REPORT NUMBER 12

MUHC -Technology Assessment Unit

The Use of Self-Expanding Metallic Stents in the Palliation of Dysphagia in Patients with Malignant Esophageal Strictures

A Technology Assessment

by

The Technology Assessment Unit (TAU)

of the McGill University Health Centre

(MUHC)

(FINAL VERSION)

This analysis was prepared for the Technology Assessment Unit (TAU)

of the McGill University Health Centre (MUHC)

by

Vania Costa, MUHC TAU

James Brophy, Department of Medicine of the MUHC

and approved and adopted by the committee of the TAU:

Ms. J. Arnoldo, Dr. J. Barkun, Mr. A. Bonnici, Dr. J. Hanley,

Mr. J. Johnston, Ms. M. Kaplow, Dr. G. Pekeles,

Dr. J. Ritchie, Dr. F. Salevsky, Mr. G. Stoopler

Dr. J. Brophy, Dr. M. McGregor

And consultant members:

Peter Szego, MD, Josée Parent, MD (Gastroenterology Service – MUHC),

John Penrod, PhD (Centre for the Analysis of Cost Effective Care, MUHC)

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e-mail: james.brophy@mcgill.ca
maurice.mcgregor@mcgill.ca

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EXECUTIVE SUMMARY

Esophageal self-expanding metallic stents (SEMS) are used primarily for the palliation of malignant dysphagia and esophagorespiratory fistulas.

Our literature review showed that SEMS immediately relieved dysphagia in approximately 89% of the patients, and the palliation was maintained for a mean of approximately 60 days (mean survival 137 days). Although complications may occur with these devices, the evidence shows a clinically meaningful reduction in the mean dysphagia score corresponding to an improved ability to eat and resulting in an overall benefit in quality of life.

The cost of each esophageal stent placement at the MUHC is CDN$ 2,254.62, with an estimate of 5-6 patients per year. The budgetary impact of this technology is therefore projected to be less than $13,528 per year. Although approximately 30% of the patients require additional procedures due to recurrent dysphagia, these additional costs are independent of the use of the esophageal self-expanding metallic stents.

Despite the variation in the results seen in the published studies, we estimate that the use of SEMS in patients with malignant dysphagia and esophagorespiratory fistulas is relatively safe, improves patients' quality of life, and has a limited budgetary impact to the MUHC.

Based on the above considerations, TAU recommends the use of esophageal self-expanding metallic stents (SEMS) in patients with malignant dysphagia and esophagorespiratory fistulas.

Foreword

On November 14, 2002 the Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC) received a request from Dr. Ewa Sidorowicz, Assistant Director, Professional Services, requesting the TAU to "give its opinion" concerning the use of esophageal stents. The objective of this report is therefore to evaluate the current available literature regarding the esophageal stents and to make recommendations regarding its use.

1. Introduction

In 1999, 1,177 and 263 cases of esophageal cancer were diagnosed in Canada (Canadian Cancer Statistics 2003), and Quebec, respectively (Statistics Canada). Although there have been advances in the diagnosis of esophagogastric cancer, 50% to 60% of the patients present inoperable disease at the time of diagnosis, and for these patients, only palliation is possible (Cwikiel). Only 10% of all cases survive more than 5 years [1].

Dysphagia may not only be caused by esophageal carcinoma, but also result from extrinsic compression from lung cancer or malignant lymphadenopathy [2]. The treatments used for palliation of dysphagia due to cancer include laser treatment, dilation [3], and most frequently self-expandable metallic stents (SEMS) [2].

The use of esophageal stents aims at relieving dysphagia and preventing malnutrition. The fact that food and liquids can be taken orally instead of intravenously or enterally, may improve the patients' quality of life [4] as well as shorten hospital stays.

An endoscopically inserted plastic prosthesis was introduced in the 70's. Metallic stents have been subsequently developed, and were first used in 1983 [3]. Use of SEMS in the esophagus have been available since 1991[4]and presently are an established treatment modality [5].

The SEMS available may vary with regards to length, outer diameter, presence or absence of cover, type of alloy and mesh architecture [4]. Although complications still occur with SEMS, such as migration, bleeding, perforation, and pain, they have advantages over plastic stents, including a small delivery system and large luminal diameter after deployment, flexible material, less operative sedation required, less frequent need for pre-placement dilation, and ease of insertion[6].

2. Technical Aspects

The different designs of SEMS vary regarding length, diameter, and presence of covering. Some of the stents are more suitable for specific tumour locations in the esophagus, or presence of fistula. Appendix 1 summarizes the characteristics of the stents currently available on the market. The most commonly used stents are the Wallstent®, the Ultraflex®, and the Z-stent®[7].Expandable metallic stents are permanent and irretrievable [8], unless stent migration occurs.

2.1 Indications of SEMS

The main indication for esophageal stents is the palliation of malignant dysphagia, but it can also be used for patients presenting with malignant tracheoesophageal fistulas, patients with dysphagia due to external compression of the esophageal lumen from a tumour, and gastric tumour encroachment on the gastroesophageal junction [4 9,10 11].

2.2 Contraindications of SEMS

Contraindications to the use of SEMS, according to the manufacturers' product label are, total esophageal obstruction, strictures that cannot be dilated to a minimum of 10mm, placement requiring positioning of the stent within 2 cm of the cricopharynx, surgical resection candidates, patients with perforated esophagus, placement of stents in actively bleeding tumours, benign disease, and polypoid lesions. The use of an uncovered stent is contraindicated for occlusion of any type of fistula [10].

Relative contraindications include, but are not limited to an uncooperative patient, coagulopathy, tracheal compression, recent myocardial infarction, cervical arthritis with fixed

cervical spine, large tumour mass occupying the mediastinum, non-obstructing tumour, gastric outlet obstruction, necrotic esophageal mucosa, and acutely angled stenosis. Caution is required in patients with strictures exceeding 12 cm [10].

The use of SEMS in patients with benign disease, such as inflammatory tracheoesophageal fistulas and diverticula, peptic or sclerotherapy strictures, is contraindicated due to the possibility of post-procedure complications including death [8]. Studies in animals showed that the tissue reaction to SEMS includes inflammation, necrosis, erosion, and ulceration, resulting in fibrosis of variable depths, which can lead to potentially fatal complications of perforation and hemorrhage [8]. These complications may be more acceptable in patients with malignant strictures for which only palliative treatment is possible and whose life expectancy is short.

The insertion technique appeared to be similar among the studies published. Acunas et al. has published a study in 2002 in which they describe the insertion technique [12]. After SEMS insertion, the patients should be instructed to start with a liquid diet, progressing to a normal diet, but avoiding large pieces of food (Acunas). The patients should also be instructed to chew thoroughly, and to drink carbonated drinks after the meals in order to clear any pieces of food that may have been retained in the stent (Acunas). Patients with stents that cross the gastroesophageal junction should be given histamine 2 receptor blockers prophylactically in order to prevent reflux esophagitis (Acunas). Meals should be avoided 2 hours before going to bed, and patients should be advised to sleep with at least two pillows[12].

2.3 SEMS selection

The selection of the stent depends on the characteristics of the tumour, such as its length, bulk, and location, and the tortuosity of the stricture [4]. The stent must be long enough to cover the stricture, and consideration must be given to a possible shortening of the stent after deployment. Using a stent that is 4 to 6 cm longer than the length of the stricture may minimize the occurrence of tumour growth around the ends of the stent[4].

