

PALLIATIVE ENDOSCOPIC ESOPHAGEAL STENTING FOR MALIGNANT ESOPHAGEAL TUMOUR COMPLICATIONS: A CLINICAL CASE AND SINGLE CENTRE EXPERIENCE IN LATVIA

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Esophageal stenting is used in patients with malignant esophageal tumours to reduce dysphagia and inanition. The objective of this study was to analyse the main reasons for esophageal stenting in Rīga East Clinical University Hospital (RECUH) and their association with dysphagia and mortality. A cross-sectional study of all patients hospitalised in RECUH who received esophageal self-expanding metal stents (SEMS) from October 2013 to December 2015 was performed. A total of 29 patients, 24 (82.8%) male and 5 (17.2%) female, with mean age 63.7 ± 11.3 years, underwent the procedure. The most common indications for stenting were tumour-related stenosis (52.9%) and fistulae (17.6%). Mean time from establishing the diagnosis of esophageal cancer to stent placement was 338.6 days. Median survival after stenting was 4.8 months. A complex case of a patient requiring placement of three palliative stents illustrates the challenges of esophageal cancer care. Esophageal stent placement is an effective palliative method for treating tumour-related symptoms but carries risks of stent complications and fistula development over time. SEMS are being successfully used in cancer patient treatment in Latvia.

Key words: palliative care, gastrointestinal cancer, dysphagia, tracheoesophageal fistula.

INTRODUCTION

Esophageal cancer is one of the most aggressive tumours of the digestive system, with a five-year survival rate of only 10%. It is the eighth most prevalent type of cancer and the sixth leading cause of cancer-related death overall. It is often diagnosed at an advanced stage, when many patients already experience local complications or have metastatic disease. Therefore, cure is unlikely, requiring a treatment focus on alleviation of symptoms and improvement of the patient's quality of life (Martinez *et al.*, 2011).

Nowadays, both globally and locally in Rīga East Clinical University Hospital (RECUH) in Latvia, the main treatment for esophageal malignancy-related complications is esophageal stent placement using self-expandable metal stents (SEMS) (Hindy *et al.*, 2012). The primary goal of esophageal stent insertion in patients with advanced disease is to relieve dysphagia and prevent malnutrition (Martinez *et al.*, 2011).

In this single centre case series, we report a two-year experience in deploying esophageal SEMS in 29 patients with dysphagia and other complications of incurable or inoperable esophageal cancer.

The aim was to analyse the main reasons for esophageal stenting in RECUH and their association with dysphagia and mortality.

MATERIALS AND METHODS

A retrospective analysis of all consecutive patients who underwent SEMS placement in the RECUH Clinic of Gastroenterology, Hepatology and Nutrition from October 2013 to December 2015 was performed. Data were obtained from patient case notes and endoscopy and radiology charts, and an originally created protocol was completed for each patient. Several variables, including demographic data, presenting complaints, nutritional status, indications for stenting, stent type, details of the procedure, including success or failure of stent insertion, morbidity and mortality, were reviewed. Esophageal pathologies and comorbidities were coded according to ICD-10 disease classification. The acquired data were analysed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Survival analysis was performed using the Mann–Whitney U-test and Wilcoxon t-test for nonparametric data and presented on a Kaplan–Meier plot. This is a cross-sectional study.

The study was approved by the RECUH Ethical Committee.

RESULTS

During the two-year period, 29 patients — 24 (82.8%) male and 5 (17.2%) female, with mean age 63.7 ± 11.3 years underwent esophageal stenting. All patients received either fully (40%) or partially covered (60%) self-expanding Wallflex™ stents (Boston Scientific, USA) (see Figures 1–7 from the RECUH Endoscopy unit archive).

Mean duration of hospital stay was 24.1 days, mean duration of hospitalisation in the Intensive Care unit was 7.4 days. Indications for esophageal stent insertion are presented in Table 1.

