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Original Article

Endoscopic stent suture fixation for prevention of esophageal stent migration during prolonged dilatation for achalasia treatment

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SUMMARY. **The aim of this study is to compare endoscopic stent suture fixation with endoscopic clip attachment or the use of partially covered stents (PCS) regarding their capability to prevent stent migration during prolonged dilatation in achalasia. Large-diameter self-expanding metal stents (30 mm × 80 mm) were placed across the gastroesophageal junction in 11 patients with achalasia. Stent removal was scheduled after 4 to 7 days. To prevent stent dislocation, endoscopic clip attachment, endoscopic stent suture fixation, or PCS were used. The Eckardt score was evaluated before and 6 months after prolonged dilatation. After endoscopic stent suture fixation, no (0/4) sutured stent migrated. When endoscopic clips were used, 80% (4/5) clipped stents migrated ($p = 0.02$). Of two PCS ($n = 2$), one migrated and one became embedded leading to difficult stent removal. Technical adverse events were not seen in endoscopic stent suture fixation but were significantly correlated with the use of clips or PCS ($r = 0.828$, $p = 0.02$). Overall, 72% of patients were in remission regarding their achalasia symptoms 6 months after prolonged dilatation. Endoscopic suture fixation of esophageal stents but not clip attachment appears to be the best method of preventing early migration of esophageal stents placed at difficult locations such as at the naive gastroesophageal junction.**

KEY WORDS: **achalasia, stent fixation, stent migration, stents.**

INTRODUCTION

Achalasia is an esophageal motility disorder characterized by progressive dysphagia due to inefficient relaxation of the lower esophageal sphincter (LES) together with either lost or inefficient motility of the esophagus. As causative therapy is not available, symptomatic treatment aims to decrease the outflow obstruction at the esophagogastric junction (EGJ). Hereby, hypothesized disruption or respective division of muscle fibers at the LES represents the base of treatment algorithms to reduce the characteristic clinical symptoms such as dysphagia, regurgitation, retrosternal pain, and consecutive weight loss.[1] Concerning the long-term symptom relief, a recently published meta-analysis favors laparoscopic cardiomyotomy (Heller's myotomy)[2] over endoscopic pneumatic balloon dilatation (PD) with success rates of only 40–50%, even after repetitive sessions.[3,4] In the elderly achalasia patient, cohort comorbid illnesses might sometimes increase intricacy of treatment. Patients with contraindications for surgery, due to their e.g. cardiopulmonary status, are usually also not good candidates for theoretically less-invasive PD; as in the case of an esophageal perforation during uncontrolled PD, necessary surgery would again be hindered.

Recent reports have described the temporary implantation of large-diameter self-expanding metal stents (SEMS) in patients with newly diagnosed achalasia to be an effective and less-invasive alternative therapeutic option.[5] Consecutively, we have started to evaluate this promising option and included patients after failed previous treatment and/or not fit for surgery.

However, stents placed across the LES in a benign indication such as achalasia, with neither strictures nor stenosis, might be prone to a high risk of migration. Earlier studies have already demonstrated that endolumenal stent suture fixation (ESSF), using a novel endoscopic suturing device, might be beneficial to prevent stent migration.[6–8] Others have described the use of endoscopic clips[9] or partially covered stents (PCS) to prevent stent dislocation.[10]

The aim of this study is to compare ESSF, endoscopic clip (EC) attachment, and the use of PCS for their ability to prevent stent migration in a difficult

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situation such as at the naive EGJ, during prolonged dilatation (PRD) in achalasia.

MATERIALS AND METHODS

Patients and stents

Patients diagnosed with achalasia (05/13 to 04/15), which had previous laparoscopic myotomy and/or serious comorbidities and thereby were no good candidates for initial (redo-) surgery, were allocated for PRD in a patient-blinded, prospective observational study. The study has been approved by the local ethical committee and has been registered with Clinical Trials.gov (NCT02518542).

In total, 11 patients (7 female) with a median age of 71 years (range: 34–86 years) diagnosed with achalasia were allocated for PRD. Seven patients (7/11) had previous treatment, such as laparoscopic myotomy ($n = 5$) and/or balloon dilatation ($n = 6$). The patients without previous laparoscopic Heller myotomy (LHM) had a median age of 76 years (range: 71–86 years), cardiovascular comorbidities, or multiple previous abdominal operations. One young female patient consulted our department and asked for PRD as her initial treatment of achalasia.

