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The evaluation of esophageal stenting complications in palliative treatment of dysphagia related to esophageal cancer

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Esophageal cancer is the seventh-most frequent cause of cancer-related deaths and it is usually diagnosed at an inoperable stage. In palliative treatment, endoscopic and non-endoscopic methods are applied to reduce dysphagia in patients with neoplastic esophageal obstruction. Because of severe complications, non-endoscopic treatment (surgery, radiotherapy, brachytherapy and chemotherapy) is applied rarely. Within the endoscopic methods, only the use of endoprostheses yields long-term effects. The aim of this study was to evaluate the safety and efficacy of implantation of self-expandable esophageal stents in palliative treatment of dysphagia related to esophageal cancer.

Material/Methods: A total number of 46 patients (41 males and 5 females) were qualified to palliative implantation of coated self-expandable stent. The mean age of the patients was 67 years (from 51 to 78 years). In all patients, Evolution-type coated self-expandable stents were used. In all cases, 24 hours after the implantation, radiological examination was performed to assess the stent location.

Results: Severe, possibly life-threatening, complications constituted 28% of all the complications and occurred in 9% of the patients. Less severe complications occurred in 17% of the observed patients and were not life-threatening.

Conclusions: In patients with neoplastic esophageal stenosis, stenting with coated, self-expandable nitinol prostheses is a safe, effective and fast method of palliative dysphagia treatment.

key words: **neoplastic dysphagia • palliative treatment • self-expandable esophageal stent • complications**

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Background

Esophageal cancer accounts for 1% of all cancers and it is the seventh-most frequent cause of cancer-related deaths [1]. The prognosis in this cancer is poor because in 50% of affected patients the diagnosis is made at an inoperable stage of the disease. The 5-year survival rate is below 20% [2,3].

Local symptoms of esophageal cancer include dysphagia, odynophagia, cough, nausea, vomiting, regurgitation and retrosternal pain. Dysphagia is a main, but not pathognomonic, symptom, as it may occur in several non-neoplastic diseases (eg, in achalasia).

In esophageal cancer, surgery is a treatment of choice if the neoplasm is in operable stage. In inoperable stage the therapeutic management is limited to palliative treatment [4]. Irresectability of esophageal cancer is related to local progression, presence of distant metastases and concurrent severe conditions. The aim of palliative treatment is to maintain digestive tract patency and to relieve pain. The latter goal is achieved by pharmacotherapy.

In palliative treatment to reduce dysphagia in patients with neoplastic esophageal obstruction, the endoscopic and non-endoscopic methods are applied.

Non-endoscopic treatment includes surgery, radiotherapy, brachytherapy and chemotherapy. Surgery is not useful for symptomatic treatment due to high perioperative mortality and frequent complications. In patients in quite good general condition, chemotherapy may reduce the intensity of dysphagia. However, in most patients with inoperable esophageal tumor, this method is not applicable due to complications and low efficacy. Radiotherapy and brachytherapy may be administered in patients in worse general condition [5]. These 3 aforementioned methods are rarely applied in palliative treatment of esophageal cancer because of severe complications such as post-irradiation esophagitis, esophageal obstruction or tracheoesophageal fistula.

Endoscopic methods are: (1) tumor mass reduction with electrocoagulation, laser therapy, argon plasma coagulation, photodynamic therapy and injection therapy; and (2) preservation of a proper diameter of esophagus lumen with the aid of dilation, implantation of esophageal endoprostheses, and use of a gastric feeding tube. Within the endoscopic methods, only the use of endoprostheses yields long-term effects; however, the other methods have high recurrence rates.

A patient with primary esophageal cancer and life expectancy over 3 months should be qualified to palliative brachytherapy. In patients with life expectancy below 3 months, as well as with recurrence of dysphagia after brachytherapy, esophageal stenting is the best therapeutic option [6–8].

Nowadays, self-expandable esophageal stents are used in esophageal stenting. Plastic stents are no longer used because of numerous complications and patient discomfort. Several types of self-expandable stents are currently available. The main differences between them concern the material they are made from, their shape, type of net braid, flexibility, diameter, length, manner of drug releasing, degree of torsion after application and the presence of an anti-reflux valve [9]. Currently, self-expanding drug-coated stents are used most often because of better long-term effect of palliation in neoplastic dysphagia. No particular type of drug-coated self-expanding stents has been proven to be superior to others in the treatment of neoplastic dysphagia. The choice of therapeutic method should be based on technical capabilities of the medical centre, and experience and skills of the operator.

