stents inserted included self-expanding metallic stents (SEMS) and biodegradable stents (BDS).

Outcomes

The primary outcomes measured were the degree of dysphagia (5) before stent insertion in all patients, and after the placement of BDS or SEMS. Dysphagia-free survival, defined as the dysphagia-free period (in days) after stent insertion of the BDS or SEMS, was also calculated. We also studied the technical and clinical success rates of the stenting procedure. Clinical success rates were divided into immediate (defined as post-procedure clinical success) and long-term (defined as the absence of dysphagia till last follow-up). We also looked at short and long-term complications, defined as complications occurring within or after 48 hours, respectively, of stent insertion. The number of dilatation

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sessions and the extent of dilatation, if carried out prior to stenting, were also recorded.

Stent placement procedure

All procedures were carried out under fluoroscopic guidance, by or under the supervision of a consultant gastroenterologist, using conscious sedation. The site and length of the stricture were assessed by reviewing previous endoscopy reports, and a standard gastroscope was then passed to confirm the upper level of the stricture. A stiff guidewire was passed through the stricture under fluoroscopic control. The stricture was marked by the placement of metal clips on the thorax of the patient and the gastroscope withdrawn while leaving the guidewire in place. An appropriately sized stent was then passed over the guidewire, across the stricture and deployed under fluoroscopic control. The guidewire was then withdrawn and the stent position confirmed by X-ray.

Follow-up

The patients' electronic charts were reviewed retrospectively and the variables of interest were extracted. Notes were reviewed up to the last clinical encounter and the patients' clinical status, including the current grade of dysphagia, were noted.

Statistical analysis

Statistical analysis was performed by using Statistical package for social sciences (SPSS) version 22. The descriptive statistical analysis was done using summary measures for categorical variables as well as continuous variables. For categorical variables percentages (proportions) were used, and for continuous variables, the mean and standard deviation was reported.

Bivariate analysis was done using the chi-square test to establish the association between two categorical variables, with $p \leq 0.05$ as the level of significance. Paired t-test was used to compare the mean difference of dysphagia free survival among different groups, with $p \leq 0.05$ taken as significant.

Results

In accordance with the above selection criteria, 17 patients, with a total of 22 stents placed for benign oesophageal or anastomotic strictures, were studied. 11 patients were female and six were male. The stents inserted included 17 metallic stents and five BDS. These findings are summarized in tables 1 and 2.

Stricture type and prior dilatation

Twelve of the strictures encountered were following radiation treatment, while five were at the site of a previous anastomosis. The mean duration after which strictures developed, post-radiation or surgery was 255 days, while the median was 97 days. The corresponding figures for post-radiation stricture were 285 and 141 days respectively, and for anastomotic strictures were 152 and 77 days respectively. Six out of the total of seventeen patients had dilatation done prior to stent insertion. All the dilatations were carried out by bougienage and five of these were done in anastomotic strictures. Four of the five BDS were inserted for anastomotic strictures,

Table 1. — **Baseline clinical characteristics and stent-related features**

Total no. of patients	17
Total no. of stents	22
Age Mean (SD) Range	 51 (13) 26-73
Gender-no. (%) Male Female	 7 (33.3) 14 (66.6)
Stricture type-no. (%) Radiation Anastomotic	 16 (76.2) 5 (23.8)
Mean dysphagia score prior to stenting post-stenting	 2.95 1.36
Stent type-no. (%) Metallic Biodegradable	 17 (77.3) 5 (22.7)
Early complications-no. (%) Pain Vomiting Pain and vomiting	 4 (18.2) 4 (18.2) 4 (18.2)
Late complications-no. (%) Vomiting Stent displacement Pain	 1 (4.5) 3 (13.6) 1 (4.5)
Technical success-no. (%)	22 (100)
Clinical success (immediate)-no. (%)	19 (86.4)
Clinical success (long-term)-no. (%)	10 (45.5)

Table 2. — **Stent specific characteristics**

	Biodegradable stent	Self-expanding metal stent
Mean dysphagia score - mean(median) Pre-stenting Post-stenting	 2.8 (3.00) 1.2 (1.00)	 3.00 (3.00) 1.41 (1.00)
Stricture type - no. (%) Anastomotic Post-radiation	 4 (80) 1 (20)	 1 (5.9) 16 (94.1)
Time to development of stricture post-surgery or radiation - days.	152 (77) ±155	285 (141) ±395
Technical success - no. (%)	5 (100)	17 (100)
Clinical success - no. (%)	5 (100)	14 (82.4)
Recurrent dysphagia - no. (%)	2 (40)	9 (53)
Time to recurrence - days	341 (190) ±304	107 (71) ±129
Dysphagia free survival - days	443 (160) ±428	159 (108) ±164

whereas in the case of metallic stents, 16 out of 17 were for radiation strictures. The choice of stent for a specific stricture type was random.