For PRD, commercially available large-diameter SEMS (diameter shaft/flare × length: 30/38 mm × 80 mm, Niti-S esophageal stent, Tae Woong Medical, Seoul, Korea) were used. All stents used come within a standard delivery system with a 22- French diameter and a length of 70 cm. For insertion of the delivery system into the esophagus, a gastroscopically placed guide wire (Radiofocus® Guide Wire, stiff type straight, 260 cm length, 0.89 mm diameter, and a distal flexible length of 3 cm; Terumo Europe, Leuven, Belgium) was used. Fluoroscopy ensured correct stent placement across the ECJ, which was routinely performed under intubation anesthesia.

To avoid potential stent, migration patients were consecutively allocated to three different methods of stent fixation:

Group A (endsocopic clip attachment)

In Group A, two or three clips (Resolution Clip, Boston Scientific, Marlborough, MA) were applied adequately to cling the proximal rim of the fully covered large-diameter stent to the esophageal mucosa as previously described.[9] Figure 1 represents endoscopic clip attachment in a patient with a severely dilated sigmoid shape esophagus.

Group B (endolumenal stent suture fixation)

The second generation of an endoscopic suturing system (OverStitch, Apollo Endosurgery, Austin, TX) was used for ESSF. The device as well as the intervention has been described previously in detail.[6] Briefly, after implantation of the fully covered large-diameter stent, the suturing arm (needle holder) of the endoscopic suturing device is mounted onto the distal end of a dual-channel endoscope (GIF-2T 180, Olympus). A system handle, mounted onto the proximal end of the endoscope, allows the movement of the curved needle holder, which can be loaded with a needle/suture (2–0 polypropylene in this study). The needle can be released from the curved arm and thereby simultaneously represents the anchoring knot after detachment at the end of endolumenal stitching. A suture-cinching tool is then used to secure the deployed suture at the opposite end. The endoscopic suturing system was introduced into the esophagus with the aid of an overtube (Guardus Overtube - Esophageal, US Endoscopy, Mentor, OH). For ESSF, the initial bite was taken around the proximal rim of the stent followed by a deep bite of the esophageal wall, and then stent and esophagus again allow sufficient attachment as previously described. After the second stitch through the esophageal wall, the anchor/needle was dropped and cinched. Care was taken to avoid cinching down the suture too firmly, and thereby ensure that the stent is only loosely sutured to the esophageal wall[6] (see Fig. 2). For the potential need to cut the sutures for stent removal, endoscopic surgical scissors (Olympus Austria, Vienna, Austria) would be used.

Table 1 again describes the procedure of ESSF.

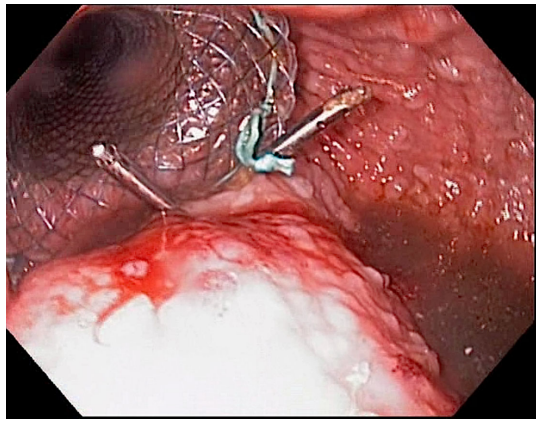


Fig. 1 Endoscopic clip attachment of the stent in a patient with a severely dilated sigmoid shape esophagus.

Group C (partially covered stents)

Furthermore, identically sized, commercially available large-diameter stents (Niti-S Esophageal Stent, Tae-Woong Medical, Seoul, Korea) not covered at the proximal and distal rim and therefore potentially less prone to migration due to their design were evaluated on their ability to prevent stent dislocation.

Figure 3a,b demonstrates the representative examples of the two stents used.

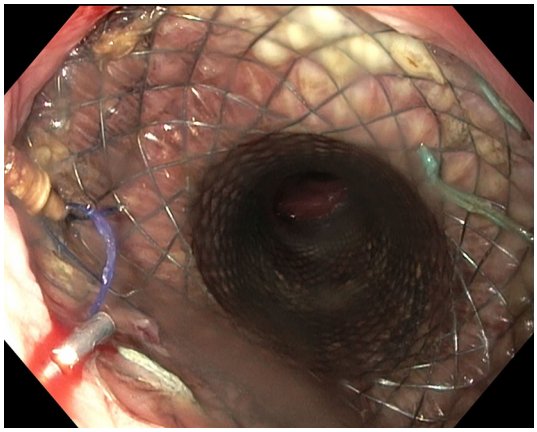
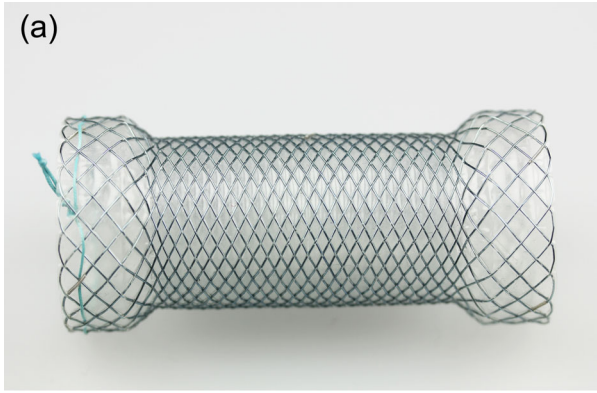