Table 1. Self-expanding stents – complications (*).

Immediate (during implantation)	Perforation Respiratory tract compression Stent dislocation Stent malposition
Early (within a week since stent implantation)	Bleeding Chest pain Nausea
Late (over a week since stent implantation)	Recurrence of dysphagia Stent migration Tracheoesophageal fistula Bleeding Gastroesophageal reflux/ aspiration

Application of self-expanding stents is not free of complications. The most common complications are presented in Table 1 [9].

Material and Methods

Patients with neoplastic dysphagia fulfilling criteria of inoperability were included into the study. In patients with dysphagia, the palliative treatment was introduced due to local progression of the lesion, presence of metastases or poor general condition. All patients had total esophageal obstruction. Within years 2009–2010, a total of 46 patients (41 males and 5 females) were qualified to palliative implantation of coated self-expandable stent (Cook Evolution, Cook Ireland Ltd.) in the Gastrointestinal Endoscopy Laboratory of the WAM Medical University Hospital in Łódź. The mean age of the patients was 67 years (from 51 to 78). In all the patients the diagnosis of esophageal cancer was confirmed by histopathological examination. Neoplastic tumor resulting in obstruction was localized in the following parts of esophagus: distal (within the distal 10 cm) in 24 patients, medial in 13 patients and proximal (up to 10 cm from the upper esophageal sphincter) in 9 patients. Tracheoesophageal fistulas in tumor mass were detected in 3 patients by means of contrast radiological examination.

In all patients Evolution type coated, fully covered, self-expandable stents, 20 mm in diameter were applied. The Evolution stent is an elastic self-expandable stent woven from a single nitinol wire. The procedures were conducted with sedation, in supine position, under fluoroscopic control. Prior to stent implantation, the endoscopic examination evaluating the size and the extent of the esophageal lesion, anatomical localization in esophagus, as well as the distance from the upper and lower esophageal sphincter, was performed in every patient. The following types of endoscopes were used:

Table 2. The results of coated stent implantation in esophageal cancer.

Tumor location	Number of patients	Improvement in terms of dysphagia	Mean time of survival (days)
Distal esophagus (up to 10 cm from a gastric cardia)	24	22/24 (91.6%)	98
Medial esophagus	13	13/13 (100.0%)	106
Proximal esophagus (up to 10 cm from the upper sphincter)	9	9/9 (100.0%)	102

GIF Q165 Ø 8.9 mm, GIF XP180N Ø 5.9 mm and GIF HI80J Ø 9 mm. In the cases of difficulty in passing the endoscope through an obstruction, balloon dilation (up to 20 mm, in accordance with the prosthesis dilatability) was carried out. During stent implantation the principles recommended by experts were strictly obeyed. The length of the stent was adjusted so that it was 4–6 cm longer than the neoplastic lesion, protruding 2 cm both above and under the lesion margins. The stents were from 8 to 15 cm in length. In the cases of tumor localization in the proximal esophagus, the patient was qualified for stent implantation provided there was a 2 centimeter margin from the upper esophageal sphincter free from the neoplastic infiltration. This condition is crucial for safe stent implantation without subsequent symptoms of pain, tracheal compression or feeling of a foreign body in the esophagus. In all cases, 24 hours after the implantation, radiological examination was performed to assess the stent location. None of patients received chemoradiation either prior to or following stent implantation.

All patients included in the study were discharged from hospital up to 48 hours from stent implantation. The patient follow-up included consultation with the laboratory physician once a week. After the procedure, proton pump inhibitor (PPI) was chronically administered in all patients in order to reduce the symptoms and not irritate the inflamed mucous membrane of the esophagus. Other drugs used by some of the patients included analgesics, received also before the implantation due to the basic disease. All patients were given instructions to eat semi-fluid products.

Results

The results of esophageal cancer treatment with coated stent implantation are shown in Table 2. Types and frequency of the complications are presented in Tables 3–5. Pictures of lesion prior to and following stent implantation are presented in Figures 1–3 (endoscopic images) and in Figure 4 (X-ray images).

