

Clinical application of self expandable medical memorial metallic stent with iodine-125 seeds in treatment of esophageal carcinoma

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【 Abstract 】

Objective	To analyze the curative effect of self-expandable medical memorial metallic stent with iodine-125 seeds in the treatment of esophageal carcinoma at advanced stage.
Methods	Forty-five patients with esophageal carcinoma at advanced stage were divided into group A and B. The patients in group A were treated with normal self-expandable stents, while those in group B received the stents with iodine-125 seeds. After the operation, the patients were followed up and their complications and survival time were analyzed.
Results	The stents were successfully implanted in all the 45 patients. The patients were obviously relieved from their difficulties in swallowing. The survival time of patients in group A were 90-300 d, with an average of 171 ± 56 d, and those in group B were 120-450 d, with an average of 316 ± 116 d. There was a significant difference between them ($t = -3.385$, $P < 0.05$).
Conclusion	Self-expandable stent with iodine-125 seeds can obviously alleviate the symptoms of difficulty in swallowing, improve the patients' life quality and survival time.

【 Key words 】

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Foreword

The esophageal stents nowadays are widely used in the treatment of esophageal stricture caused by esophageal cancer. And the results show that they can relieve the dysphagia. But the esophageal stent has no effect on the growth of tumor. Therefore to load the radioactive seeds in the esophageal stent and implant it into the diseased region may relieve the dysphagia as well as control the growth of tumor. During June, 2004 to May, 2005, our hospital used the ¹²⁵I Seeds Self-Expanding Esophageal Stent in treating 20 patients with middle/late stage esophageal cancer and achieved preliminary results. The

reports are as following:

Material & Method

1.1 Material

1.1.1 General Information

45 patients, 35 male and 10 female, aging from 55 to 85 in an average of 68. After taking barium meals and endoscopy, all the cases were diagnosed as esophageal cancers. Their dysphagia degrees can be classified according to the Stooler Classification Standard [7]. They were divided into Group A and Group B, depending on whether they were willing to

accept the therapy of ^{125}I seeds self-expanding nitinol stents. Group A was the common self-expanding nitinol stent treatment group and Group B was the ^{125}I seeds self-expanding nitinol stent treatment group. Group A consisted of 25 patients, 19 male and 6 female. Their average age was 68.9. In Group A, 18 patients were of squamous cell carcinoma and 7 adenocarcinoma. 16 cases were in Grade III and 9 cases were in Grade IV. Their average score of Dysphagia was 3.36. Group B consisted of 20 patients, 16 male and 4 female. Their average age was 69.4 and lesion lengths were between 4.0cm to 7.0cm. 12 cases were in Dysphagia Grade III and 8 cases were in Dysphagia Grade IV. Their average score of dysphagia was 3.40. In this group, 15 patients were of squamous cell carcinoma and 5 adenocarcinoma and the lesion lengths were between 4.0cm to 9.0cm. There were no significances of dysphagia and pathological type classification in these two groups. All of the patients were not suitable for or refuse the surgical treatment because of their weakness, senility, heart & lung diseases or tumor metastasis. All of the patients didn't receive any radiotherapy or chemotherapy.

1.1.2 Radiative Particle

We selected the sealed ^{125}I seeds that produced by Beijing Hi-Tech Atomic Technology Inc. The seeds were cylindrical shaped and their lengths were 4.5mm, diameters were 0.8mm, half lives were 59.43 days. They emitted pathognomonic photons and electrons. The electrons were absorbed by ^{125}I sealed sheath. The main emitted energies of electrons were 27.4 keV X-ray, 31.4keV X-ray and the 35.5keV γ -ray. And the synchronously activated silver stick could also emit 22.1keV and 25.5keV fluorescent X-ray. Its surface activity was 0.3-1.0mCi.

1.1.3 Develop the Radioactive Stent

We chose the suitable Coated Nitinol Esophageal Stent (manufactured by Micro-Tech (Nanjing) Co., Ltd.) according to the lengths of patients' esophageal lesions. The specific sheaths of seeds were already fixed on the stent. According to the lengths and characteristics of lesions, we then loaded the radioactive seeds in the specific sheaths with tweezers and loaded the stent in the esophageal stent introducer.

1.1.4 Devices

The EG-2930K endoscope manufactured by PENTAX, the GIF-Q260 endoscope manufactured by OLYMPUS, the nitinol stent and its introducer made by Micro-Tech.

