

Dr. Marco Scarpa, PhD, Series Editor

Quality of life in patients with esophageal stenting for the palliation of malignant dysphagia

Giorgio Diamantis, Marco Scarpa, Paolo Bocus, Stefano Realdon, Carlo Castoro, Ermanno Ancona, Giorgio Battaglia

Giorgio Diamantis, Marco Scarpa, Paolo Bocus, Stefano Realdon, Carlo Castoro, Giorgio Battaglia, Veneto Oncological Institute (IOV-IRCCS), Via Gattamelata 64, Padua 35128, Italy

Ermanno Ancona, Giorgio Battaglia, Department of Surgical and Gastroenterological Sciences, University of Padua, Via Giustiniani 2, Padua 35128, Italy

Author contributions: Diamantis G, Scarpa M, Castoro C, Ancona E and Battaglia G designed the research; Diamantis G, Scarpa M, Bocus P, Realdon S and Castoro C performed the research; Castoro C, Ancona E and Battaglia G contributed analytic tools; Diamantis G, Scarpa M, Bocus P, Realdon S and Castoro C analyzed the data; Diamantis G and Scarpa M wrote the paper; all authors revised and approved the final version of the manuscript.

Correspondence to: Giorgio Diamantis, MD, Veneto Oncological Institute (IOV-IRCCS), Via Gattamelata 64, Padua 35128, Italy. giodiamantis@gmail.com

Telephone: +39-49-8218840 Fax: +39-49-8211707

Received: September 2, 2010 Revised: October 16, 2010

Accepted: October 23, 2010

Published online: January 14, 2011

or palliative intervention. To date, only a few published studies can be found on Medline examining HRQoL in patients with advanced EC treated with SEMS implantation. The aim of this study was to review the impact on HRQoL of SEMS implantation as palliative treatment in patients with EC. All Medline articles regarding HRQoL in patients with advanced EC, particularly those related to SEMS, were reviewed. In most studies, relief of dysphagia was the only aspect of HRQoL being measured and SEMS implantation was compared with other palliative treatments such as brachytherapy and laser therapy. SEMS insertion provides a swift palliation of dysphagia compared to brachytherapy and no evidence was found to suggest that stent implantation is different to laser treatment in terms of improving dysphagia, recurrent dysphagia and better HRQoL, although SEMS insertion has a better technical success rate and also reduces the number of repeat interventions.

© 2011 Baishideng. All rights reserved.

Key words: Esophageal cancer; Health-related quality of life; Self-expandable metal stents

Peer reviewers: Piero Marco Fisichella, MD, Assistant Professor of Surgery, Medical Director, Swallowing Center, Loyola University Medical Center, Department of Surgery, Stritch School of Medicine, 2160 South First Avenue, Room 3226, Maywood, IL 60153, United States; David Ian Watson, Professor, Head, Flinders University Department of Surgery, Room 3D211, Flinders Medical Center, Bedford Park, South Australia 5042, Australia

Diamantis G, Scarpa M, Bocus P, Realdon S, Castoro C, Ancona E, Battaglia G. Quality of life in patients with esophageal stenting for the palliation of malignant dysphagia. *World J Gastroenterol* 2011; 17(2): 144-150 Available from: URL: <http://www.wjg-net.com/1007-9327/full/v17/i2/144.htm> DOI: <http://dx.doi.org/10.3748/wjg.v17.i2.144>

Abstract

Incidence of esophageal cancer (EC) is rising more rapidly in the Western world than that of any other cancer. Despite advances in therapy, more than 50% of patients have incurable disease at the time of presentation. This precludes curative treatment and makes palliative treatment a more realistic option for most of these patients. Dysphagia is the predominant symptom in more than 70% of patients with EC and although several management options have been developed in recent years to palliate this symptom, the optimum management is not established. Self-expanding metal stents (SEMS) are a well-established palliation modality for dysphagia in such patients. Health-related quality of life (HRQoL) is becoming a major issue in the evaluation of any therapeutic

INTRODUCTION

Esophageal cancer (EC) is a devastating disease with an incidence that is rising more rapidly in the Western world than that of any other cancer^[1]. Despite advances in therapy, more than 50% of patients have incurable disease at the time of presentation and only 5%-10% of patients survive 5 years later^[2]. The incidence rates of EC are highly variable across geographic areas. Whereas rates are relatively low in many parts of the world, exceptionally high incidence rates have been reported from some regions of China. Moderate to high incidence rates have been reported from other areas or populations, including parts of Central Asia, South Africa, South America, northern France, and among African-Americans in the United States^[3,4]. A marked change in the male to female ratio of age-adjusted incidence rates has also been observed^[5].