In 4 patients of the study group, tracheoesophageal fistulas were found before stent implantation. In 3 cases they were consequences of the neoplasm, while 1 was iatrogenic due to prior esophageal dilation. Endoscopic esophageal dilation prior to stent implantation was required in 21 patients. In all 4 cases, application of the coated stent provided entire sealing of fistulas, and in the subsequent follow-up no complications related to fistulas were observed.

Among the aforementioned complications, summarized in Table 6, 2 groups may be distinguished. The first group includes life-threatening complications – perforation, respiratory tract compression, bleeding and death. In the study group they accounted for 28% (5/18) of complications and occurred in less than 9% of patients (4/46). The second group comprises non-life threatening complications, which only required application of an additional procedure. Those complications include stent malposition, chest pain, nausea, gastroesophageal reflux and stent occlusion by food material. This group accounted for 72% (13/18) of all complications, and they occurred in 17% (8/46) of patients. The total percentage of complication occurrence was 19%.

Discussion

The stage of neoplastic disease, general patient condition and (in consequence) life expectancy, should be taken into account in choosing a method for palliative treatment of dysphagia caused by esophageal cancer [4]. Patients with life expectancy over 3 months are qualified for esophageal stenting [8].

Our study confirmed the usefulness of this method in palliative treatment of neoplastic dysphagia. In 44 of 46 patients the degree of dysphagia improved from stage 5/6 (inability to swallow any food or saliva) to stage 1 (ability to swallow solid food). These results are consistent with literature data [10–12]. Satisfactory remission of dysphagia was not reached in 2 cases in which the tumor was localized in the area of the gastric cardia. In these cases, second stent application was necessary for dysphagia alleviation. Average time of survival in all the patients was 102 days.

In our research, the percentage of patients in which any complications occurred as a result of esophageal stenting with coated nitinol prosthesis was 39%. Severe complications such as perforation, respiratory tract compression, bleeding and death occurred in 11% of the patients under therapy. Non-severe complications such as stent malposition, chest pain, nausea, gastroesophageal reflux and stent occlusion by food material occurred in 17% of the analyzed patients. In comparison with results from the literature, the obtained results may be considered to be very good [13–18].

Immediate complications occurring during stent implantation include perforation, aspiration pneumonia, fever, bleeding, stent malposition, respiratory failure and death*. In our research these complications occurred in 11% (5/46) of the patients. In 2 cases, a perforation caused by balloon dilation of the esophagus occurred and in 1 case stent malposition, was verified in the next endoscopic investigation and the reposition was made with the aid of pincers. The 2 most severe complications occurred in 1 patient in poor

Table 3. Immediate complications.

Tumor location	Perforation	Stent malposition	Respiratory tract compression	Death	Total
Distal esophagus (up to 10 cm from a gastric cardia)	2/24	1/24	0/24	0/24	2/24
Medial esophagus	0/13	0/13	1/13	1/13	2/13
Proximal esophagus (up to 10 cm from the upper sphincter)	0/9	0/9	0/9	0/9	0/9
Total	2/46	1/46	1//46	1/46	5/46 (~11%)

Table 4. Early complications.

Tumor location	Bleeding	Chest pain	Nausea	Stent migration	Total
Distal esophagus (up to 10 cm from a gastric cardia)	1/24	2/24	0/24	2/24	5/24
Medial esophagus	0/13	1/13	0/13	0/13	1/13
Proximal esophagus (up to 10 cm from the upper sphincter)	0/9	1/9	1/9	0/9	2/9
Total	1/46	4/46	1/46	2/46	8/46 (~17%)

Table 5. Late complications.

Tumor location	Recurrence of dysphagia	Stent migration	Tracheoesophageal fistula	Bleeding	Stent overgrowth	Gastroesophageal reflux	Total
Distal esophagus (up to 10 cm from a gastric cardia)	1/24	0/24	0/24	0/24	0/24	2/24	3/24
Medial esophagus	0/13	0/13	1/13	0/13	0/13	0/13	1/13
Proximal esophagus (up to 10 cm from the upper sphincter)	1/9	0/9	0/9	0/9	0/9	0/9	1/9
Total	2/46	0/46	1/46	0/46	0/46	2/46	5/46 (~11%)

general condition – respiratory failure led to the patient's death. This patient had a left lung cavity tumor, infiltrating the bronchi and the esophagus, with metastases to the liver. Due to the bronchus infiltration it was impossible to secure it with simultaneous bronchus stenting according to recommendations found in the literature [19,20].