Technical and clinical success

The technical success rate was 100%, while the immediate clinical success rate, defined as some relief of dysphagia immediately following stent placement, was 86.4%. The long-term clinical success rate, defined as the absence of dysphagia at the time of the last clinical encounter, was 45.5%, overall. For the SEMS group, this was 47% and for BDS, it was slightly lower, at 40%. With respect to stricture types, anastomotic strictures had a long-term clinical success rate of 60%, while post-radiation stricture had a corresponding success rate of 45.5%. Metallic stents were placed for a median duration of 6 weeks (mean=8.4±11.5, range=2-52) and then removed. (Tables 1 and 2)

Complications

More than half (54.6%, n=12) of our patients experienced pain, vomiting or both soon after the procedure, in the majority of whom (45.5%, n=10) this settled within 48 hours. One patient had more prolonged pain and one had persistent vomiting. Three patients experienced stent migration, in all of whom this was more than 48 hours after stent placement i.e. a long-term complication. Of the three patients who had stent migration, two had prior dilatation done. Migration was seen in case of two SEMS and one BDS. Recurrent dysphagia was observed in 54% (n=12) of patients. In case of metallic stents, this occurred after a median duration of 71 days (mean=107±129, range=1-432) post-stent insertion. In case of BDS, dysphagia recurred after a median duration of 190 days (mean=341±304, range=142-691) post-insertion. Overall, stenting of radiation strictures was associated with a higher rate of both early and late complications as compared to those with anastomotic strictures, with the majority of complications, including vomiting, pain or stent migration occurring in the radiation stricture cohort (59% vs. 20% p=0.03) (Table 3). Five patients required repeat stent insertion due to recurrent dysphagia. All of these patients had post-radiation strictures and all of them had fully covered stent placement prior. The mean time (in days) after which a repeat stenting was required was 293 ±227 (median=219). The remaining patients with recurrent dysphagia were either lost to follow-up or deceased.

Table 3. — **Complications with radiation and anastomotic stricture**

Variables	Complications (early and late)	*p-value*
Radiation strictures	59%	0.03
Anastomotic strictures	20%	

Table 4. — **Mean dysphagia scores, overall, and according to stent type**

Stent type	Mean dysphagia score before stent insertion	Mean dysphagia score after stent insertion	*p-value*
Overall	2.95	1.36	0.0001
SEMS	3	1.4	0.0002
BDS	2.8	1.2	0.0824

Dysphagia

The overall mean dysphagia score pre- and post-stent insertion was 2.95 and 1.36 respectively which was statistically significant (p=0.0001). The dysphagia score for the SEMS group prior to stenting and post-stent removal was 3 and 1.4 respectively, which was also statistically significant (p=0.0002). The corresponding scores for BDS were, 2.8 and 1.2 respectively, (p= 0.0824) (Table 4). The dysphagia-free survival comparison of the patients with anastomotic strictures and those with radiation-induced strictures yielded similar results, statistically, with $p=0.22$.

When BDS and SEMS were compared head to head, the mean dysphagia-free survival was again statistically comparable with $p=0.055$.

Discussion

Benign oesophageal strictures arise due to a number of conditions. Peptic strictures used to be the most commonly encountered cause of benign oesophageal strictures, but with the widespread use of proton pump inhibitors, these are less common, and other causes, such as caustic ingestion, mucosal resection, radiotherapy and surgical anastomosis-related strictures are being identified more frequently (6). Initial success rates with dilatation of benign strictures are as high as 80-90%. The recurrence rate, however, is around 30-40% in the long-term. This is especially so with the post-oesophagectomy anastomotic site and radiation-induced strictures, which are usually complex and difficult to manage, with a tendency to recur (7, 8).