Squamous cell carcinoma is the predominant histologic type of EC in the world^[4]. Nevertheless, a shift in proportion of EC type from SCC to adenocarcinoma (AC) has been reported to have occurred in Western countries, notably from the 1970s in the United States and from the 1980s and early 1990s in some European countries^[6-8]. The reason for this shift is not clear, but it may be related to several factors, including transitions in lifestyle and diet, being overweight, and declining rates of *Helicobacter pylori* infection in the Western world^[7,9]. In Europe, while incidence of SCC has remained stable or declined during the past few decades, the incidence of esophageal AC has been rising. This increase has been more prominent in Northern Europe, notably in the United Kingdom and Ireland, but smaller increases have also been reported from other parts of the continent^[7,8].

Most ECs are diagnosed at an advanced stage and in patients with co-morbidity. This precludes curative treatment and makes palliative treatment a more realistic option for most of these patients^[10]. Dysphagia is the predominant symptom in more than 70% of patients with EC^[11]. Several management options have been developed in recent years to palliate malignant dysphagia. These include mechanical measures such as endoluminal stenting or surgery and antineoplastic methods such as external beam radiation, brachytherapy, chemotherapy, chemoradiotherapy, laser treatment, photodynamic therapy or ablation using injection of alcohol or chemotherapeutic agents. The optimum management of dysphagia caused by advanced primary EC is not established although continued progress has been made in recent years to achieve this goal^[10,12,13]. However, palliation remains an important aspect of treatment, with goals of relieving dysphagia, reducing the risk of aspiration, maintaining a patent orogastric pathway and nutritional status and improving the quality of life.

Esophageal intubation for the palliation of dysphagia from malignant esophageal obstruction has been practiced for over a hundred years. In 1959, Celestin^[14] described the palliation of esophageal malignancy with a plastic endoprosthesis introduced at laparotomy. In the 1970s,

Atkinson *et al*^[15] introduced an endoscopically inserted plastic prosthesis, with a more reduced complication rate. Plastic stents have been superseded by the newer range of metallic self-expanding stents that are safer and easier to place^[14-22]. The first description of the endoscopic placement of an expanding metallic spiral stent was made by Frimberger^[23] in 1983. Nevertheless, some series report little difference in the degree of palliation from dysphagia between plastic and metal stents^[14,24], although the complication rates with metallic stents are significantly lower.

However, the use of self-expanding metal stents (SEMS) is not without problems. Stent migration, incomplete expansion of the stent and tumour ingrowth and overgrowth may require further intervention for recurrent dysphagia. Insertion of stents beyond the gastro-esophageal junction has been observed to result in acid reflux^[25,26]. More recently, developments in SEMS design have resulted in the increasing use of anti-reflux SEMS^[27,28] and retrievable SEMS^[29]. Although SEMS insertion is now reported to be the most common palliative method for treating dysphagia in EC^[30], there is a paucity of evidence regarding its effectiveness in improving the quality of life and nutritional status of the patients.

The aim of this study was to review the impact on health-related quality of life (HRQoL) of SEMS implantation as palliative treatment in patients with EC. A text word literature review was performed using the PubMed and Medline databases. Although this was not a systematic review, the search terms used were as follows: esophageal AND cancer OR carcinoma AND quality of life OR HRQoL OR health-related quality of life OR patient reported outcome AND self-expandable metal stents OR esophageal stents. The reference lists of identified articles were searched for further relevant publications. Two researchers (Diamantis G and Scarpa M) independently selected the studies, limited to clinical studies published between January 1980 to July 2010 and in the English language. Unpublished data and data published in abstract form only were excluded, because these were unlikely to contain sufficient methodologic information to allow valid conclusions to be made. Whenever there was discordance regarding study inclusion the two researchers negotiated an agreement.

HRQOL AS MEASURE OF OUTCOME AFTER TREATMENT OF EC

Defining HRQoL is a complex matter and a universally accepted definition does not exist. Usually, the term quality of life (QoL) and, more specifically, HRQoL, refers to a multidimensional construct which encompasses patients' perceptions of both negative and positive aspects in at least 4 dimensions: physical, emotional and social functions, as well as disease and treatment-related symptoms^[31]. More recently, the assessment of other dimensions of QoL (e.g. spiritual well-being or sexual function) has received more attention. QoL data provide direct measures of benefit as perceived by the patients and may be

Table 1 Examples of quality of life questionnaires used to assess quality of life in patients with esophageal cancer

Category	Type of questionnaire	Advantages	Disadvantages
Generic	SF-36	Good psychometric properties	
	EQ-5D	Reliable	Limited number of domains
Cancer-specific	Spitzer QoL index	Brief and easy to complete	Limited number of domains
	EORTC QLQ C30	Fully validated The most widely used specific instrument Clinical significance assessed	Ceiling effect Site-specific modules may add to patient burden
EC-specific	HAD scale	Well validated and widely used with RSCL	Only assesses anxiety and depression
	EORTC QLQ-OES18	Fully validated	Needs to be used with QLQ-C30
	EORTC QLQ-STO22	Fully validated	Limited supporting psychometric data
	FACT-E	Provides overall summary score	

Modified from Conroy *et al*^[55]. SF-36: Medical Outcomes Study 36-Item Short Form Health Survey; HAD: Hospital Anxiety and Depression; QoL: Quality of life; EORTC QLQ: European Organization for Research and Treatment QoL Questionnaire; FACT: Functional Assessment of Cancer Therapy.

useful for helping them clarify their treatment preferences. The data are also intended to help physicians' decisions by allowing them to understand patients' experiences of treatment, and there is evidence that QoL data may have prognostic value, especially in metastatic disease.