Due to early complications (occurring in the first 7 days after the stent implantation) we observed 1 bleeding, 2 stent migrations and 4 patients complained of chest pain. The bleeding that occurred in patient with a gastric cardia tumor was caused by mechanical damage to the tumor mass and was controlled pharmacologically; endoscopic intervention was unnecessary in this case. Retrosternal pain is an often reported complication after stent implantation [21]. Galder et al. reported the occurrence of chest pain after esophageal self-expanding stent implantation in 30% of the patients. In other papers the frequency of this complication was estimated at from 5% to 50% [13,14,16,17]. In our study the percentage of patients reporting chest pain was lower than 9%. All of these cases were successfully controlled with non-steroidal anti-inflammatory drugs within 48 hours after the stent implantation.

Late complications (occurring more than 1 week after the procedure) included: recurrent dysphagia, stent migration, fistulas, bleeding, symptoms of gastroesophageal reflux and neoplasm overgrowth. According to the literature, prosthesis migration occurs in approximately 5–15% of the cases, as an early, immediate or late complication [13,15,18,22]. The most frequent re-intervention methods after stent migration are second stent implantation or stent reposition with the aid of a loop or pincers. In our research this complication occurred in 5% of the cases and concerned stent implantation in patients with tumor of the distal part of the

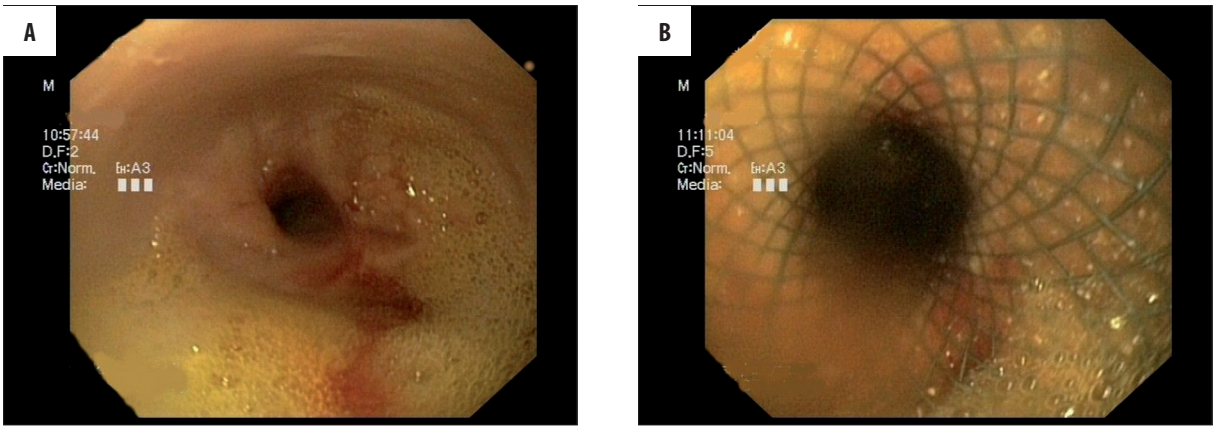

Figure 1. (**A**) Tumorous narrowing (up to 3 mm in diameter) of esophageal-stomach junction. (**B**) Dilation of lesion up to 20 mm in diameter after self-expandable stent implantation.