Mean time from establishing the diagnosis of esophageal cancer to stent placement was 338.6 days. Median survival time after tumour diagnosis confirmation was 19.73 months (10.2–29.3). Median survival after stenting was 4.8 months (2.4–7.2). The one-month survival rate was 73.4%, 3-month survival rate — 30.6% and 12-month survival rate was 16.3%, which reflects disease progression (see Fig. 8). SEMS placement was successful in all 29 patients.

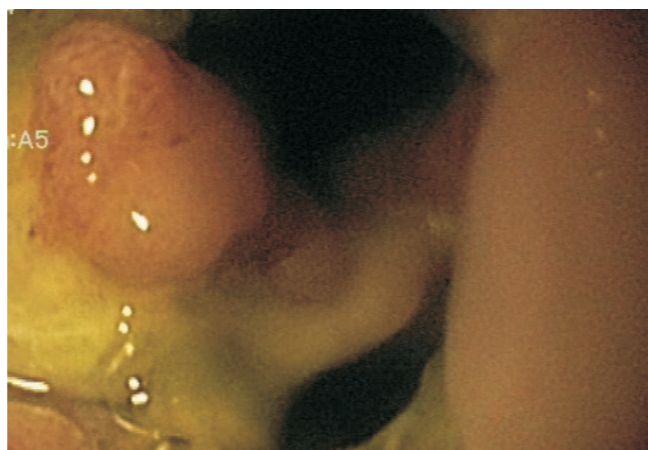


Fig. 1. Esophagomediastinal fistula after esophageal resection.

A representative RECUH case of repeated palliative stenting required to treat complications of esophageal malignancy emphasises the complexity of these patients.

CLINICAL CASE

A 47-year-old man was diagnosed with Grade II squamous cell carcinoma of the proximal third of the esophagus in 2013. Tumour tissue was localised 20–26 cm from the incisors and was classified as T3N0M0 stage II. The patient un-

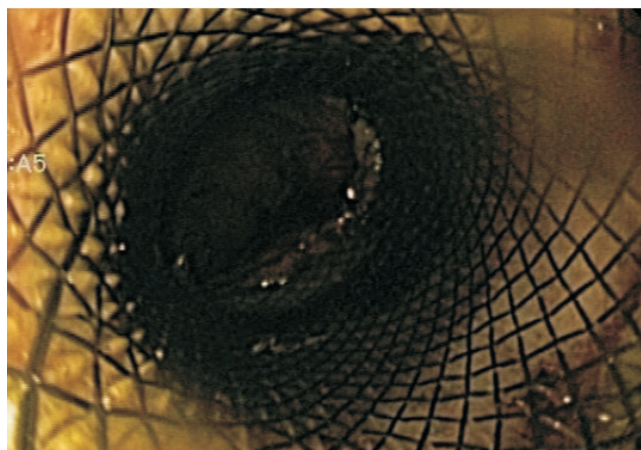


Fig. 2. View after SEMS insertion.

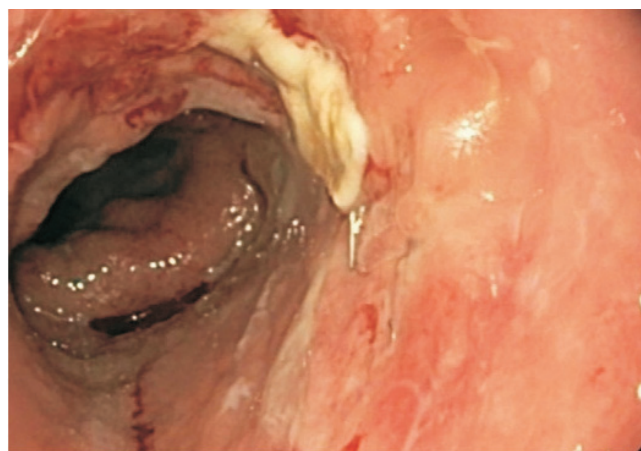


Fig. 3. Fistula closure after stent evacuation.