Questionnaires are the most frequently used tools to measure QoL. Multitudes of HRQoL instruments have been described providing adequate coverage of the basic HRQoL dimensions (i.e. physical, functional, social, and emotional function). As the patients represent the most appropriate source of information for their own QoL, the patient self-report is the usual means of assessing QoL. There is no consensus as to which instruments are more appropriate. However, not all QoL instruments have been shown to have acceptable psychometric properties such as reliability, validity and responsiveness. These tools can be classified into 3 main categories: generic instruments, symptom-focused questionnaires and cancer-specific instruments (Table 1).

Esophagectomy, of all elective or emergency surgical oncology procedures performed, is currently one of the most highly rated for morbidity and mortality. Mortality rates vary between 1% and 8% and major morbidity occurs in almost 50% of the patients undergoing resection^[32,33]. The impact of surgery on QoL has been investigated in several prospective studies using validated reliable questionnaires^[34-36]. These investigations generally showed that early in the postoperative phase most aspects of QoL significantly deteriorate. Probably the only aspect of QoL that does not dramatically deteriorate after surgery is emotional function^[34-37]. Several studies have shown that scores for emotional function remain stable after surgery and this may represent patients' relief that the procedure is over, despite the slow physical recovery. Dysphagia scores are generally improved or stable after surgery and patients report fewer problems swallowing solid and soft foods than before the operation. Relief of dysphagia, however, is replaced with other symptoms such as anorexia, change in taste, nausea and diarrhea. The combined impact of multiple symptoms and general deterioration in key aspects of well-being leads to reduced overall QoL scores, but these

gradually recover within 9 mo. Although longitudinal studies show QoL recovery after surgery, one of the difficulties with interpreting these studies relates to missing data due to attrition. The 1-year survival rate after esophagectomy is about 65%; therefore, most papers reporting a recovery of QoL only include data from patients who are alive and sufficiently well to complete questionnaires.

Safieddine *et al*^[38] suggested that although combined modality therapy (chemotherapy/radiation therapy/surgical intervention) is arduous and prolonged, its effect on HRQoL in patients with operable EC is transient, since HRQoL scores return to baseline levels after induction and before surgical intervention. Similarly, surgical intervention has a significant effect on HRQoL because FACT-E scores (Functional Assessment of Cancer Therapy-Esophageal; a validated tool to measure the effect of treatment on functional, social, physical, and emotional well-being that incorporates the EC subscale and allows for a systematic evaluation of QoL specifically in the context of EC) decrease significantly 1 mo after surgical intervention but again return to baseline levels within 3 mo of surgical intervention. Significantly greater increases in FACT-E scores were observed in patients who were still alive 1 year after surgical intervention with or without disease but were observed to decrease in those who died within 1 year of surgical intervention. These researchers had similar findings in patients after esophagectomy who had not been treated with induction chemoradiotherapy.

HRQOL AFTER SEMS IMPLANTATION IN PATIENTS WITH INOPERABLE EC

Since their introduction in the early 1990s^[39,40], SEMS have virtually supplanted not only conventional prostheses but also most forms of ablative therapy in the palliation of malignant dysphagia^[41,42]. The reasons for this range from perceived to real benefits. The latter include smaller delivery systems (precluding the need for excessive dilation), ability to curve around acute angulations, and the larger internal diameter of most SEMS compared with conventional prostheses. The perceived, as opposed to proved,

Table 2 Characteristics of conventional and anti-reflux mechanism self-expanding metal stents

	Material	Length	Inner diameter	Constrainability	Foreshortening	Anti-reflux mechanism
Conventional SEMS						
Ultraflex	Nitinol	10 cm (7 cm CS)	18 mm with 23 mm PF	Braided nylon wire	20% to 40%	
	Polyurethane sheath	12 cm (9 cm CS) 15 cm (12 cm CS)	23 mm with 28 mm PF	Not reconstrainable when partially deployed		
Z stent	Stainless steel	8, 10, 12, 14 cm	18 mm with 25 mm PF and DF	Polyethylene sheath	None	
	Polyurethane covering			Reconstrainable when partially deployed		
Wallstent	Elgiloy	10 cm (8 cm CS)	20 mm with 23 mm PF and DF	Polyethylene sheath	Up to 28%	
	Polyurethane sheath	15 cm (13 cm CS)		Reconstrainable when partially deployed		
SEMS with an anti-reflux mechanism						
Dua Z-stent						Polyurethane sleeve (collapses with gastric pressure)
DO stent						Tricuspid valve
Fer-X-Ella stent						Stainless steel with polyethylene covering and windsock type valve