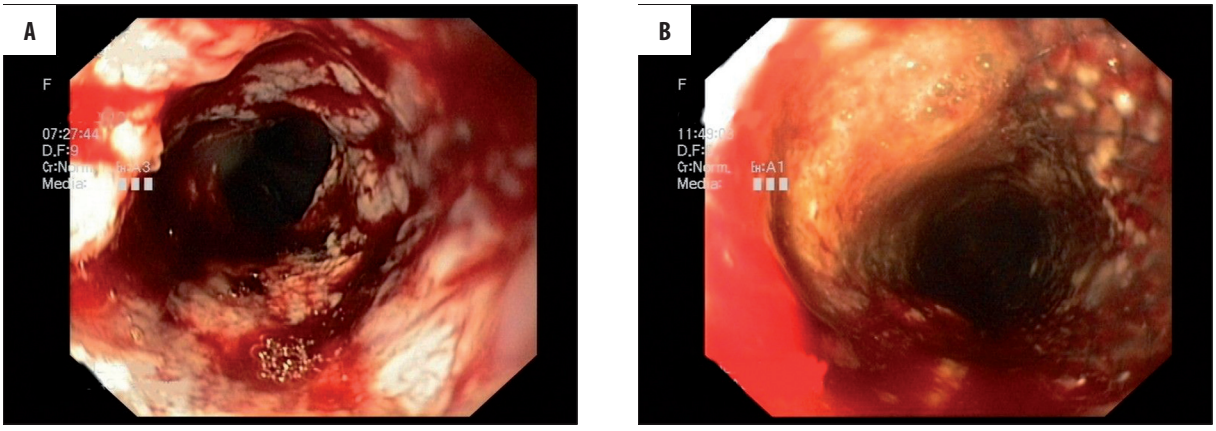

Figure 2. (**A**) Esophageal cancer completely blocking the lumen of esophagus (image presents the state following dilation of esophagus with balloon). (**B**) Esophageal cancer – after the implantation of self-expandable stent.

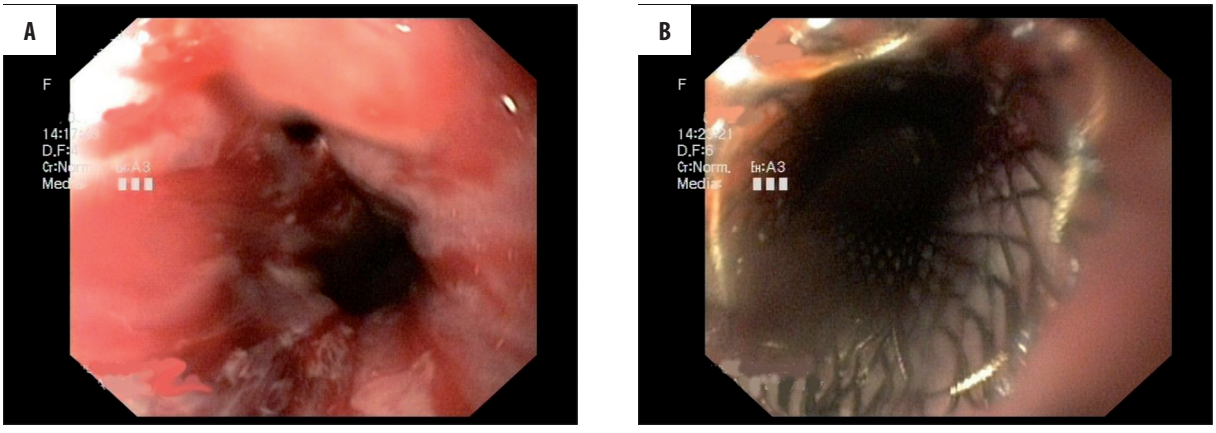

Figure 3. (**A**) Tumorous narrowing along with fistula. (**B**) After implantation of fully-covered stent.

esophagus. In 1 of those cases, for the correct placement of the prosthesis, it was enough to perform reposition with the aid of pincers. In the second case it was necessary to apply a second stent to obtain patency of the esophagus; in our research this was an early complication.

Gastroesophageal reflux is a common complaint of patients with neoplasms located in the distal part of the esophagus, when the distal end of the prosthesis goes through the lower esophageal sphincter. As a preventive method, a prosthesis with an anti-reflux valve or pharmacological treatment may be applied. Some randomized studies confirmed the efficacy of the anti-reflux valve [23,24]. Other studies, due to the lack of clear proof of efficacy of stents with an anti-reflux valve, do not recommend their application in patients with dysphagia caused