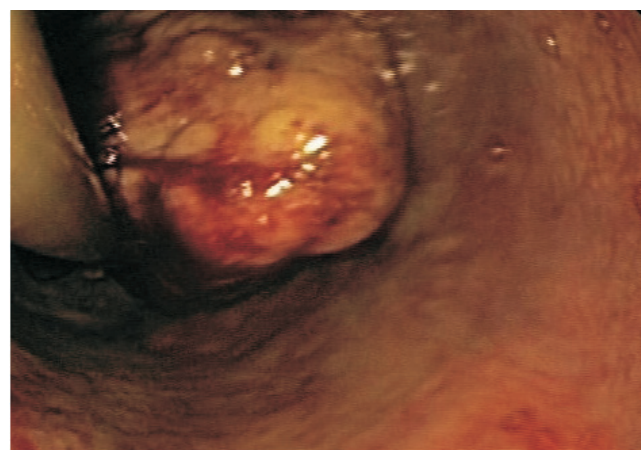


Fig. 4. Esophageal tumour.

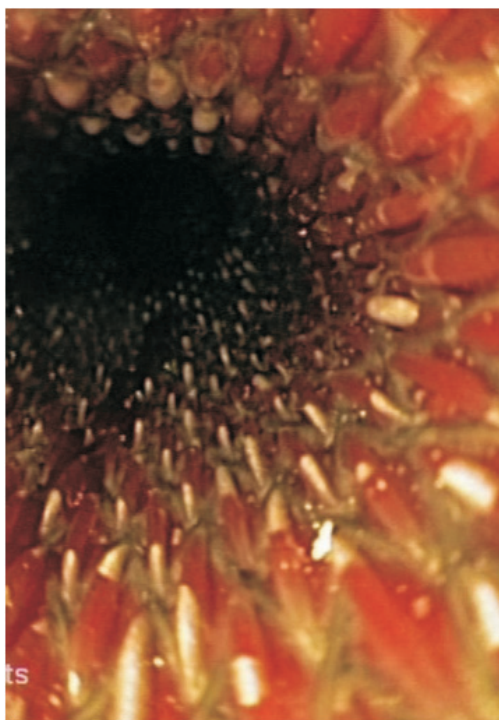


Fig. 5. View after self-expanding stent placement.

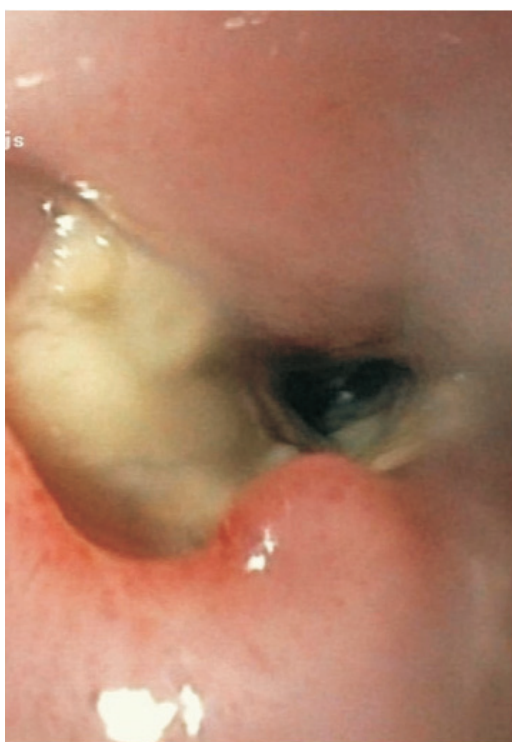


Fig. 6. Esophageal tumour. Tracheobronchial fistula.

derwent 28 external beam irradiation sessions with total radiation dose 56 Grey and 3 brachytherapy sessions with total radiation dose of 5 Greys per day.