Fig. 2 An endoscopically applied suture secures the esophageal stent.



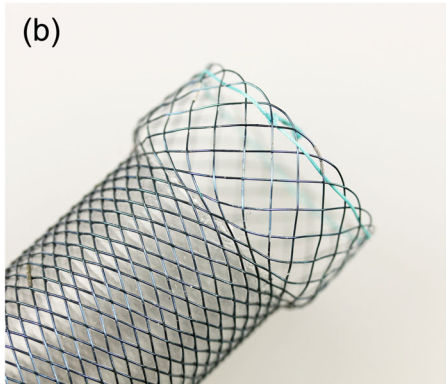


Fig. 3 (a) A representative picture of the fully covered esophageal stent used in Groups A and B. (b) A representative picture of the proximal end of the partially covered stent used in Group C.

After stent implantation, patients were put on liquid diet overnight. All patients were put on double-dose PPI. To confirm stent location, gastrografin esophagogram was performed on the following morning and elective stent removal was scheduled after 4–7 days. If stents were found dislocated to the stomach on the first postinterventional day, removal was scheduled as soon as possible.

After elective stent removal, another gastrografin swallow was performed to ensure the integrity of the esophageal wall and patients were discharged on the next morning. Six months after PRD, the clinical follow-up was performed by evaluating the Eckardt symptom scores and/or the outflow obstruction by timed-barium-swallow (TBS) studies.

Figure 4 demonstrates patient enrollment.

Statistical analysis

Statistical analysis was performed using the Mann–Whitney U-test or Pearson's coefficient as appropriate. The SPSS 21.0 (SPSS, Inc., Chicago, IL) statistical software was used for analysis. Values are shown as median with range and p values less than 0.05 were considered significant.

RESULTS

Efficacy of stent-fixation procedure

Implantation of the large-diameter SEMS was performed without any adverse events (0/11). All patients received the stents as described above. Overall, early spontaneous dislocation, defined as stent migration observed at the esophagograms on the first postinterventional day, was observed in 45% (5/11).

In Group A ($n = 5$) where clip attachment was used to avoid stent migration, 4 of the 5 patients (80%) experienced stent dislocation.

In patients with ESSF (Group B, $n = 4$), no early stent migration was observed ($p = 0.02$). All sutures had to be cut for stent removal, which was performed without any adverse events in all patients.

Table 1 A stepwise description of ESSF

(1) After implantation of the stent, the suturing arm or the needle holder of the endoscopic suturing device is mounted onto the distal end of a dual-channel endoscope. Then, the system handle is mounted onto the proximal end of the endoscope as described by the manufacturer.
(2) The curved needle holder is loaded with the needle together with the attached suture as described by the manufacturer.
(3) After introducing the endoscope with the mounted endoscopic suturing system into the esophagus until right above the proximal end of the stent, the initial stitch is taken around the proximal rim of the stent.
(4) This is followed by a stitch proximal to the rim through the esophageal wall.
(5) This is followed by another 'bite' through the proximal flare of the stent and then again through the esophageal wall above.
(6) After the second stitch through the esophageal wall, the anchor/needle is dropped.
(7) A suture-cinching tool is then used to loosely cinch the deployed suture at the opposite end.
(8) For the potential need to cut the sutures for later stent removal, endoscopic surgical scissors are used.