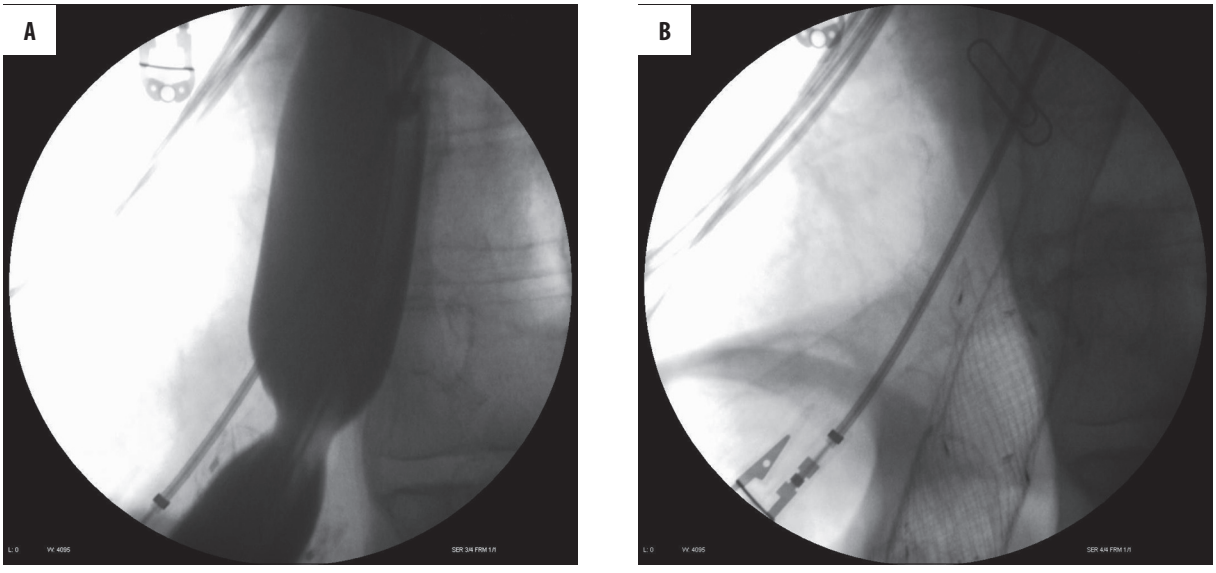

Figure 4. (**A**) The dilation of tumorous metastasis with balloon above the upper edge of previously implanted prosthesis. (**B**) Implantation of stent into previously implanted prosthesis due to tumorous hypertrophy over the old prosthesis.

Table 6. Summary of complications.

Complication	Frequency
Perforation	3/46
Stent malposition	1/46
Respiratory tract compression	1/46
Bleeding	1/46
Chest pain	4/46
Nausea	1/46
Stent migration	2/46
Gastroesophageal reflux	2/46
Death	1/46
Recurrence of dysphagia	2/46
Total	18/46

by neoplastic stenosis of the distal part of the esophagus and cardia [9].

Bleeding most often occurs as a late complication; the etiology of this complication is not fully agreed upon. Both prosthesis placement and disease progression may equally contribute to its occurrence. The presence of the stent often makes the precise localization of the bleeding impossible. The procedures in case of severe hemorrhage include blood transfusion and pharmacological treatment. In our study, bleeding as a late complication did not occur.

In 1 case we observed the occurrence of a tracheoesophageal fistula. This lesion appeared in the fourth week of observation as a consequence of esophageal wall weakening by a pathological neoplastic mass that did not withstand the centrifugal force exerted by the stent. The fistula occurred in the area where the coated and uncoated parts of the stent are joined. This complication was treated with the application of a second coated prosthesis.

The most common late complication, occurring 2–4 months after the stent implantation, is neoplasm infiltration at the ends of the prosthesis. Both ends are affected with comparable frequency in this complication,which has been observed in 10–20% of patients [15,16,18,25]. In such a case, the method of choice is implantation of a second stent. In our observation, adhering to the rule that both ends of the prosthesis protrude by 2–3 cm of the neoplastic stenosis allowed avoidance of the infiltration of the prosthesis by the neoplastic mass.

In our observation, in 2 cases the reoccurrence of dysphagia appeared as a result of stent occlusion with food material. It was a late complication in both cases, it resulted from violating the rules of proper food consumption, and it was easily treated by endoscopic stent cleaning. The frequency of this complication is estimated at 15% in the literature [15,16,18,25].

Conclusions

In patients with neoplastic esophageal stenosis, stenting with coated, self-expandable nitinol prostheses is a safe, effective and quick method of palliative dysphagia treatment. Severe, possibly life-threatening, complications constituted 28% of all the complications and occurred in 9% of the patients. Other complications, which were less severe, occurred in 17% of the observed patients and were not life-threatening. Future research to enhance the quality of the available stents, as well as the introduction of new stent types (biodegradable, with radioactive coating, delivering drugs) will help to decrease of the number of complications and enhance the quality of life of patients in the terminal phase of the disease.

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