The luminal diameter of the obstructing tumour must allow the passage of the stent-introducer catheter, otherwise it must be pre-dilated to at least 6mm. The small applicator size

of the self-expanding metal stents requires less aggressive dilation of the tumour when compared to the rigid plastic prostheses, which have a fixed outer diameter. Larger endoluminal tumours require smaller diameter stents [4].

If the stricture is located at the lower third of the esophagus or at the cardia, esophageal reflux is likely to occur, which may lead to aspiration [3]. Stents with an anti-reflux valve such as the Dua Z-stent® may be more suitable in these cases [3]. The more flexible stents such as the Ultraflex stent, allow curved luminal patency with less local trauma [4].

3. Other Treatment Modalities

Other modalities of therapies include endoluminal laser treatment (Nd:YAG), dilation, photodynamic therapy (PDT), argon beam or bipolar electrocoagulation therapy, absolute ethanol for tumour necrosis, intracavitary brachytherapy, and external beam radiotherapy [3].

Laser therapy has been used for several years as a palliative treatment for esophageal cancer, and it has shown an improvement in dysphagia in approximately 88% of the cases [13], however, it has to be repeated every 4-6 weeks [12]. Prior dilation is required in approximately 30% of the patients who undergo laser treatment, and is associated with a 6-8% risk of perforation [5].

Radiation therapy is successful in palliating dysphagia in approximately 40% of the cases, but may take two months before the results are seen [12].

Plastic prostheses are inexpensive, however, perforation may occur in 7-8% of the patients, and stent migration, tumour overgrowth, and bleeding may also occur [12]. They have now been replaced as randomized studies have shown that metallic stents achieve better palliation, with fewer complications[14].

4. Literature review methodology

The databases used for the literature review were Medline, Pubmed, and Technology Assessment Agencies websites, including the International Association for Health Technology

Assessment (INAHTA). This report contains information mainly from studies published after 1995, as this coincides with the start of use of the presently available SEMS, however, the studies published before 1995 were also reviewed and were included in the report if relevant information was found. The literature review focused on studies that used SEMS that are currently marketed in Canada. According to the distributors, none of the stents not presently marketed in Canada are expected to be available in the near future.

5. Cost Analysis Methodology

Information concerning cost generating procedures was supplied by the departments in which the procedures were performed. The costs included nurses, technicians, and office personnel time, materials, and medications needed during the procedures. Hospital overhead costs are not included.

A weighted average of the rates of re-interventions reported in the studies was used as a reference in our report.

Foreign currencies in published studies were converted according to the exchange rate of the Bank of Canada (May 2003).

6. Literature Review

The studies used in this review included patients with inoperable malignant dysphagia due to primary esophageal carcinomas, secondary lung or gastric cancers, or lymphomas [15] [16] [1,17] [18] [19] [20] [5] [21] [22] [23] [24] [25] [26], although some studies also included patients with fistulas [6] [27] [28] [29]. The studies included a mix of patients with tumours located in the proximal, middle and distal portion of the esophagus, and the cardia. Covered and uncovered stents, as well as different stent designs, mainly the Wallstent I®, Wallstent II®, the Strecker® stent, which was replaced by the Ultraflex® stent, and the Z-stent® with or without anti-reflux mechanism were used in the published studies. In general, the study results could not be stratified according to stent type, with some exceptions. Studies specifically focusing on the distal portion of the esophagus and the cardia, the cervical esophagus, or esophagorespiratory fistulas are discussed separately. The mix of patients and stents varied between the studies, which may be partially responsible

for differences in the results seen among the studies. As these differences may also be due to the sample sizes, the rates of outcomes and events are presented as a weighted average of all study results. In cases where stent characteristics or tumour location were considered to be mostly responsible for the complications or differences in efficacy, an attempt was made to describe their rates separately by type of stent or tumour location, where the literature permitted.

6.1 Clinical outcomes with SEMS

Advantages of SEMS include ease of insertion, avoidance of general anesthetic, shorter hospital stay compared to plastic prostheses, narrower delivery system, and the ability to continue other forms of treatment concomitantly [28]. SEMS can also be inserted on an outpatient basis [30]. When the insertion device is removed, the stent expands to a larger diameter [7].

Dysphagia was evaluated on a 5 grade scale in most studies, as follows: 0-ability to eat a normal diet, 1-some solid food, 2-some semisolids only, 3-liquids only, 4-inability to tolerate any solid intake [18 18,27 22 26 25 31], although other studies used a slightly different scale [1 16 6 20 21]. A varying number of cases, i.e., 4% to 100%, required dilation before or immediately after stent placement [21 22 18 6 19 16]. Technical success occurred at a mean rate of 96% [26 19 1,27 6 18 29 22].

Immediate improvement of dysphagia after stent placement occurred, on average, in 89% of the patients [19 16 20,21 28 29 1,5]. The dysphagia score was reduced by 0.9 - 2.5 grades after stent implantation [1 6 16 19,27 20 21 22 23 25 26 27 29 18]. The average dysphagia score before stent implantation was approximately 3 (ability to ingest liquids only), and it decreased to a mean of approximately 1 (ability to ingest some solid food) after stent implantation [1, 6, 18, 27, 16,20 29, 26, 25, 31, 21, 22].

Despite dysphagia recurring, on average, in 34% of the patients [29 31 18,27 5,16,19,23,25], palliation lasted for a mean of approximately 60 days [16 26 31], and quality of life improved in 81% of the patients after stent placement [6].

Mean survival ranged from 49 days to 207 days [27 31 26 21 23 18 5 1 20]. At the time of death, 42% of the patients in a study by Cwikiel et al. had no dysphagia, and 81% had no or mild dysphagia [1]. On the other hand, others have observed a progressive worsening of dysphagia in 68% of long-term survivors after a median of 74 days (range 1-474 days) [20].

Appendix 2 has more detailed information on the clinical outcomes of SEMS in malignant dysphagia.

6.2 Complications with SEMS

Immediate complications associated with SEMS placement included problems with stent deployment or expansion, stent misplacement, perforation, and chest pain. Late complications included migration, occlusion of the stent due to tumour ingrowth or overgrowth, or food impaction [32]. Bleeding may occur either as an immediate or as a late complication [32]. Potentially life-threatening complications may include immediate respiratory compromise, aspiration, fistula formation, sepsis, and procedure-related death [32]. Some authors [4 30], but not all [6 18], have observed a higher rate of complications if the stent was placed after chemotherapy or radiotherapy.

Mortality as a consequence of the stent implantation occurred, on average, in 3% of the patients [6,16,18,20,25,27,29 15]. Tumour ingrowth or overgrowth occurred in 5.9% - 32% [6,15 18,28 1,21,22,27] of the patients, and tumour ingrowth appears to be more intensive with uncovered stents. Pain following stent insertion is common, but it normally resolves after a few days[14]. On the other hand, persistent severe pain occurs in a small number of patients, and it appears to be related to the more rigid stents, such as the Z-stent®, and the Wallstent®, than with the Ultraflex® stent[14]. Foreign-body sensation occurs more frequently when a stent is placed in the cervical esophagus, however, it may occur more frequently if larger diameter stents are used [33].