Modified from Sreedharan *et al*^[56]. SEMS: Self-expanding metal stents; CS: Covered segment; PF: Proximal flare; DF: Distal flare.

benefits have been heavily touted by the manufacturers and include more precise placement (contradictory data because of prosthesis foreshortening in many of the SEMS), fewer long-term complications, and long-term survival advantages. In the 20 years since their introduction, both the SEMS themselves and their delivery systems have undergone multiple modifications. As such, most SEMS have evolved from an uncovered to a covered form, diameters of the prostheses have often been increased, and attempts have been made to minimize migration, gastroesophageal reflux, and tissue ingrowth (Table 2). Although it is safer and easier to place expandable stents, they are not devoid of complications. The major complications include stent migration, stent block, bleeding, and perforation, while the minor ones are foreign body sensation, regurgitation, and chest pain. The main complication of metal stents is distal migration, with an incidence rate ranging between 10% and 30%^[43]. It is more commonly (50%) seen when covered endoprosthesis are used to treat distal esophageal lesions involving the gastroesophageal junction^[44,45]. Stents can become blocked either due to tumor ingrowth through the stent mesh (17%-36%) or tumor overgrowth (10%)^[46,47].

As mentioned in the introduction, the primary aim of treatment in patients with inoperable EC is to relieve dysphagia with minimal morbidity and mortality, and thus improve their QoL. Implantation of a SEMS has become established as a treatment modality for the palliation of malignant dysphagia. SEMS relieves dysphagia rapidly and improves the nutritional status. However, in most studies, relief of dysphagia is the only aspect of HRQoL being measured, although physical, mental and social functioning and other EC-specific aspects of HRQoL are additional important outcome measures, as explained before.

A randomized clinical trial comparing SEMS with plastic endoprosthesis published in 2002 by O'Donnell *et al*^[48]

included 50 patients suffering from dysphagia due to an inoperable EC, and measured QoL using EORTC QLQ-30, a multi-dimensional cancer-specific QoL questionnaire and an EC specific questionnaire (EORTC OES-24), allowing QoL to be measured over 26 components relating to cancer in general and EC in particular. Although the authors found no statistical significance in any of the 26 components, 21 of the 26 components showed a trend towards the metal group, five were neutral and none favored plastic stents.

Shenfine *et al*^[49] in a randomized controlled trial regarding the cost-effectiveness of palliative therapies for patients with inoperable EC studied QoL in detail using four different questionnaires including Spitzer QoL index, Karnofsky performance scale, Euroqol EQ-5D and EORTC QLQ-30. They also used proxy and self-administered questionnaires. These authors reported differences in the baseline quality of life index favoring the non-SEMS group and went on to report 1 and 6 wk QoL data for the different treatment groups. Mean QoL index for the SEMS group at 6 wk was significantly lower than for the QoL index at baseline for the same group. The authors concluded that decreased QoL in the SEMS group at 6 wk, although not statistically significant, reflected the presence of pain following the intervention; the effect of pain on quality of life may have significant implications for treatment with SEMS.

Bergquist *et al*^[50], in their randomized controlled clinical trial published in 2005, compared endoluminal brachytherapy with endoscopic stent placement for newly diagnosed patients with advanced EC or gastroesophageal junction cancer, with a primary outcome being the detailed evaluation of HRQoL. Sixty-five patients eligible for the study were enrolled; 34 were randomized to stent treatment and 31 to brachytherapy. The authors assessed dysphagia improvement as a part of disease-specific HRQoL question-

Table 3 Quality of life results after self-expanding metal stents placement for malignant dysphagia