The use of stents for treating benign oesophageal strictures is still a matter of debate, particularly since this has not yet been standardized (9). In recent years, various types of stents, including SEMS, BDS and self-expanding plastic stents (SEPS), have been used to treat benign oesophageal strictures, with variable rates of success. (9, 10, 11)

Griffiths et al reported the results of BDS for benign and malignant oesophageal strictures. A total of seven BDS were inserted for benign strictures. Aetiologies were variable, and included one patient each with post-oesophageal perforation stricture, anastomotic and Barrett's related strictures, post-radiation and reflux-related strictures, while the remaining two were strictures associated with achalasia. In comparison, four of the

five patients in whom we inserted BDS had anastomotic strictures, while one had a post-radiation stricture (10).

El-Oubeidi et al, in a prospective analysis, looked at the efficacy and safety of SEMS in the treatment of benign esophageal diseases. A total of 19 patients were studied, of whom seven had an anastomotic stricture, and two had a post-radiation stricture. 21% of the patients with benign strictures did not require re-intervention following SEMS removal. In comparison, in our study group, 47 % (n=8/17) required no further intervention following SEMS insertion and removal (12). The improvement in pre- and post-procedure dysphagia scores, for benign strictures, was comparable to our own study group and, like ours, was statistically significant (p<0.001). The long-term clinical success rate in the stricture group, however, was 21% compared to our success rate of 45%.

In a prospective study, Canena et al reported on 30 patients, divided equally into three cohorts, undergoing SEPS vs. BDS vs. SEMS placement for refractory benign oesophageal strictures. At the end of the study period, the proportion of patients free of dysphagia in the BDS and SEMS groups was reported to be 30 and 40% respectively. These numbers approach our figures of 40 % for the BDS group, and 47% for the SEMS group (13).

In a relatively recent prospective study conducted by Yano et al, data on 18 patients was presented, that had undergone curative treatment for oesophageal cancer and developed strictures, in which BDSs were inserted. Overall, improvement in the dysphagia score was observed in 66% (n=12) of the patients, compared to our BDS group that showed improvement in 40% of the patients. The median dysphagia free survival reported by the author was 14.1 weeks. In comparison, our patients undergoing BDS placement had a dysphagia free survival of 190 days that translates to 27 weeks. Thus our corresponding patient group benefitted less frequently, but those who benefited remained dysphagia free for a longer duration, compared to the study under consideration (14).

In another multicenter retrospective study, Suzuki et al analysed the effects of SEMS in 70 patients with benign oesophageal strictures. Of these, 13 patients had anastomotic strictures. The clinical success rate in this group, however, was much lower (23.1% (n=3)), compared to our patients with anastomotic strictures that had a long-term clinical success rate of 60% (4).

In view of the limited number of studies on this subject, and the small numbers of patients in most studies, Halsema et al. conducted a meta-analysis reviewing the effects of all three types of stents i.e. SEPS, BDS, and SEMS. This meta-analysis reviewed the results in 232 patients with refractory benign esophageal strictures who had stents inserted to provide relief of dysphagia. These were SEMS in 85, BDS in 77 and SEPS in 70. The overall clinical success rate was 24.2%. Individually it was 14.1% for SEMS, 32.9% for BDS and 27.1% for SEPS. In comparison, our clinical success rate was 45.5%, overall and 47% and 40% respectively for SEMS and BDS. We did not use SEPS in our patients. With regard to complication rates, however, our patients fared less well (50%) compared to the results in this meta-analysis (31%), although the majority (57%) of complications observed in our group were transient and relatively minor in nature, such as pain, vomiting or both, as discussed above (16).

Recently, Alder demonstrated the use of lumen-apposing metal stents (LAMS) in four patients with benign oesophageal strictures, two of which were anastomotic in nature. The clinical success rate in these patients was reported to be a 100% and there were no major complications observed (17).

We conclude that stents, both SEMS and BDS, offer an effective and safe method for treating benign oesophageal strictures, particularly post-radiation and anastomotic site strictures following major oesophageal resection, both of which are often difficult to manage by more traditional means. We have also observed better clinical outcomes post-stenting than those reported in the literature. Lastly, our study showed that BDS and SEMS seem to be equally effective with regard to dysphagia-free survival. Lastly, LAMS may appear to be an additional newer modality for treating benign oesophageal strictures, however larger prospective studies will be needed to prove its efficacy.

Our study is limited by the fact that it is a retrospective review, and, in common with most studies in this area, contains a relatively small number of patients. As with all retrospective series, more prolonged and regular follow up would have been useful. Stents, whether metallic or biodegradable, offer a safe, well-tolerated and highly effective means of treatment of benign oesophageal strictures arising particularly in the course of treatment of oesophageal cancer.

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Conflict of interest

The authors have no conflicts of interest to declare.

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