Stent migration occurred in 0 - 17% of the patients [27 18 6 1 28,29 16 21 22 23 15]. This rate may be higher if only covered stents are used or if they're placed across the cardia [3].

Perforation has occurred at a mean rate of 2.4% [1 6 27 18 16 29].

Appendix 3 details the specific complications and their rates. No significant differences in complication rates could be seen between the different stent models [16 19].

6.3 Treatments for complications

Tumour ingrowth or overgrowth may be treated with endoscopic laser therapy and/or additional stents [12], or balloon dilation [34]. Food impaction can be treated endoscopically, and fistulas can be treated with a covered stent [1], or with tissue glue [15]. If a stent migrates, it is replaced by another stent, and attempts are made to remove the stent that migrated [16]. Chest pain is treated with analgesics, including opioids in some cases [27]. Gastroesophageal reflux is treated with proton pump inhibitors and or a gastric motility enhancing agent [15]. Blood transfusion or radiotherapy may be used for bleeding [6].

6.4 Re-interventions

O'Sullivan et al. [28], in a study with 121 patients with malignant esophageal stricture reported that most patients were discharged on the same day of the procedure, when topical pharyngeal anesthesia with mild intravenous sedation was used.

An average of 28.5% of the patients required re-interventions in the studies published [1,6,16 18,19,29 35 17,25 15,21,36]. The types of re-interventions were: closure of fistula, 5% [20], hemostasis, 8% [20], endoscopic food disimpaction, 3.2% [1,17 18,19,29,36 37], laser therapy, 13.5% [1,25 6,19,26,35,36,38]. Additional stent implantation was required at a mean rate of 13.2% [1 1,18,18,25,25 6 19 35 26,36 38 29 21]. Gastrostomy was required at an average rate of 3.6% [16,21], dilation was required at an average rate of 25% [19 26 21 38], sclerotherapy was required in 17% of the patients [19], and surgical retrieval of a stent was reported in 5% of the patients in one study [25]. Non-opioid and opioid analgesics were used to treat chest pain in 19% and 9% of the patients in one study respectively [16].

Appendix 4 has more detailed information on the rates of complications reported in the studies found in the literature.

6.5 Malignant strictures at the gastroesophageal junction

The use of SEMS in patients with unresectable malignant strictures located in the lower esophagus or gastroesophageal junction may not always improve the patients quality of life. While providing relief for dysphagia, it may, on the other hand, cause gastroesophageal reflux and aspiration pneumonia [39]. Gastroesophageal reflux may be caused by the fact that the use of a stent in the cardia requires the distal end to be in the stomach[40]. As a consequence, treatment with proton pump inhibitors, and in some cases, with properistaltic agents is required, which not only adds to the cost of treatment, but also obliges a patient with dysphagia to take further regular medication [40]. For this reason, the use of a stent with an anti-reflux mechanism is recommended for tumours in this area [40]. Another problem caused by the use of a stent in the cardia is that there is a higher propensity for migration, i.e., 1.4 times the rate of migration of stents placed in the mid- and upper esophagus [40]. Elevation of the head of the bed may decrease reflux in patients with stents placed across the gastroesophageal junction [16].

The Dua Z-stent with an anti-reflux valve has a design that allows the valve to invert into the stent at high pressure gradients such as coughing, sneezing and vomiting in order to allow the patients to belch or vomit, as a consequence however, the patients may experience daytime reflux symptoms [41].

A summary of the results of studies that evaluated the use of SEMS in patients with inoperable esophageal carcinoma is shown below and in Appendix 5.

Patients who used stents with an anti-reflux mechanism, such as the Ultraflex stent with anti-reflux mechanism, or the Dua Z-stent with anti-reflux mechanism, had a lower mean rate of esophageal reflux than patients who used stents without the anti-reflux mechanism, i.e., 8.3% and 31% respectively [39,40]. One study reported one death (14%) due to aspiration pneumonia, in a patient who used a stent without the anti-reflux mechanism [39]. The rate of re-interventions was compared between stents with and without an anti-reflux mechanism, i.e., 32% versus 16% respectively, although the difference was not statistically significant [40]. However, as the sample used in these studies was small, varying from 7 to 25 patients (Osugi,

Dua, Laasch), the possibility that these results were due to chance cannot be ruled out, and therefore, these results should be interpreted with caution.

6.6 Use of SEMS in the upper esophagus

Seven to ten percent of the esophageal tumours occur in the cervical segment, where the spread of the disease occurs more rapidly [42 43]. Endoscopists may avoid using plastic prostheses in this area due to possible foreign-body sensation and airway compression, and there is a concern that SEMS would cause the same problems [42]. Foreign-body sensation is a result of the proximity to the cricopharyngeal muscle [43]. Other expected complications of the use of stents in the cervical esophagus are proximal migration, intractable pain [33], perforation, and pulmonary aspiration[44]. All treatments in the upper esophagus are difficult due to the anatomy of the region, for instance. For example, laser therapy can be risky and does not result in satisfactory results, and radiotherapy may cause tight stenoses that are difficult to treat[43].

According to the stents label [9 10 11], the use of stents within 2 cm of the cricopharyngeus is contra-indicated, although some authors [42,43 33] have used SEMS within 2-3 cm of the cricopharyingeus with 50% to 100% [42 43 33] success rates. Immediate improvement of dysphagia occurred in 87% to 100% of the patients, and mean decrease in dysphagia score ranged between 1.0 to 2.5 grades, but complication rates were increased when stents were used in this region of the esophagus [42 43 33].

The Ultraflex stent has a lower radial force [42] and is more flexible than the other stents [43], it may therefore be more suitable for use in this region of the esophagus.

Pain requiring opiates occurred at a mean rate of 4.7% of the patients, and pain not requiring opiates occurred at a mean rate of 7% of the patients [42 43 33]. Mortality related to the stent or insertion procedure was only reported in one of the studies, and the rate was 15% [42]. Stent migration was reported in one of the studies at a rate of 13% [33]. Aspiration pneumonia occurred at an average rate of 35% [42 43].

In general, the authors of these studies[42 43 33] considered that overall results were favourable. Conio et al. pointed out that upward growth of the tumour cannot be controlled by the stent, and that recurrent dysphagia still occurs in long-term survivors, and these patients will therefore need other modalities of treatment in order to control the local growth of the tumour such as photodynamic therapy, re-stenting, and/or brachytherapy, and ultimately, gastrostomy[43]. The characteristics of the stents to be placed in the upper esophageal region should be considered, for instance, the diameter of the stents used in the studies[42 43 33]was up to 18mm, and as Bethge pointed out, larger diameters stents should be avoided as they may cause problems[33].

Two cases of airway complications have been reported with the Wallstent®, as the proximal flange of 28 mm compressed the respiratory tract[14], however, it was not possible to assess if the patients were using the new generation of the stent, or if this type of complication would occur with another stent design.

The results of these studies must be interpreted with caution due to their extremely small sample sizes, i.e., 6[43], 8[33], and 22[42].

6.7 Use of SEMS in esophagorespiratory fistulas

Fistulas are often difficult to treat and may decrease not only the patients life expectancy, but also their quality of life[45], due, in part, to aspiration pneumonia and malnutrition [46]. Esophagorespiratory fistulas occur in approximately 5-15% of the patients with esophageal cancer or other mediastinal malignancies[46].