Ref.	Yr	Study type	Investigation	Type of questionnaire	Results
Dallal <i>et al</i> ^[52]	2001	Randomized trial	Endoscopic thermal ablation <i>vs</i> SEMS in patients with inoperable EC	EORTC QLQ-30 EORTC OES-24 SF-36 HAD scale	HRQoL deteriorated in the stent group but not in the group treated with thermal ablation
Siersema <i>et al</i> ^[53]	2001	Prospective, randomized study	comparison between Ultraflex stent, Flamingo Wallstent, and Gianturco-Z stent in 100 consecutive patients with dysphagia caused by EC or carcinoma of the gastric cardia	WHO performance status Dysphagia score	Mean WHO performance status before and at 4 wk after stent placement was not different among the 3 patient groups
O'Donnell <i>et al</i> ^[48]	2002	Randomized clinical trial	SEMS <i>vs</i> plastic endoprostheses	EORTC QLQ-30 EORTC OES-24	QoL in patients with SEMS was better than in plastic stents (no statistical significance)
Homs <i>et al</i> ^[51]	2004	Randomized trial	Stent placement <i>vs</i> single dose brachytherapy for the palliation of EC	EORTC OES-23 Visual analogue pain scale EORTC QLQ-C30 Euroqol EQ-5D EQ-VAS	Treatment with single dose brachytherapy gave better overall scores on HRQoL scales compared with stent placement for the palliation of EC
Shenfine <i>et al</i> ^[49]	2005	Randomized controlled trial	Cost-effectiveness of palliative therapies for patients with inoperable EC	Spitzer QoL index Karnowsky performance scale Euroqol EQ-5D EORTC QLQ-30	Mean QoL index for the SEMS group at 6 wk was significantly lower than the QoL index at baseline for the same group
Bergquist <i>et al</i> ^[50]	2005	Randomized controlled clinical trial	Endoluminal brachytherapy <i>vs</i> endoscopic stent placement in patients with advanced EC or gastroesophageal junction cancer	EORTC OES-23 EORTC QLQ-30	Insertion of SEMS offered a more instant relief of dysphagia compared to endoluminal brachytherapy, but HRQoL was more stable in brachytherapy treatment
Madhusudhan <i>et al</i> ^[54]	2009	Prospective study	QoL after palliative stenting in patients with inoperable EC	EORTC QLQ-C30 EORTC QLQ-OES 18	Palliative stenting using SEMS resulted in significant improvement in all scales of QoL

QoL: Quality of life; HRQoL: Health-related quality of life; EC: Esophageal cancer; SEMS: Self-expanding metal stents.

naire EORTC OES-23 and found a statistically significant improvement in dysphagia grade, ability to swallow saliva, choking and coughing compared to baseline scores. There was no improvement in these outcomes for patients treated with brachytherapy. In an interim inter-group analysis at 1 mo a significant improvement in dysphagia scale favored the SEMS group. At 3 mo, some of the dysphagia-related parameters continued to show clinical improvement in the SEMS group but these did not achieve statistical significance. In the brachytherapy group, clinically significant improvements were noted in some of the parameters related to dysphagia at 3 mo and these were maintained at 6 mo. However, these data did not achieve statistical significance. General health QoL was measured using the EORTC QLQ-30 scale. In the stent group all functional scales and single symptom scales deteriorated compared to mean scores at inclusion. The largest deterioration was found for social function, followed by pain, role function and insomnia. In the brachytherapy group, a clinically relevant deterioration was found for most variables on the function and single symptom scales with physical function, global QoL and pain scales reaching statistical significance.

The same type of comparison between these two types of palliative procedures, brachytherapy and stent placement, in patients with advanced EC was published from Homs *et al*^[51] who prospectively compared generic and disease-specific HRQoL between single dose brachy-

therapy and SEMS placement. Treatment with single dose brachytherapy gave better overall scores on HRQoL scales compared with stent placement for the palliation of EC. Major improvements were seen on the dysphagia and eating scales of the disease-specific EORTC OES-23, in contrast to other scales of this disease-specific measure which remained almost stable during follow-up. In addition, pain levels remained stable or slightly increased during follow-up, indicating that adequate pain management during follow-up is important.

In a randomized trial carried out at the Western General Hospital in Edinburgh (United Kingdom)^[52], patients presenting with advanced inoperable EC were randomized to palliative therapy by endoscopic thermal ablation (34 patients) or insertion of a SEMS (31 patients), assessing HRQoL. The authors evaluated cancer-specific and EC-specific questionnaires (EORTC QLQ-30 and OES 24) along with a generic questionnaire (SF-36) and a psychometric questionnaire (HAD Scale). The baseline QoL data were reported to be similar in the two groups. However, at 1 mo the SEMS group was significantly worse in parameters of physical function, physical health, pain and emotional health. Results of the cancer-specific questionnaires were reported to be significantly worse in the SEMS group for fatigue, emotional, cognitive and social function and troublesome taste. No differences were noted in dysphagia, deglutition and eating scores.

Several randomized studies comparing different types

of SEMS have been published over the last 10 years but only a few of them have assessed HRQoL as an outcome. Siersema *et al*^[53] performed a prospective, randomized study comparing the Ultraflex stent, the Flamingo Wallstent, and the Gianturco-Z stent in 100 consecutive patients with dysphagia caused by EC or carcinoma of the gastric cardia. All patients were evaluated before stent placement and at 4-wk intervals until death. The authors used the WHO performance status in addition to the dysphagia score to evaluate QoL. The mean WHO performance status before and at 4 wk after stent placement was not different among the 3 patient groups.