At the end of 2014, the patient was hospitalised with progressive dysphagia, non-productive cough, fever and weight loss. X-ray and CT scan results showed tumour in the proximal third of the esophagus, mediastinal perforation and destruction. The patient was diagnosed with mediastinitis and

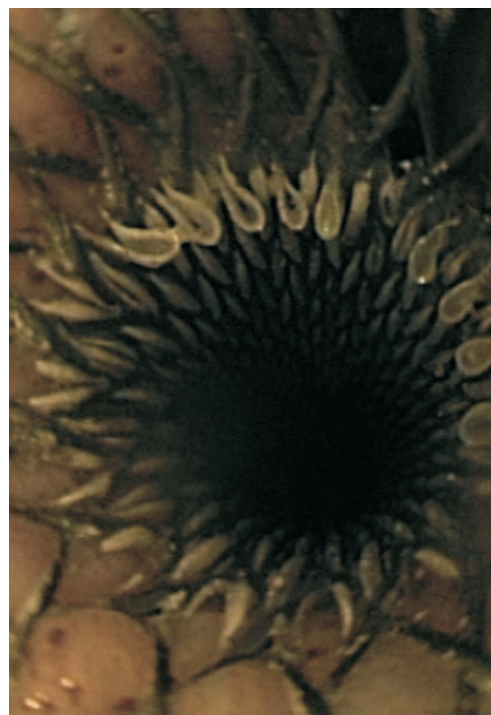


Fig. 7. View after self-expanding stent placement.

Table 1. Indications for stent placement

Indication	Percentage of stents placed
Tumour-related stenosis	52.9%
Fistula	17.6%
Anastomosis insufficiency	11.9%
Tumour ulceration	5.9%
Stent dysfunction	5.9%
Iatrogenic injury	2.9%
Esophageal burns	2.9%

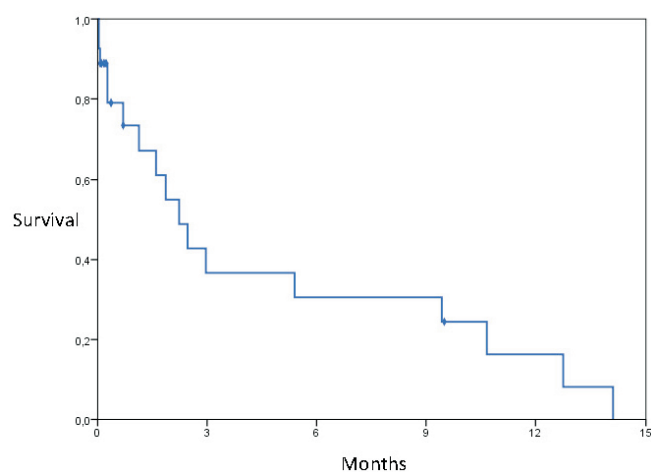


Fig. 8. Patient survival after esophageal stenting.

aspiration pneumonia and started on broad spectrum antibiotic therapy. Considering the patient's status, a covered Wallflex™ esophageal SEMS (23 mm × 125 mm) was placed under fluoroscopic guidance. Bronchoscopy additionally revealed a tracheoesophageal fistula (TEF) and tumour in-growth into the trachea. TEF was localised 2.5 cm

below the proximal end of the esophageal stent and 3 cm above the tracheal bifurcation. The trachea was narrowed by about 30–40% at the fistula level.

A month later, the patient was admitted to the hospital with complaints of heartburn and severe cough. Since bronchoscopy showed a TEF, an uncovered Ultraflex™ tracheo-bronchial SEMS (16 × 40 mm) was placed in the middle third of the trachea.