Studies in the literature using SEMS to seal esophagorespiratory fistulas have shown technical success in all cases, with a mean rate of fistula sealing of 85% [45 46 47]. The mean reduction in dysphagia was 2 grades [45 46 47]. One study reported that 91% of the patients did not present with any recurrent symptoms until completion of follow-up [45], however, recurrent dysphagia occurred in 3 out 6 (50%) patients in a study by Tomaselli et al. [46].

Dumonceau et al. [47] reported a 12% rate of procedure-related death. Tumour ingrowth or overgrowth occurred at a mean rate of 9% [45 46 47]. Retroesternal pain occurred at a mean rate of 64% [45 46], and severe pain was reported in one patient (17%) in a study by Tomaselli et al. [46]. Fistula enlargement and relapse occurred in 6% and 30% of the patients studied by Dumonceau et al. [47] respectively.

Another study reported a rate of overall complications of 37.9%, with life-threatening complications occurring in 7.9%, but no procedure-related death [14].

The mean cost per patient of esophagorespiratory fistula sealing, assessed in 14 patients that used the Ultraflex stent or the Wallstent in Belgium was CDN$ 11,043, including the initial procedure, re-hospitalizations and other procedures [47].

The results presented above should be interpreted very cautiously, as few studies with the currently available SEMS were found in the literature, and the three studies together [45 46 47] added up to only 34 patients.

6.8 SEMS versus Laser Therapy

Laser treatment has been reported to relieve dysphagia with a low rate of complications compared to SEMS or plastic prostheses, however, it has to be repeated at regular intervals, normally every 4-5 weeks [25]. It also requires esophageal dilation in 30% of the cases, which has been associated with perforation in 6%-9% of the cases [5]. According to Gevers et al. [26], laser therapy does not seal fistulas, but it should be the therapy of choice especially for tumours of the lower third of the esophagus, and in patients with a short life expectancy. Mason et al. [48] mentioned that laser therapy is best suited for small polypoid intraluminal tumours and intubation for mural and extramural disease.

The results of the studies found in the literature are in Appendix 7. No significant differences between SEMS and laser therapy were noted in success or complication rates in two randomized trials [25 31], however, the sample sizes were too small for conclusive results to be inferred.

In a non-randomized study [26], major complication rates were higher with SEMS than laser therapy, but the small sample size and lack of randomization limits the strength of any conclusion based on this study.

The mean rate of perforation was 4.7% with SEMS, and 1.1% with laser therapy [26 25 31].

6.9 Economic Studies

A randomized study by Konigsrainer et al. [31] compared the costs of SEMS used alone (n=10), or combined with laser treatment (n=8), and laser treatment plus radiotherapy (n=21) in Austria. The costs including initial and subsequent hospitalizations, endoscopic treatment and radiotherapy, were CDN$ 6,587, CDN$ 15,859, and CDN$ 30,391and the mean total number of days in hospital were 7.1 (3.1), 18.9 (4.2), and 30 (5.4) for SEMS alone, laser plus SEMS, and laser plus radiotherapy respectively [31]. In the SEMS groups (with or without laser), no complications such as fistula, bleeding, and mortality were reported, which is lower than what was reported by other published studies.

A randomized study by Dallal et al. [49] in Scotland, compared the costs of treatment with SEMS and laser therapy in 65 patients with inoperable esophageal and esophagogastric cancer. The mean cost of each individual treatment was CDN$2,500 for the SEMS group, and CDN$4,615 for the laser group, and the mean total cost of treatment, from the initial procedure until death was CDN$ 7,677 and CDN$ 14,170 in the SEMS and laser groups respectively [49]. According to the authors, the higher cost of laser therapy is due to the longer length of stay in this group, i.e, 23 days compared to 12 days with SEMS [49]. The mean number of admissions was also higher with the laser group, 4 compared to 2 with SEMS, as was the cost of each hospital stay, i.e., CDN$ 9,550 versus CDN$ 5,177 in the laser and SEMS groups respectively [49]. The median survival was statistically significantly higher in the laser group, 125 days, compared to 68 days in the stent group [49]. However, although randomized, the number in each group was small and the two groups might have been different. The survival was almost twice as long in the laser treatment group and it was not possible to evaluate if the longer survival was responsible, at least partially, for the higher cost in the laser group. Consequently, if both

groups had had a similar survival time, the difference in cost between them may not have been significant, but the authors did not discuss these issues.

A non-randomized study by Sihvo et al. [37] compared the cost of palliative treatment between SEMS and laser therapy in Finland, in 52 patients with esophageal or esophagogastric adenocarcinomas. The overall cost of treatment, from the initial procedure until death, was similar between the two groups, CDN$ 8,882 and CDN$ 8,735 for the laser and SEMS groups respectively, however, the cost per day survived was CDN$ 139 and CDN$ 285 respectively[37]. The number of interventions was higher in the laser group, 3.4 (1-23), than in the stent group, 1.9 (1-7, p=0.0048) [37]. The higher morbidity and mortality seen in the stent group could be due to clinical baseline differences, for instance, the stent group had a higher mean tumour length, 7.9 cm, compared to 6.4 cm in the laser group, and 65% of the patients in the stent group had advanced disease compared to 47% in the laser group, however, the authors considered the two groups similar as the differences in baseline characteristics were not statistically significant[37]. The study was retrospective, and included patients seen over a 9-year period, and it seems that laser therapy was predominantly used earlier, with SEMS being introduced in the later years. This may also partially account for differences between the groups.

Based on the evidence from the literature, it seems that laser treatment may have a higher cost than SEMS, although both treatments apparently have similar success rates, however, as the sample sizes of the studies were small, and as it cannot be assessed if the population in the two groups were similar, it is not possible to infer any conclusive results from the information available.

7. Costs of SEMS implantation for the MUHC

Considering that 6 patients will require SEMS implantation per year, and considering the average number of re-insertions at the initial procedure in the literature, 1.06, the direct cost for the MUHC of the initial SEMS implantation, is as follows:

Table 1 – Estimated direct costs of procedures involved in the insertion of esophageal stents in the MUHC

Procedure	Unit cost (CDN$)	Number of procedures	Total Cost
Barium swallow (pre- and post-stenting)	39.5	12.8	505.6
Upper endoscopy	103.09	6.4	659.8
Stent insertion (including stent acquisistion)	1931.62	6.4	12,362.37
Total Cost			**13,527.74 (2,254.62/patient)**

According to the literature, approximately 28.5% of the patients need an additional procedure in order to relieve recurrent dysphagia, however, due to the patients short survival, i.e., mean of 137 days according to the literature, we are assuming that the additional costs incurred as a consequence of additional procedures are independent of the original stent insertion.

Cost components and sources

Barium swallow: 2 technicians – 20 minutes, $22. Office staff –20 minutes, $10. Barium and other materials: $7.50. **Estimated cost: $39.50 /**

Source: Radiology Department, Mrs. Patricia Smith

Upper endoscopy: **Estimated cost: 103.09**

Source: Published study in 2002 by Crott et al., that evaluated the cost of upper endoscopy at the Montreal General Hospital[50]

Esophageal stent insertion: 1 nurse and 2 technicians – 60min, $104. Office staff – 20 min., $10. Stent acquisition cost, $1,500. Guidewire acquisition cost, $250. Medication, $23.62. 1 hour in recovery room – 1 nurse – 60min, $44. **Estimated cost: $1,931.62**

Source: Radiology Department, Mrs. Patricia Smith

According to Dr. Peter Szego, esophageal stent insertion is normally performed as an outpatient procedure in the MUHC, not requiring hospitalization, therefore, hospitalization related costs were not included.