Madhusudhan *et al*^[54] in their prospective study assessed the QoL using EORTC QLQ-C30 (version 3) and EORTC QLQ-OES 18 questionnaires before stenting, and at 1, 4, and 8 wk following placement of the stent. The results showed significant improvement following stenting. The general health scale and function scores increased significantly. Most symptom scores, except pain, showed improvement. The pain score deteriorated at 1 wk, as initial expansion of SEMS following its placement led to an increase in pain sensation. Over a period of 2 mo, the pain scores decreased to baseline values. The financial strain scores also showed a significant improvement.

The QoL results after SEMS placement for malignant dysphagia are displayed in Table 3.

CONCLUSION

The prime objective of palliative treatment in patients with inoperable esophageal or gastro-esophageal junctional cancers is to achieve adequate improvement in dysphagia and QoL in a short span of time with a reduced need for additional interventions. In summary, the above analysis confirms that SEMS insertion provides a swift palliation of dysphagia compared to brachytherapy. However, this difference gradually diminishes over time and, in the long run, brachytherapy appears to provide better dysphagia improvement and improved disease-specific QoL scores along with better general health-related QoL scores in these gradually deteriorating patients. On the other hand, no evidence was found to suggest that stent implantation is any better than laser treatment in terms of improving dysphagia, recurrent dysphagia or in yielding a better QoL. Nevertheless, SEMS insertion has a better technical success rate and also reduces the number of repeat interventions. Finally, QoL seems to be similar between different types of conventional SEMS.

REFERENCES

- 1 Pera M, Cameron AJ, Trastek VF, Carpenter HA, Zinsmeister AR. Increasing incidence of adenocarcinoma of the esophagus and esophagogastric junction. *Gastroenterology* 1993; **104**: 510-513
- 2 Mason R. Palliation of oesophageal cancer. *Surg Oncol* 2001; **10**: 123-126
- 3 Kmet J, Mahboubi E. Esophageal cancer in the Caspian littoral of Iran: initial studies. *Science* 1972; **175**: 846-853

- 4 Blot WJ, McLaughlin JK, Fraumeni JF. Esophageal cancer. In: Schottenfeld D, Fraumeni JF, editors. *Cancer epidemiology and prevention*. New York: Oxford University Press, 2006: 697-706
- 5 Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; **55**: 74-108
- 6 Trivers KF, Sabatino SA, Stewart SL. Trends in esophageal cancer incidence by histology, United States, 1998-2003. *Int J Cancer* 2008; **123**: 1422-1428
- 7 Karim-Kos HE, de Vries E, Soerjomataram I, Lemmens V, Siesling S, Coebergh JW. Recent trends of cancer in Europe: a combined approach of incidence, survival and mortality for 17 cancer sites since the 1990s. *Eur J Cancer* 2008; **44**: 1345-1389
- 8 Steevens J, Botterweck AA, Dirx MJ, van den Brandt PA, Schouten LJ. Trends in incidence of oesophageal and stomach cancer subtypes in Europe. *Eur J Gastroenterol Hepatol* 2010; **22**: 669-678
- 9 Robins G, Crabtree JE, Bailey A, Forman D. International variation in *Helicobacter pylori* infection and rates of oesophageal cancer. *Eur J Cancer* 2008; **44**: 726-732
- 10 Weigel TL, Frumiento C, Gaumintz E. Endoluminal palliation for dysphagia secondary to esophageal carcinoma. *Surg Clin North Am* 2002; **82**: 747-761
- 11 Brierley JD, Oza AM. Radiation and chemotherapy in the management of malignant esophageal strictures. *Gastrointest Endosc Clin N Am* 1998; **8**: 451-463
- 12 Allum WH, Griffin SM, Watson A, Colin-Jones D. Guidelines for the management of oesophageal and gastric cancer. *Gut* 2002; **50** Suppl 5: v1-v23
- 13 Bown SG. Palliation of malignant dysphagia: surgery, radiotherapy, laser, intubation alone or in combination? *Gut* 1991; **32**: 841-844
- 14 Celestin LR. Permanent intubation in inoperable cancer of the oesophagus and cardia: a new tube. *Ann R Coll Surg Engl* 1959; **25**: 165-170
- 15 Atkinson M, Ferguson R. Fibreoptic endoscopic palliative intubation of inoperable oesophagogastric neoplasms. *Br Med J* 1977; **1**: 266-267
- 16 Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. *N Engl J Med* 1993; **329**: 1302-1307
- 17 De Palma GD, di Matteo E, Romano G, Fimmano A, Rondinone G, Catanzano C. Plastic prosthesis versus expandable metal stents for palliation of inoperable esophageal thoracic carcinoma: a controlled prospective study. *Gastrointest Endosc* 1996; **43**: 478-482
- 18 Roseveare CD, Patel P, Simmonds N, Goggin PM, Kimble J, Shepherd HA. Metal stents improve dysphagia, nutrition and survival in malignant oesophageal stenosis: a randomized controlled trial comparing modified Gianturco Z-stents with plastic Atkinson tubes. *Eur J Gastroenterol Hepatol* 1998; **10**: 653-657
- 19 Davies N, Thomas HG, Eyre-Brook IA. Palliation of dysphagia from inoperable oesophageal carcinoma using Atkinson tubes or self-expanding metal stents. *Ann R Coll Surg Engl* 1998; **80**: 394-397
- 20 Sanyika C, Corr P, Haffeejee A. Palliative treatment of oesophageal carcinoma--efficacy of plastic versus self-expandable stents. *S Afr Med J* 1999; **89**: 640-643
- 21 Birch JF, White SA, Berry DP, Veitch PS. A cost-benefit comparison of self-expanding metal stents and Atkinson tubes for the palliation of obstructing esophageal tumors. *Dis Esophagus* 1998; **11**: 172-176
- 22 Siersema PD, Hop WC, Dees J, Tilanus HW, van Blankenstein M. Coated self-expanding metal stents versus latex prostheses for esophagogastric cancer with special reference to prior radiation and chemotherapy: a controlled, prospective study. *Gastrointest Endosc* 1998; **47**: 113-120
- 23 Frimberger E. Expanding spiral--a new type of prosthesis for