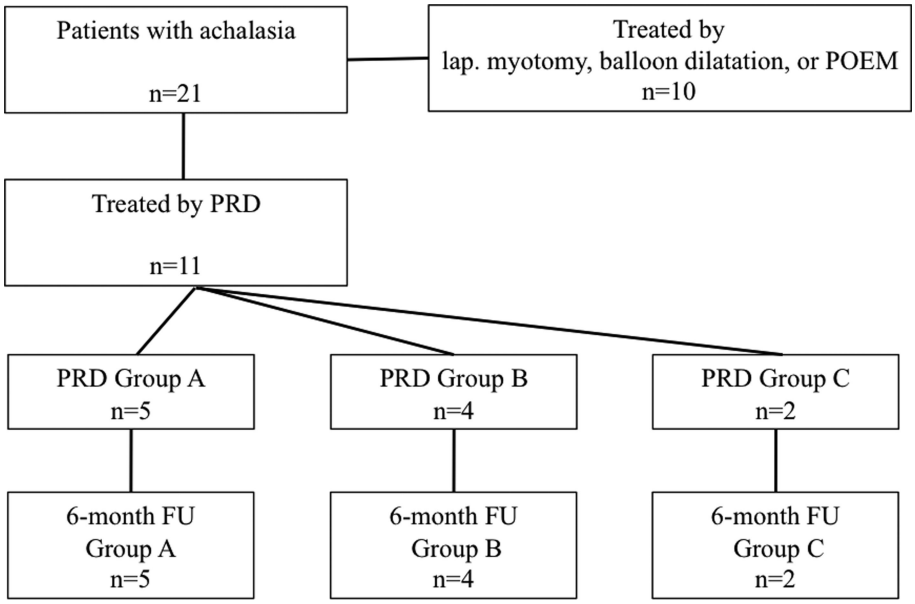


Fig. 4 The flow diagram displays the patient enrollment (PRD, prolonged dilatation).

The use of PCS (Group C, $n = 2$) led to stent migration in one patient but was abandoned after the second patient, as it led to seriously ingrown tissue with difficult consecutive stent removal after only 6 days. A stent-in-stent removal procedure had to be performed as described previously,[11] increasing the PRD period to 13 days in this patient.

Patients without stent dislocation ($n = 6$) had the stent electively removed after a median period of 5 days (range: 4–13 days).

Although no technical adverse events were observed in patients where stents were secured by ESSF, in six of seven patients (85%) either stent dislocation or difficult removal occurred with alternative methods, which was significantly correlated ($r = 0.828$, $p = 0.02$).

Short-term efficacy of prolonged dilatation

Overall, 72% of patients (8/11) were in remission 6 months after PRD. Five of 6 patients (83%) were either naive or dilated previously, and 3 of 5 patients (60%) had previous laparoscopic myotomy. Prior to PRD, the initial Eckardt score ranged from 4 to 9. The Eckardt score after PRD (range: 1–8) had sufficiently improved (≤ 3) in 64% of patients (7/11). One patient could only be reevaluated by TBS as her symptom score could not be clearly evaluated due to a cerebrovascular insult in her history (# 8). Her TBS demonstrated sufficient esophageal clearance (4 cm/1 min; 0 cm/2 min; 0 cm/5 min).

In 2 patients (# 5; # 10), describing sufficient subjective symptom relief, high-resolution manometry was performed 6 months post PRD. Both had normalized LES resting pressure (51 mmHg vs. 22 mmHg; 62 mmHg vs. 15 mmHg) as well as decreased integrated relaxation pressure (IRP: 47 mmHg vs. 18 mmHg; 59 mmHg vs. 16 mmHg). Both also presented partial restitution of esophageal peristalsis.

Overall, no correlation between the length of PRD and remission of achalasia symptoms was found in this study.

Table 2 demonstrates patient demographics, previous treatments, stent migration, and short-term outcome of PRD.

DISCUSSION

This is the first clinical study comparing the effectiveness of endoscopic suture fixation, with endoscopic clip attachment or the use of PCS for preventing esophageal stent migration at difficult locations. As all stents were placed only at identical locations (EGJ) without impaired integrity of the mucosa, this study allows a more precise analysis compared to previous studies.[7,12,13]

De Palma and Mukherjee initially described the role of stent implantation as treatment after failed standard achalasia treatment.[14–16] Later, the use of only temporary stent implantation has been reported to be successful in up to 85% of newly diagnosed achalasia patients.[17,18] Interestingly, in these series stent migration was reported to be less than 10% as PCS were used. This low migration rate eventually might be explained by a special stent design used in these studies or the eventual use of PRD only in certain types of achalasia. In the current study, the use of PCS was discontinued, after tissue ingrowth led to difficult removal using a stent-in-stent procedure.[11] This observation again emphasizes that PCS should preferably