8. Conclusions

SEMS are used for the palliation of inoperable malignant esophageal or esophagogastric strictures, and esophagorespiratory fistulas.

Although complications are reported at a mean rate of 20%, with reinterventions required in approximately 28.5% of the cases in the studies published, dysphagia was reduced on an average of 89% of the patients studied. Mean dysphagia score decreased from 3.1 (ability to ingest only liquids) to 1.1 (ability to ingest some semi-solids). The palliation lasted for approximately 60 days, whereas the mean survival time was approximately 137 days in the literature.

In two randomized studies, no significant differences in success or complication rates were observed between SEMS and laser therapy. However, laser therapy has to be repeated every 4-5 weeks, which may result in longer hospital stays and higher costs, according to these studies.. According to information given by Dr. Peter Szego, laser treatment is normally performed as an outpatient procedure in the MUHC. Other alternative therapies such as plastic prostheses, have not been used in the past 5 years and can be very unpleasant to the patient. Gastrostomy is also very uncomfortable to the patient. Photodynamic therapy has been approved for use in the MUHC, but only in cases in which SEMS cannot be used. Moreover, in patients with fistulas, SEMS is the only alternative available.

The estimated cost per stent insertion is CDN$ 2,254.62. Approximately 5-6 patients are expected to use SEMS each year at the MUHC, therefore the total yearly cost to the MUHC is estimated to be CDN$ 13,527.74.

A wide variation was seen in the results of the published studies. This variation can be at least partially explained by different study designs, as well as small sample sizes. Besides,

SEMS have been constantly modified with the intent to minimize associated complications, and the fact that different studies used different generations or different types SEMS, in addition to different mix of tumour location or other prognostic factors may have also have contributed to differences in the study results. According to Raijman et al. [6], the efficacy and the occurrence of complications can also be related to the insertion technique used, and the experience of the operator. As a consequence, the rates of events presented in this report may differ from the ones that will be seen in the patient population of the MUHC. However, as a newer generation of SEMS will be used, improvements in the outcomes or lower rates of complications may also be seen.

Despite the variation in the results observed in the literature, it appears that the use of SEMS for the palliative treatment of malignant dysphagias and esophagorespiratory fistulas represents an improvement for the patients status and quality of life, with an additional cost of only CDN$ 13,246.10 to the MUHC (based on 6 treated patients / year).

9. Recommendation

Based on the above considerations, TAU recommends the use of esophageal self-expanding metallic stents in patients with malignant dysphagia and esophagorespiratory fistulas.

APPENDIX 1 – CHARACTERISTICS OF SEMS

Table 1 – Types and Characteristics of Metallic Esophageal Stents Approved in Canada

Stent	Material	Cover	Shortening after insertion	Length (cm)	Size of delivery catheter (Fr)	Outer diameter (mm)	Cost
Ultraflex*	Nitinol	Covered or uncovered	No	7, 10, 12, 15	15	18-23	CDN$ 1,800 - 2,000
Wallstent II**	Stainless steel	Covered	Yes	10, 15	18	20-28	CDN$ 2,000
Z-stent	Stainless steel	Covered or Uncovered	No	8, 10, 12, 14	31	18-25	CDN$ 1,500 – 1,700
Dua Z-stent (with anti-reflux valve)	Stainless steel	Yes	Not reported	8, 10, 12, 14	31	18-25	CDN$ 2,000 – 2,500

Source: Boston Scientific, Wilson Cook, Medtronics website and product labeling.

Cost information was given by representatives from these Companies

* Previously called the Strecker stent.

**The Wallstent II is a modification of the Wallstent I, which had a dog-bone form and was placed with a 38-Fr delivery system. The Wallstent II has a more gradual flare at its ends and requires a 18-Fr delivery system, it is covered, it is not covered at each end in order to allow for tissue ingrowth and anchoring of the stent (Mauro).

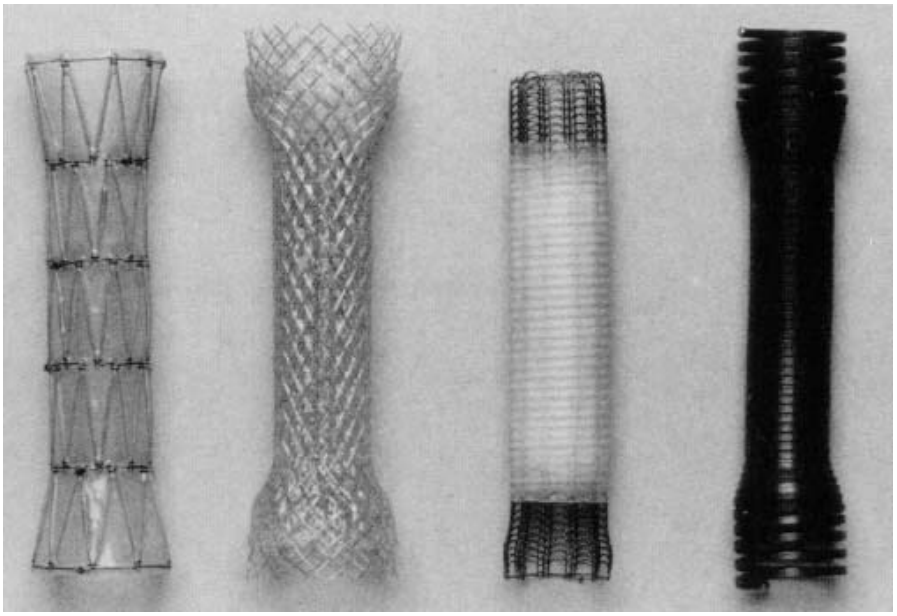
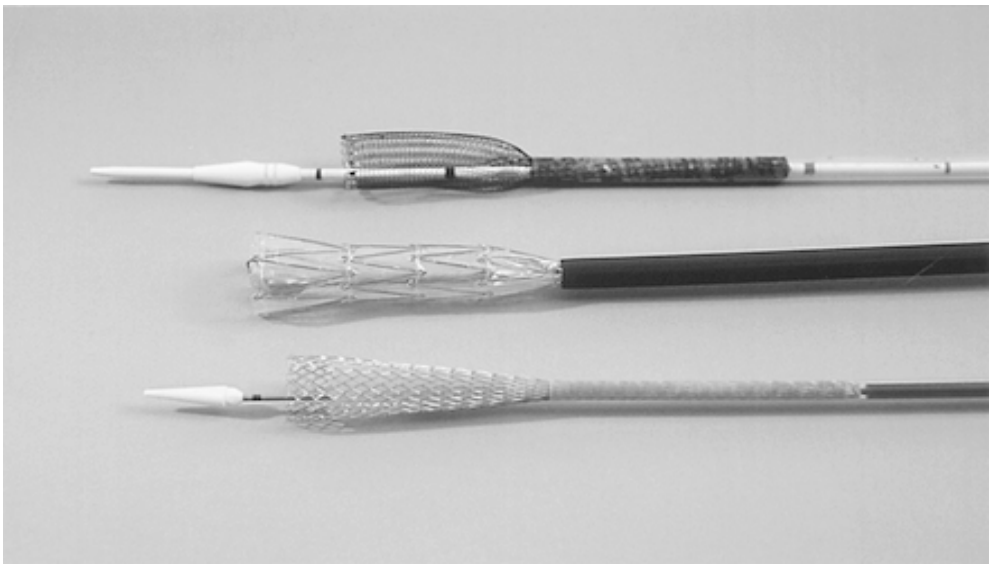