- the palliative treatment of malignant esophageal stenoses. *Endoscopy* 1983; **15** Suppl 1: 213-214
- 24 **Gevers AM**, Macken E, Hiele M, Rutgeerts P. A comparison of laser therapy, plastic stents, and expandable metal stents for palliation of malignant dysphagia in patients without a fistula. *Gastrointest Endosc* 1998; **48**: 383-388
 - 25 **Adam A**, Ellul J, Watkinson AF, Tan BS, Morgan RA, Saunders MP, Mason RC. Palliation of inoperable esophageal carcinoma: a prospective randomized trial of laser therapy and stent placement. *Radiology* 1997; **202**: 344-348
 - 26 **Sabharwal T**, Hamady MS, Chui S, Atkinson S, Mason R, Adam A. A randomised prospective comparison of the Flamingo Wallstent and Ultraflex stent for palliation of dysphagia associated with lower third oesophageal carcinoma. *Gut* 2003; **52**: 922-926
 - 27 **Dua KS**, Kozarek R, Kim J, Evans J, Medda BK, Lang I, Hogan WJ, Shaker R. Self-expanding metal esophageal stent with anti-reflux mechanism. *Gastrointest Endosc* 2001; **53**: 603-613
 - 28 **Laasch HU**, Marriott A, Wilbraham L, Tunnah S, England RE, Martin DF. Effectiveness of open versus antireflux stents for palliation of distal esophageal carcinoma and prevention of symptomatic gastroesophageal reflux. *Radiology* 2002; **225**: 359-365
 - 29 **Song HY**, Lee DH, Seo TS, Kim SB, Jung HY, Kim JH, Park SI. Retrievable covered nitinol stents: experiences in 108 patients with malignant esophageal strictures. *J Vasc Interv Radiol* 2002; **13**: 285-293
 - 30 **Gilbert FJ**, Park KGM, and Thompson AM. Scottish Audit of Gastric and Oesophageal Cancer. Report 1997-2000. Edinburgh: Scottish Executive Health Department, 2002
 - 31 **Fayers P**, Hays R. Assessing quality of life in clinical trials. 2nd ed. New York: Oxford University Press, 2005
 - 32 **Jamieson GG**, Mathew G, Ludemann R, Wayman J, Myers JC, Devitt PG. Postoperative mortality following oesophagectomy and problems in reporting its rate. *Br J Surg* 2004; **91**: 943-947
 - 33 **de Boer AG**, Stalmeier PF, Sprangers MA, de Haes JC, van Sandick JW, Hulscher JB, van Lanschot JJ. Transhiatal vs extended transthoracic resection in oesophageal carcinoma: patients' utilities and treatment preferences. *Br J Cancer* 2002; **86**: 851-857
 - 34 **Zieren HU**, Jacobi CA, Zieren J, Müller JM. Quality of life following resection of oesophageal carcinoma. *Br J Surg* 1996; **83**: 1772-1775
 - 35 **Brooks JA**, Kesler KA, Johnson CS, Ciaccia D, Brown JW. Prospective analysis of quality of life after surgical resection for esophageal cancer: preliminary results. *J Surg Oncol* 2002; **81**: 185-194
 - 36 **Blazeby JM**, Farndon JR, Donovan J, Alderson D. A prospective longitudinal study examining the quality of life of patients with esophageal carcinoma. *Cancer* 2000; **88**: 1781-1787
 - 37 **de Boer AG**, van Lanschot JJ, van Sandick JW, Hulscher JB, Stalmeier PF, de Haes JC, Tilanus HW, Obertop H, Sprangers MA. Quality of life after transhiatal compared with extended transthoracic resection for adenocarcinoma of the esophagus. *J Clin Oncol* 2004; **22**: 4202-4208
 - 38 **Safieddine N**, Xu W, Quadri SM, Knox JJ, Hornby J, Sulman J, Wong R, Guindi M, Keshavjee S, Darling G. Health-related quality of life in esophageal cancer: effect of neoadjuvant chemoradiotherapy followed by surgical intervention. *J Thorac Cardiovasc Surg* 2009; **137**: 36-42
 - 39 **Domschke W**, Foerster EC, Matek W, Rödl W. Self-expanding mesh stent for esophageal cancer stenosis. *Endoscopy* 1990; **22**: 134-136