Two weeks later, the patient was re-admitted with severe cough, heartburn, fever, periodic pain in the esophagus and weight loss. Bronchoscopy showed a gap in the posterior wall of the trachea with esophageal stent protruding into the trachea and narrowing the lumen. A native CT scan showed a 1.1 × 1.6 cm TEF and a 50% tracheal stenosis. As the patient had severe symptoms, an additional uncovered Ultraflex™ tracheobronchial SEMS 16 x 40 mm was placed. The procedure was successful and fistula closure was complete. Nevertheless, a month later percutaneous endoscopic gastrostomy was performed due to cancer progression.

DISCUSSION

In 2018, there were 6.7 cases of esophageal cancer per 100 000 people in Latvia. 54% of cases represented an advanced disease — stage III and stage IV (Anonymous, 2018). Despite advances in diagnostics, neoadjuvant care and perioperative care of esophageal cancer patients, the five-year survival rate remains less than 20%, and chemotherapy has shown limited survival benefit. Therefore, patients with incurable esophageal malignancies often require palliative treatment of advanced cancer complications — dysphagia and/or tracheoesophageal fistulae (Hindy *et al.*, 2012). Esophageal stenting can be used as a definitive treatment, a bridge to surgery or a palliative measure in patients who are not candidates for surgical resection. In contrast to other treatment modalities like brachytherapy, stents are more accessible, and their use is not restricted to specialised centres (Pavlidis and Gorard, 2011).

About 5–15% of patients with primary esophageal carcinomas develop a TEF (Hürtgen and Herber, 2014), and 9% develop fistulae after esophageal stent placement (Hindy *et al.*, 2012). Once fistulae become symptomatic, the natural history involves continued contamination of the respiratory tract, eventual sepsis and death. Median survival is 1 to 6 weeks (Chauhan and Long, 2004). Survival was noted to be significantly lower in patients who underwent only airway stenting compared to those who received esophageal or double (airway plus esophageal) stents (F-test $p = 0.023$) (Herth *et al.*, 2010). Interestingly, in the previously described case from RECUH both malignancy associated TEF and TEF after stent placement developed, the latter being a delayed complication of stenting. Previous radiotherapy and large SEMS size were possible risk factors for fistula formation. As the posterior wall of the trachea lacks cartilage (pars membranacea) it may be also predisposed to fistulisation and easier destruction by pressure necrosis.

Delayed complications have been reported in 53–65% of cases and include tumour ingrowth, stent migration, stent occlusion, and recurrence of strictures (Hindy *et al.*, 2012). Development of complications can depend on stent-related factors (length, diameter) and tumour characteristics (site, histological type) (Kim *et al.*, 2017). Table 2 lists the most common complications after SEMS insertion (Sharma and Kozarek, 2010). In a study of patients with more than six months survival after stent placement, the complication rate was 48.8%, with a more complication rate progressing with longer time after stent insertion (Bakheet *et al.*, 2019).

Table 2. The most common complications after SEMS placement

Immediate:
Aspiration
Airway obstruction
Malposition
Stent dislodgement
Perforation
Early (up to 1 week after stent placement)
Upper gastrointestinal bleeding
Chest pain
Delayed (2–4 weeks after stent placement):
Recurrent dysphagia
Tracheoesophageal fistula
Stent migration
Upper gastrointestinal bleeding

Recurrent dysphagia affects approximately one-third of patients (Reijm *et al.*, 2019). Sharma *et al.* (2003) describe a similar case of a TEF developing after palliative stenting because of dysphagia. Four months after the procedure, esophageal dilation and a TEF at stent level were discovered. The previous stent was removed and a modified Wilson-Cook prosthesis was inserted to close the fistula (Sharma *et al.*, 2003). Whether the stent caused the formation of fistula is unclear in both this and the presented case.

In a study by Paganin *et al.*, time between esophageal stenting and emergency admission for respiratory complications in patients with TEF was 8.5 ± 9 days (range 2–29) (Paganin *et al.*, 2008). In the presented case, the second TEF developed later — 30 days after the first esophageal stent and 42 days after the tracheal stent placement.