FIGURE 1 • SEMS (left to right): Z-stent, Wallstent I, Ultraflex, and Esophacoil.
From: **Raltz: Gastroenterol Nurs, Volume 22(6).November/December 1999.249-253**



Stent deployment systems. Top: *Ultraflex* knitted nitinol stent delivered with a 20F outer-diameter delivery system. Middle: *Z-stent* delivered with a 28F outer-diameter delivery system. Bottom: Covered *Wallstent Esophageal II* delivered with an 18F outer-diameter delivery system From Mauro MA, Koehler RE, Baron TH. Radiology. 2000;215:659-669.

Other types of stents such as the Flamingo Wallstent®, and the Ultraflex® stent with an anti-reflux mechanism have been developed and studied, however, they will not be marketed due to problems with their design, according to information from Boston Scientific (Francine Paradis).

The Polyflex® esophageal stent will not be marketed in Canada due to licensing issues between companies, according to a representative from Rush Canada. Other stents seen in the literature such as the Memotherm® esophageal stent is currently not marketed in Canada, and there is no estimate of when or if it will be marketed, according to information from Guy Ringuette, from Bard Canada.

APPENDIX 2 – Clinical Outcomes with SEMS in Malignant Dysphagia and Esophagorespiratory Fistulas

Use of SEMS in Malignant Dysphagia (all esophageal locations)

Studies Type of study	Cwikiel [1] N=100 Prospective non-randomized	Raijman[6] N=101 Retrospect.	Siersema[18] N=100 Prospect / non-randomized	Siersema[27] N=57 Prospect. Non-randomized	Christie[16] N=100 Retrospect	Dorta[19] N=82 Retrospet.	Ludwig[20] N=40 Prospective, non-randomize	Rozanes[5] N=116 Retrospective	McGrath[29] N=200 Non-comparative
Period of Observation	1998 (P)*	94 – 96	98 – 99	95 – 99	95 – 99	92 – 95	92 – 95	93 – 2002	96 – 2000
Types of Stents	Strecker/Ultraflex	Wallstent I	Flamingo Ultraflex Z-stent	Flamingo Ultraflex Z-stent	Ultraflex Wallstent	Ultraflex Wallstent	Ultraflex Wallstent	Flamingo Ultraflex Wallstent	Ultraflex
Technical Success	97%	100%	95%	86%	100%	85%		94%	100%
Need for dilation	7.5% - complete 92.5 – partial	-	7%	-	77%	53%			
Mean reduction in dysphagia	1.8	2.2	2.5**	2.0**	Measured in a different scale	1.8**	1.5	-	1.7**
% immediate improvement of dysphagia	97%	-	-	-	85%	75%	90%	98%	93%
Pre-stent dysphagia	-	3.6	3.2**	3.6**	Measured in a different scale	-	2.0	-	3.2**
Post-stent dysphagia	-	1.4	0.7**	1.6**	Measured in a different scale	-	0.5	-	1.5**
Duration of palliation (days)	42% had no dysph at death	-	-	-	Time to reintervention: 82 days	-	-	-	-
% recurrent dysphagia	58%	-	28%	34%	51%	46%	Long-term survivors: 68%	51%	10%
Mean survival (days)	186	-	107 (median)	61 (median)	-	84 (median)	141 (median)	121	-

*The period of observation was not available, therefore, the publication year was provided instead.

**Only the studies that used a similar dysphagia scoring scale were used for the weighted average calculation.

Cont. APPENDIX 2 - Use of SEMS in Malignant Dyspahgia (all esophageal locations)

Studies **Type of study**	**Raltz[21]** **N=75** **Prospective** **Non-randomized**	**De Palma[22]** **N=92** **Retrospective**	**Decker[23]** **N=37** **Retrospective**	**Gevers[26]** **N=26** **Prospective** **Non-randomized**	**Adam[25]** **N=42** **Randomized**	**Konigsrainer[31]** **N=10** **Randomized**	**Weighted Average**
Period of Observation	87 - 97	92 – 97	92-97	92 - 96	94 - 95	92 – 94	**-**
Types of Stents	Z-stent Wallstent Ultraflex Esophacoil	Ultra unc Ultra cov Esophacoil	-	-	Strecker Wallstent	Wallstent	**-**
Technical Success	-	96.7%	-	81%	100%	-	**96%**
Need for dilation	4%	40%			100%		**53%**
Mean reduction in dysphagia	2.0	2.5**	2.0**	0.9**	2.0**	2.0**	**1.9****
% immediate improvement of dysphagia	77%	-	-	81%	-	-	**89%**
Pre-stent dysphagia	2.9	3.0**	-	2.5**	3.0**	2.5**	**3.1****
Post-stent dysphagia	0.85	0.5**	-	1.6**	1.0**	0.4**	**1.1****
Duration of palliation	-	-	-	66	-	60	**64 (using Gevers et al. & Konigsrainer et al.)**
% recurrent dysphagia			25.9%	-	16%	5.5%	**33.6%**
Mean survival (days)	84	207	134	49	54 (median)	205	**137 (not using median values)**

*The period of observation was not available, therefore, the publication year was provided instead.

**Only the studies that used a similar dysphagia score were used for the weighted average calculation.

APPENDIX 3 – Complications with SEMS

SEMS - Complications (all esophageal locations)

Studies Type of study	Cwikiel[1] N=100 Prospective / non-randomized	Raijman[6] N=101 Retrospective	Siersema[18] N=100 Prospective/ non-randomized	Siersema[27] N=57 Prospective Non-randomized	Christie[16] N=100 Retrospective	Mason[48] N=60 Randomized	Ludwig[20] N=40 Prospective / non-randomized	McGrath[29] N=200 Non-comparative
Period of Obs.	1998 (P)*	94 – 96	98 – 99	95 - 99	95 - 99	1996 (P)*	92 – 95	96 – 00
Types of stents	Strecker/Ultraflex	Wallstent I	Flamingo Ultraflex Z-stent	Flamingo Ultraflex Z-stent	Ultraflex Wallstent	Strecker Wallstent	Ultraflex Wallstent	Ultraflex
Major complications	-	8.9%	26%	23%	-	-	-	-
Minor complications	-	21%	19%	-	-	-	-	-
Death related to procedure	-	0	2%	1.8%	1%	-	0	0
Tumour ingrowth/overgrowth	17%	5.9%	10%	32%	-	-	-	-
Esophageal reflux	-	-	-	-	11%	22%	-	-
Stent Migration	4%	2.9%	13%	1.7%	11%	-	-	7%
Severe pain	-	-	1%	1.7%	1.6%	-	-	-
Chest pain	47%	12.9%	-	-	-	-	20%	-
Perforation	4%	0	6%	3.4%	0.8%	-	-	0
Food impaction	5%	-	5%	1.7%	-	-	-	3.5%
Bleeding	-	6.9%	14%	9%	-	-	8%	2.5%
Aspiration	-	0	-	1.7%	-	-	-	4%
Erosion	-	-	-	-	2.3%	-	-	-
Airway compression	-	-	-	-	0	-	-	-
Sep cover	-	-	-	-	-	-	-	-
Resp insuf	-	-	-	-	-	-	-	-
Foreign body sen	-	-	-	-	-	-	-	-
Space btw stent and wall	-	-	-	-	-	-	-	-

* *The period of observation was not available, therefore, the publication year was provided instead.