1.2 Methods

1.2.1 Regular Stent Implantation Method

25 patients accepted the stent implantation method under the X-ray surveillance. The endoscope was regularly inserted to the stricture, and then the guide wire into the endoscopic working channel until it reached the Gastric antrum. We chose the suitable Savary Gilliard esophageal dilator, inserted it along with guide wire and dilated the esophagus step by step until the diameter of esophagus was bigger than 13mm. The endoscope was re-inserted to affirm the distal end of diseased area, which was marked with lead markers under X-ray and then the endoscope was drawn out. We chose the appropriate stent (3-4cm longer than the lesion length) according to the distance between lead markers and loaded it into the delivery system. Then we deployed the delivery system along guide wire until it reached the diseased area. Then we deployed it under the X-ray surveillance after confirming its position. After deployment, we reinserted the endoscope to observe active hemorrhage, the stent position, and the dilation situation. The operation was completed.

1.2.2 ^{125}I Seeds Self-Expanding Esophageal Stent Implantation Method

We ordered the personalized coated nitinol esophageal stent according to the lengths and situation of patients' strictures. The specific sheaths containing radioactive seeds were fixed on the stents in advance. Technical staff loaded the ^{125}I seeds in the specific sheaths of the stent (Fig 1). Firstly the layers of the seeds were confirmed. Generally speaking, one layer of ^{125}I seeds would be loaded per 1.5cm long in the stent, each layer consisted of 3-4 ^{125}I seeds and they were placed in an angle of 90-120°. Each three ^{125}I seeds in the nearby 2 layers were interleaved. The procedure of deploying the ^{125}I seeds was the same as deploying the normal stent (Fig 2-4).

1.2.3 Follow-up

Meglumine diatrizoate contrast was given to patients 3 days after stent implantations and observed the stent positions and their expanding situations. Then we checked patients in a clinic or interviewed patients via telephone about their stent clarity situation as well as life qualities 1,2,3,6,8,12 and 18 months after operations separately. We treated the patients with stent blockages in time and made a specific record about the reasons of deaths as well as the clarity situations of the stents. We also carried CT scan on the patients implanted with ^{125}I Seeds Stent and took photos of the stent and strictures to see whether the seeds fell off about 2 months after operations.

Statistical Treatment The data was treated with SPSS 10.0 Statistical software, the measurement data was expressed as mean±SD and the enumeration data was expressed as frequencies, chi-square test, t test and rank-sum test.

Result

2.1 The Deployment of Stent

The dysphagia were significantly relieved 1 week after operation (Sheet 1). The average score of dysphagia in Group A reduced from 3.36 to 0.96, obviously improved (Wilcoxon $W = 325.000$, $P < 0.01$). And the average score of dysphagia in Group B reduced from 3.4 to 0.90 (Wilcoxon $W = 210.000$, $P < 0.01$). There was no statistical significance of the degree of dysphagia relieved between the group implanted normal stents and the group implanted the radioactive stents.

2.2 The Relief Effect of Dysphagia

The dysphagia were significantly relieved 1 week after operation (Sheet 1). The average score of dysphagia in Group A reduced from 3.36 to 0.96, obviously improved (Wilcoxon $W = 325.000$, $P < 0.01$). And the average score of dysphagia in Group B reduced from 3.4 to 0.90, obviously improved (Wilcoxon $W = 210.000$, $P < 0.01$). There were no statistical significances of relieving dysphagia between the group implanted normal stents and the group implanted the radioactive stents.

2.3 The Complications During & After Operation

1) The retrosternal and midsection pains: in Group A, 20 patients out of 25 had the retrosternal and midsection pain and the pain sharpened when patients were taking food. The incidence rate was 80%. In Group B, 18 patients out of 20 had the retrosternal and midsection pains and the pain sharpened when patients were taking food. The incidence rate was 90%.
 2) Hemorrhage: 6 patients in Group A and 2 patients in Group B were found with melena afteroperation.
 3) Reflux esophagitis: 8 patients in Group A had the symptoms of food reflux, acid regurgitation and retrosternal burning sensation, etc. The incidence rate was 33.3%. 6 patients in Group B had these symptoms and the incidence rate was 30%.
 4) Stent Blockage: During follow-up, 7 cases in Group A (32%) were found to have the obstructive symptoms. The obstruction in 1 case caused by swallowing of unfully chewed mutton was endoscopically found. The medical staff then took out the mutton with foreign body forceps and the obstruction of this patient was relieved. The obstructions in other 6 cases were caused by the

esophageal tumors invasion. The symptom was remitted after implanting another stent in the obstructive position. 2 cases in Group B (10%) were found to have the obstructive symptoms. The obstruction caused by eating the jujube seed in 1 case was endoscopically found. The medical staff then took out the jujube seed with foreign body forceps and the obstruction of this patient was relieved. The obstruction in another case was caused by the esophageal tumor invasion.

5) Others: there were no perforations, stent's migrations or deaths caused by implantations. And there were also no leucopenia, gastrointestinal reaction or other complications caused by radiotherapy in Group B.