 - 40 **Kozarek RA**, Ball TJ, Patterson DJ. Metallic self-expanding stent application in the upper gastrointestinal tract: caveats and concerns. *Gastrointest Endosc* 1992; **38**: 1-6
 - 41 **Kozarek RA**. Intestinal tract stenting. In: Classen M, Tytgat GNJ, Lightdale CJ, editors. Gastroenterological endoscopy. Stuttgart: Thieme, 2002: 372-386
 - 42 **Mohan V**, Kozarek RA. Placement of conventional and expandable stents for malignant esophageal stenoses. *Tech Gastrointest Endosc* 2001; **3**: 166-175
 - 43 **Cowling MG**, Hale H, Grundy A. Management of malignant oesophageal obstruction with self-expanding metallic stents. *Br J Surg* 1998; **85**: 264-266
 - 44 **Warren WH**. Palliation of dysphagia. *Chest Surg Clin N Am* 2000; **10**: 605-623, x-xi
 - 45 **Loizou LA**, Grigg D, Atkinson M, Robertson C, Bown SG. A prospective comparison of laser therapy and intubation in endoscopic palliation for malignant dysphagia. *Gastroenterology* 1991; **100**: 1303-1310
 - 46 **Rozanes I**, Poyanli A, Acunaş B. Palliative treatment of inoperable malignant esophageal strictures with metal stents: one center's experience with four different stents. *Eur J Radiol* 2002; **43**: 196-203
 - 47 **McGrath JP**, Browne M, Riordan C, Ravi N, Reynolds JV. Expandable metal stents in the palliation of malignant dysphagia and oesophageal-respiratory fistulae. *Ir Med J* 2001; **94**: 270-272
 - 48 **O'Donnell CA**, Fullarton GM, Watt E, Lennon K, Murray GD, Moss JG. Randomized clinical trial comparing self-expanding metallic stents with plastic endoprotheses in the palliation of oesophageal cancer. *Br J Surg* 2002; **89**: 985-992
 - 49 **Shenfine J**, McNamee P, Steen N, Bond J, Griffin SM. A pragmatic randomised controlled trial of the cost-effectiveness of palliative therapies for patients with inoperable oesophageal cancer. *Health Technol Assess* 2005; **9**: iii, 1-iii121
 - 50 **Bergquist H**, Wenger U, Johnsson E, Nyman J, Ejnell H, Hammerlid E, Lundell L, Ruth M. Stent insertion or endoluminal brachytherapy as palliation of patients with advanced cancer of the esophagus and gastroesophageal junction. Results of a randomized, controlled clinical trial. *Dis Esophagus* 2005; **18**: 131-139
 - 51 **Homs MY**, Essink-Bot ML, Borsboom GJ, Steyerberg EW, Siersema PD. Quality of life after palliative treatment for oesophageal carcinoma -- a prospective comparison between stent placement and single dose brachytherapy. *Eur J Cancer* 2004; **40**: 1862-1871
 - 52 **Dallal HJ**, Smith GD, Grieve DC, Ghosh S, Penman ID, Palmer KR. A randomized trial of thermal ablative therapy versus expandable metal stents in the palliative treatment of patients with esophageal carcinoma. *Gastrointest Endosc* 2001; **54**: 549-557
 - 53 **Siersema PD**, Hop WC, van Blankenstein M, van Tilburg AJ, Bac DJ, Homs MY, Kuipers EJ. A comparison of 3 types of covered metal stents for the palliation of patients with dysphagia caused by esophagogastric carcinoma: a prospective, randomized study. *Gastrointest Endosc* 2001; **54**: 145-153
 - 54 **Madhusudhan C**, Saluja SS, Pal S, Ahuja V, Saran P, Dash NR, Sahni P, Chattopadhyay TK. Palliative stenting for relief of dysphagia in patients with inoperable esophageal cancer: impact on quality of life. *Dis Esophagus* 2009; **22**: 331-336
 - 55 **Conroy T**, Marchal F, Blazeby JM. Quality of life in patients with oesophageal and gastric cancer: an overview. *Oncology* 2006; **70**: 391-402
 - 56 **Sreedharan A**, Harris K, Crellin A, Forman D, Everett SM. Interventions for dysphagia in oesophageal cancer. *Cochrane Database Syst Rev* 2009; CD005048

S- Editor Sun H L- Editor Logan S E- Editor Zheng XM