Cont. APPENDIX 3- SEMS – Complications (all esophageal locations)

Studies **Type of study**	**Raltz[21]** **N=75** **Prospective** **Non-randomized**	**De Palma[22]** **N=92** **Retrospective**	**Decker[23]** **N=37** **Retrospective**	**Wang[15]** **N=82**	**Adam[25]** **N=42** **Randomized**	**O'Sullivan[28]** **N=121** **Retrospective**	**Acunas[12]** **N=59** **Non-randomized**	**Weighted Average**
Period of Observation	87 – 97	92 –97	92 – 97	93 – 97	94 – 95	92 - 97	93 – 95	**-**
Types of stents	Z-stent Wallstent Ultraflex Esophacoil	Ultraf. Unc Ultraf cov Esophacoil	-	Ultraflex (c/u) Wallstent (c/u) Z-stent	Strecker Wallstent	Ultraflex Wallstent Z-stent	Ultraflex ?	**-**
Major complications	-	-	-	-	-	-	-	**18.6%**
Minor complications	-	-	-	-	-	-	-	**20%**
Death related to procedure		1%	3%	15.9%	7%			**2.6%**
Tumour ingrowth/overgrowth	17%	11%	-	28%	-	11%	36%	**16.7%**
Esophageal reflux	-	3.3%	-	4.9%	-	-	-	**9.4%**
Stent Migration	17%	2%	0	6.1%	-	6%	-	**7.1%**
Severe pain	-	-	-	-	-	1%	-	**1.3%**
Chest pain	-	3.3%	-	6.1% (persistent)	-	-	-	**18.3%**
Perforation	2.6%	-	0	7.3%	-	-	-	**2.4%**
Food impaction	1%	3.3%	-	6.1%	-	2.5%	-	**3.6%**
Bleeding	4%	2%	0	7.3%	-	2.5%	-	**5.3%**
Aspiration	5%	-	-	-	-	-	-	**2.9%**
Erosion	4%	-	-	-	-	-	-	**3%**
Airway compression	1%	-	-	6.1%	-	-	-	**2.2%**
Sep cover	4%	1%	-	-	-	-	-	**2.3%**
Resp insuf	-	1%	-	-	-	-	-	**1%**
Foreign body sen	-	1%	-	-	-	-	-	**1%**
Space btw stent and wall	-	-	-	8.5%	-	-	-	**8.5%**

APPENDIX 4 – Re-interventions with SEMS

Studies **Type of study**	**Cwieckl[1] N=100 Prospective non-randomized**	**Raijman[6] N=101 Retrospective**	**Siersema[18] N=100 Prospective non-randomized**	**Siersema[27] N=57 Prospective Non-randomized**	**Christie[16] N=100 Retrospective**	**Dorta[19] N=82 Retrospetive**	**Ludwig*[20] N=40 Prospective non-randomized**	**McGrath[9] N=200 Non-comparative**	**Adam[25] N=42 Randomized**	**McManus[35] N=165 Prospective**	**Gevers[26] N=26 Prospect. Non-randomzied**	**O'Donnel[34] N=25 Randomized**
Period of Obs.	1998 (P)	94 - 96	98 - 99	95 - 99	95 - 99	92 - 95	92 - 95	96 – 2000	94 - 95	94 - 98	92 - 96	2002 (P)
Types of stent	Strecker/Ultraflex	Wallstent I	Flamingo Ultraflex Z-stent	Flamingo Ultraflex Z-stent	Ultraflex Wallstent	Ultraflex Wallstent	Ultraflex Wallstent	Ultraflex	Strecker Wallstent	Flamingo Ultraflex Wallstent II	NA	Flamingo Ultraflex Wallstent
Hoslp. Stay 1st	-	82% - outpatients	-	-	2.0	-	-	-	2.0	-	-	-
Hosp. stay over.	-	-	-	-	-	-	-	-	-	-	-	7.1
# stents initially	1.09	1.02	-	1.1	1.01	1.04	1.15	1.04	-	-	-	-
# stents overall	1.15	1.09	1.10	-	1.27	1.26	1.25	1.15	1.21	1.16	1.19	1.32
Re-interventions	24%	30%	11.5%	-	51%	46%	-	11%	36%	27%	-	40%
Stents	6%	7% (7st.)	9.6%	-	-	21%	10%	11%	-	13%	19%	-
Laser	16%	2%	-	-	-	22%	60%	-	5%	18%	11.5%	20%
Dilation	-	-	-	-	-	39%	80%	-	-	-	19.2%	-
Endoscopic food dis.	5%	-	4%	-	-	9%	58%	0.15%	-	-	-	0
Sclerotherapy	-	-	-	-	-	17%	-	-	-	-	-	-
Gastrostomy	-	-	-	-	4%	-	18%	-	-	-	-	-
Blood transfusion	3%	-	-	-	-	-	-	-	-	-	-	-
Surg.l retriev	4%	-	-	-	-	-	-	-	5%	-	-	-
Survival (days)	186	-	107 (median)	61 (median)	-	84 (median)	141	35	-	100	-	205

Cont. - APPENDIX 4 – Re-interventions with SEMS

Studies **Type of study**	**Raltz[21] N=75 Prospective non randomized**	**Knyrin N=21 Randomized**	**Roseveare[51] N=15 Randomized**	**Dallal [49] N=31 Randomized**	**Davies [38] N=41 Prospective**	**Nicholson [52] N=32**	**Sihvo[37] N=20 Retrospective**	**Wang [15] N=82**	**Weighted Average**
Obs.Period	87 - 97	91 – 92	1998 (P)	2001 (P)	1998 (P)	1999 (P)	90 – 98	93 – 97	-
Types stents	Z-Stent Wallstent Ultraflex Esophacoil	Wallstent	Z-stent	Ultraflex Walllstent	Strecker Wallstent	Ultraflex Z-stent	Esophacoil Ultraflex Wallstent	Ultraflex (c/u) Wallstent (c/u) Z-stent	-
Hoslp. Stay 1st	-	4	4	-	3	-	-	-	**2.5**
Hosp. stay over.	-	-	8	12.0	3	12.7	12.9	-	**9**
# stents initially	1.12	-	-	-	-	-	-	1.10	**1.06**
# stents overall	1.55 (?)	-	-	-	-	-	1.4	-	**1.20**
Re-interventions	22%	-	-	-	-	-	-	52.4%	**28.5%**
Stents	37%	-	-	-	7.3%	-	-	-	**13.2%**
Laser	-	-	-	-	7.3%	-	-	-	**13.5%**
Photdynamic	-	-	-	-	-	-	-	-	-
Dilation	19%	-	-	-	12%	-	-	-	**25%**
Endoscopic food dis.	-	-	-	-	-	-	0.3%	-	**3.2%**
Sclerotherapy	-	-	-	-	-	-	-	-	**17%**
Gastrostomy	3%	-	-	-	-	-	-	-	**3.6%**
Blood transfusion	-	-	-	-	-	-	-	-	**5%**
Alcohol injection	-	-	-	-	5%	-	-	-	**5%**
Surg.l retriev	-	-	-	-	-	-	-	-	**4.3%**
Survival (days)	84	-	96	68	-	112	139	-	**98 (not using median values)**