The reported overall median survival of 19 months was comparable with other studies of patients with esophageal malignancy. Median survival after stent placement was also consistent with previously reported literature data (Whiteoak *et al.*, 2012; Forootan *et al.*, 2018). Some studies reported even shorter survival times after palliative treatment — mean survival time of 137.6 days and median 103 days (Besharat *et al.*, 2008).

Different changes in SEMS design have been introduced with the intention of minimising complication risk, with different materials, shapes, coverings and antimigration features (van Boeckel *et al.*, 2010; Uitdehaag *et al.*, 2010). New advances in palliative esophageal stenting provide an option of radioactive stents loaded with iodine 125 beads,

thus combining the benefits of stenting with radiation therapy. In a meta-analysis of six studies, radioactive stents showed comparable success rate in relief of dysphagia and prolonged survival after stenting when compared to conventional stents (Chen *et al.*, 2017). Another study with 122 patients showed a decreased rate of restenosis with radioactive stents (11.9% vs 27.0% with conventional stents) (Wang *et al.*, 2019). A double-covered modified segmental SEMS was developed to combat the drawbacks of conventional stents, which are not bendable and not suitable for circuitous esophageal lesions. This type of stent seems to be as safe and effective and can possibly improve outcome in patients in need of palliative stenting (Bi *et al.*, 2019).

The limitations of this study include small sample size and retrospective design. The study did not examine esophageal tumour histology and tumour type correlation with subsequent complications, but the investigators plan to continue data collection in a future prospective study that would include additional parameters such as patient nutritional status, specific cancer therapy, histological analysis and tumour staging.

CONCLUSIONS

Despite the implementation of guidelines, esophageal cancer is a fast-progressing disease with a low survival rate. Esophageal stent placement is an effective palliative method for treating tumour-related symptoms but carries risks of stent complications and fistula development over time. SEMS are successfully used in cancer patient treatment in Latvia. Advances in radiotherapy and stent technology may improve therapy outcome for future esophageal cancer patients.

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PALIATĪVA ENDOSKOPISKA BARĪBAS VADA STENTĒŠANA ĻAUNDABĪGU BARĪBAS VADA AUDZĒJU KOMPLIKĀCIJU ĀRSTĒŠANĀ: KLĪNISKAIS GADĪJUMS UN VIENA CENTRA PIEREDZE LATVIJĀ

Barības vada stentēšana tiek pielietota pacientiem ar ļaundabīgiem barības vada audzējiem, lai samazinātu disfāģiju un inanīciju. Šī pētījuma mērķis bija analizēt galvenos cēloņus barības vada stentēšanai Rīgas Austrumu klīniskajā universitātes slimnīcā (RAKUS) un to saistību ar disfāģiju un mirstību. Tika veikts šķērsgrīzuma pētījums ar visiem RAKUS stacionētajiem pacientiem, kuriem no 2013. gada oktobra līdz 2015. gada decembrim tika ievietoti pašizpletoši metāla stenti (PIMS). Kopā 29 pacientiem, 24 (82,8%) vīriešiem un 5 (17,2%) sievietēm ar vidējo vecumu $63,7 \pm 11,3$ gadi tika ievietoti barības vada stenti. Biežākās stentēšanas indikācijas bija audzēja izraisīta stenoze (52,9%) un fistulas (17,6%). Vidējais laiks no barības vada vēža diagnozes noteikšanas līdz barības vada stentēšanai bija 338,6 dienas. Vidējais dzīves ilgums pēc stentēšanas bija 4,79 mēneši. Sarežģīts klīniskais gadījums, kurā pacientam bija nepieciešama trīs paliatīvu stentu ievietošana, ilustrē izaicinājumus barības vada vēža pacientu aprūpē. Barības vada stentēšana ir efektīva paliatīva metode audzēja izraisītu simptomu ārstēšanai, bet pastāv ar stentu saistītu komplikāciju un fistulu attīstības risks. PIMS tiek veiksmīgi izmantoti vēža slimnieku ārstēšanā Latvijā.