Table 2 Demographic and procedural data as well as outcome of study patients

Patient #	Age/sex	Chicago	p.t.	Eckardt	Group	Dislocation	PRD	Eckardt 6 mo
1	70/m	1	M, D	4	A	No	**4 d**	1
2	86/w	1	—	4	A	Yes	(1 d)	2
3	34/w	2	—	9	A	Yes	(1 d)	2
4	48/w	2	M, D	8	B	No	**5 d**	7
5	71/w	1	D	4	B	No	**8 d**	2
6	35/m	2	M	4	B	No	**5 d**	1
7	74/w	2	D, M	9	B	No	**5 d**	8
8	74/w	2	D, M	8	A	Yes	**(4 d)**	†
9	76/m	2	—	‡	C	Yes	(1 d)	‡
10	79/w	2	—	9	C	Ingrown	**13 d**	0
11	73/m	2	D	5	A	Yes	**(7 d)**	2

†The Eckardt score could not be explored, but timed barium swallow indicated sufficient esophageal clearance; ‡Due to language barrier, the Eckardt score could not be explored, but subjective symptoms did not improve. Chicago, Achalasia type according to Chicago classification; D, dilatation; Eckardt, Eckardt score; M, myotomy; PRD, time of prolonged dilatation; p.t., previous treatment. Days in parentheses describe migrated stents, where the proximal flange was still placed at the EGJ with potential ongoing dilatation until stent removal.

not be used in routine clinical practice for benign indications.

The use of a fully covered stent design for consecutive safe stent removal as well as the integrity of the mucosal surface in achalasia patients, without any fibrotic fistulas tissue, anastomoses, or strictures, might lead to a higher stent migration rate, which indeed has been observed in our study.

As demonstrated earlier in an ex vivo preclinical study,[6] ESSF with only one or two sutures appears to significantly enhance stent attachment. The first clinical ESSF cases described also included two patients with fully covered SEMS placed at the EGJ without any stricture. No stent migration had been observed but some sutures were found to have already migrated out of the mucosa within a short period of time. This potential drawback led to the hypothesis to tie down sutures more loosely to avoid suture migration in consecutive cases, which has also been pursued in the current study. Another initial case series also included two patients without strictures[7] in their analysis. No stent migration was observed in this small subgroup.

It was argued that the use of an endoscopic suturing device to anchor SEMS would only be relatively effective for antimigration prevention as a study by Fujii and colleagues observed a dislocation rate of 33% despite endoscopic suturing.[12] However, looking closer into these data, it appears that only one out of 7 patients (14%) had stent migration despite suture fixation in the case of benign nonstricture indications. A more recently published retrospective analysis regarding ESSF found a significantly reduced migration rate when endoscopically applied sutures were used to attach SEMS.[13] In this study, 11 patients appeared to be with neither strictures nor stenosis. Unfortunately, it was not described whether migration of suture-attached stents (11%) occurred in patients with or without initial strictures.

In contrast to our current study, others favored endoscopic clips to be effective in significantly reducing stent migration.[19] Unfortunately, the authors included strictures together with fistulas and perforations as well as different stent diameters and brands into their analysis. The authors, though, hypothesized that the mechanical effect of clips during the first days after stent insertion might explain prevention of migration. However, two recent ex vivo studies observed clip attachment to be biomechanically not effective at all.[6,20]

A recently described novel technique used an over-the-scope clip for stent fixation in comparison with endoscopic suture fixation.[8] Similar pullout forces were found in this animal study. Although in the first clinical case stent removal was described to be uncomplicated, further clinical studies will have to evaluate whether the disengagement of the clip's teeth is as simple and safe as endoscopically cutting the previously placed sutures. Others have also demonstrated a similar procedure with a different clip used in an over-the-scope technique. Although the authors reported the feasibility of clip removal, a possible remaining risk of perforation was emphasized.[21] The external stent fixation using a dental floss thread has also been recently demonstrated as a successful option to prevent stent migration.[22] However, this procedure might impair patient comfort.

Endoscopic suture fixation of esophageal stents could also have an important clinical impact, when temporary stents are placed in other benign indications e.g. esophageal perforations or bleeding from esophageal varices, where a nonmigration design would be mandatory.[23] However, the migration rate in these indications is still high.[24] For example, when SEMS, such as 'Ella Danis' stents, are implanted for severe esophageal bleeding, migration has been reported to be as high as 20%.[25] ESSF could eventually reduce these migration rates, which would be interesting to evaluate in further studies.

The small sample size of our study certainly represents a limitation and it does not yet allow drawing sufficient long-term conclusions regarding the use of PRD and its effect in symptomatic achalasia.

Factors responsible for the success of PRD have to be defined in larger studies. Another interesting option for PRD would be to use biodegradable stents and thereby overcome the need for a second intervention for the stent removal.[26]

In conclusion, this study indicates that endoscopic suture fixation of esophageal stents performed with a novel endoscopic suturing device but not clip attachment appears to prevent early migration of esophageal stents placed at difficult locations such as at the naive mucosa of the EGJ.

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