2.4 Related follow-up results

2.4.1 Survival time

45 patients accepted the postoperative follow-up. The clinical follow-up lasted from 30 to 540 days (sheet 2). 3 patients in Group A are still alive until now. The average survival time of Group A is 184 days so far. And 7 patients in Group B are still alive until now. The average survival time of Group B is 336 days so far. According to statistical analysis, the average survival time of Group B is obviously longer than that of Group A ($t = -3.385$, $P < 0.05$). What's more, 7 patients are still alive in Group B; the average survival time of Group B can be longer than the number so far.

2.4.2 Cause of Death

17 patients in Group A died of tumor metastasis and systemic failure; 3 died of pulmonary infection; 2 died of gastrointestinal hemorrhage. 9 patients in Group B died of tumor metastasis and systemic failure; 2 died of angiocardiopathy; 2 died of gastrointestinal hemorrhage.

2.4.3 Others

During review, no stent migrations, stent fall-offs, gastrointestinal perforations or radioactive seed fall-offs were found in all the patients.

Discussions

The malignant obstructions are the main causes of dysphagia and the patients suffered a lot of pains such as painful swallow and inability to eat. Because of many reasons, the surgery is of high risks, little curative effect and high recurrence rate. The stent can relieve the patients' dysphagia, improve the patients' ability to eat, strengthen the patients' confidence and disease resistance. Therefore the patients' life qualities can be significantly improved and their life time can be prolonged. The

esophageal stent can dilate the esophagus, effectively relieve the patients' symptoms and has satisfactory curative effects. 1 week after implanting the normal esophageal stents, the average score of dysphagia reduced from 3.36 to 0.96, the average life time is 171 ± 56 days. This is similar to the results in literatures in and out of China.

The self-expanding metal esophageal stent can relieve the dysphagia but has no effect on the growth of tumor. 80% of the patients were found in middle/late stage when they got diagnosed. The radiotherapy is the main treatment. The 5a survival rate was 10% [9]. The external beam radiation therapy was the main therapy for middle or late stage esophageal cancer and its curative effect was good. But its complication rate was high; its complication rate as 14.9% reported once [10], including esophago-tracheal fistula, radiation pneumonitis, esophageal stricture and esophageal ulcer, etc. Any of the complications could cause serious consequences, even death. ¹²⁵I seeds are the low-energy radioactive seeds with good curative effects which can make tumor cells lose their multiplication capacity and are effective in killing tumors constantly [11-14]. However, simply implanting the ¹²⁵I seeds in patients with esophageal cancer have slow effect in relieving the dysphagia. Its operation procedure is complex and the seed are easy to fall off [15]. We loaded the seeds in the stent and then deploy the stent into patient's diseased area, then the stent could relieve the dysphagia and control the tumor growths. The radioactive professionals fixed ¹²⁵I seeds on the stent. During the fixing, the professionals should avoid direct contact with the radioactive seeds. Then we loaded the stent into the delivery system of esophageal stent. In theory, the stent with radioactive seeds fixed on added the diameter of stent as well as the friction forces between stent and the delivery system and should affect the deployment of stent. But we found the ¹²⁵I seed esophageal stent can be deployed with normal delivery system and its procedure showed no difference between that of normal stent. The

stents were successfully implanted in 20 patients with accurate position. No seeds fell off. Compared with that of normal stents, no serious complications happened after deploying the ¹²⁵I seed esophageal stent. 2 cases who suffered chest pain got better after symptomatic treatment. The patients with ¹²⁵I seed esophageal stent implanted lived significantly longer than those implanted normal stents. The average survival time of the former was 316 ± 116 d and the average survival time of the later was 171 ± 56 d. There were still 35% patients alive in the former group. Therefore the average survival time of this group should be longer.

20 patients in this group received endoscopy and chest CT scan 2 months after operation, and the results showed that 13 patients' diseased areas shrank, 4 patients' diseased areas had not significant changes and 3 patients' diseased areas enlarged, which can explained by the different dosages of seeds and the pathological types of patients. The tumor's invasive growth into esophageal was found in 1 patient of this group. And the tumor's invasive growths into esophageal and blockages of the stent were found in 6 patients of the normal esophageal stent group. This result showed that the radioactive seeds had significant inhibiting effects to the esophageal tumors.

Although the ¹²⁵I Seeds were sealed in the specific sheaths, would they leak after being positioned in the esophageal PH environment for a long time? Jinhe Guo, et al [16] worked on the radiation range of radioactive seeds according to the ECT images of postoperative tests to see whether there were ectopic autoradiography or leakages of ¹²⁵I Seeds. The results showed that no ¹²⁵I seeds leaked.

This research was carried out for a short time with few cases and short follow-up time, but it showed that the internal radioactive esophageal stent was feasible. It's proven to be safe and effective clinically. It can effectively control the growth of malignant tumor, significantly relieve the dysphagia, improve the patient's life quality and prolong the life time of patient. It's worthy of further promotion and practice in clinic.

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