***** Higher rates compared to the other studies, this study was not included in the weighted average calculation

APPENDIX 5 – Use of SEMS in the Lower Esophagus

Self-Expanding Metallic Stents in the Lower Esophagus

Studies Type of study	Osugi[39] Prospective	Dua[41] Prospective	Laasch[40] Prospective	Weighted Average
Types of stents	Ultraflex N=7	Z-stent with anti-reflux valve N=11	Z-stent with anti-reflux N=25	-
Period of Observation	1995 – 1998	2001 (P)*	00 – 01	-
Technical success	86%	-	92%	**90.7%**
Immediate imprv. of dysphagia	100%	-	-	**100%**
Mean decrease in dysphagia	2.0	2.3	3.0	**2.7**
Complications	-	64%	-	**64%**
Tumour ingrowth/overgrowth	14%	18%	4%	**9.2%**
Esophageal reflux	43%	0 – nocturnal symptoms some daytime by design	12%	**18.8%**
Aspiration pneumonia	14% (death)	-	-	**14%**
Stent Migration	0	18%	16%	**13.9%**
Mortality related to stent	14%	0	-	**5.4%**
Perforation	-	-	4%	**4%**
Air embolism	-	9%	-	**9%**
Chest pain	-	18%	-	**18%**
Survival (days)	173	-	103	**118**
Reinterventions	-	-	32%	**32%**

*The period of observation was not available, therefore, the publication year was provided instead.

APPENDIX 6 - Use of SEMS in esophagorespiratory fistulas

Clinical Outcomes with SEMS in esophagorespiratory fistulas

Studies Type of study	May[45] N=11 Prospective/non-randomized	Tomaselli[46] N=6 Prospective	Dumonceau[47] N=17 Prospective / non-randomized	Weighted average
Period of Observation	Dec. 93 on	96 – 2000	94 – 96	-
Types of Stents	Z-stent	Ultraflex	Wallstent / Ultraflex	-
Technical Success	100%	100%	100%	**100%**
Mean reduction in dysphagia	2.4 (3 – 0.6)	2.1 (3.2 – 1.1)	2.0 (3.5 – 1.5)	**2.1**
% Fistula sealing	91%	100%	76%	**85%**
% recurrent dysphagia	-	50%	-	**50%**
Mean survival (days)	121 days (median)	78	-	**78**
Mean hospital stay	-	4.6 (3-9)	-	**4.6**

Complications with SEMS in esophagorespiratory fistulas

Studies Type of study	May[45] N=11 Prospective / non-randomized	Tomaselli[46] N=6 Prospective Non-randomized	Dumonceau[47] N=17 Prospective / non-randomized	Weighted Average
Period of Observation	Dec. 93 on	96 –2000	94 –96	-
Types of stents	Z-stent	Ultraflex	Wallstent / Ultraflex	-
Death related to procedure	-	-	12%	12%
Tumour ingrowth/overgrowth	(1) 9%	(1) 17%	6%	9%
Esophageal reflux	-	17% (100% in GE)	-	17%
Stent Migration	0*	-	18%	11%
Severe pain	-	17%	-	17%
Restroesternal pain	45%	100%	-	64%
Perforation	0	17% (fistula)	6%	8.9%
Food impaction	-	17%	6%	8.9%
Bleeding	0	-	-	0
Fistula enlargement	-	-	6%	6%
Fistula relapse	-	-	30%	30%
Foreign body sens	9% (slight)	-	-	9%
Survival (days)	121	78	-	105.8

*No fistula in the distal portion of the esophagus

APPENDIX 7 – SEMS compared to laser treatment in malignant strictures

Self-Expandable Metallic Stents vs Laser treatment

Studies **Type of study**	**Gevers* [26] Prospective / Non-randomized**		**Adam[25] Randomized**		**Konigsrainer[31] Randomized**		**Weighted average**	
	SEMS N=21	Laser N=70	SEMS N=42	Laser N=18	SEMS N=10	Laser N=21	**SEMS**	**Laser**
Period of Observation	92 - 96	86 -96	94 - 95	94 -95	92– 94	-	**-**	**-**
Types of stents	NA	-	Strecker Wallstent	-	Wallstent	-	**-**	**-**
Technical Success	-	-	100%	83%	-	-	**100%**	**83%**
Need for dilation	-	-	-	-	-	-		
Mean reduction in dysphagia	0.86	0.8	2.0	1.0	2.0	2.0	**1.7**	**1.1**
% immediate improvement of dysphagia	80.8%	82.9%	-	-	-	-	**80.8%**	**82.9%**
Dur. of palliation	66	98	-	-	-	-	**66**	**98**
% recurrent dysphagia	-	-	17%	12%	5.5%	43%	**14.8%**	**28.7%**
Mean survival (days)	49	172	54	56	205	237	**73.2**	**165.4**
Procedure related mortality	4.8%	0	7.1 %	6%	0	9.5%	**5.5%**	**2.8%**
Complications	-	-	-	-	0	19%	**0**	**19%**
Early Complications	50%	8.6%	-	-	-	-	**50%**	**8.6%**
Late complications	34.6%	0	-	-	-	-	**34.6%**	**0**
Major compl.	30.8%	4.3%	-	-	-	-	**30.8%**	**4.3%**
Minor compl	84.6%	4.3%	-	-	-	-	**84.6%**	**4.3%**
Migration	11.5%	NA	19%	NA	-	-	**16.5%**	**-**
Tumour in- / overgrowth	35%	NA	48%	NA	-	-	**43.7%**	**-**
Perforation	3.8%	2.9%	0	6%	0	9.5%	**1.1%**	**4.7%**
Hosp. stay	-	-	2.0	2.0	7.1	30	**3.0**	**17.1**
Re-intervent.	-	-	36%	100%	-	-	**36%**	**100%**
# of sessions	-	6.8	-	-	-	-	**-**	**6.8**

*Complication rates are higher due to design problems, experience of physician placing the stent

Laser does not seal fistulas – should be the therapy of choice especially for tumours of the lower third and in pts with a short life expectancy.

Patients in laser group started to be seen in 86, and those in the stent group in 92

Reference List

1. Cwikiel W, Tranberg KG, Cwikiel M, Lillo-Gil R. Malignant dysphagia: palliation with esophageal stents--long-term results in 100 patients. Radiology 1998; 207:513-8.

2. Baron TH. Expandable metal stents for the treatment of cancerous obstruction of the gastrointestinal tract. N Engl J Med 2001; 344:1681-7.

3. Lee SH. The role of oesophageal stenting in the non-surgical management of oesophageal strictures. Br J Radiol 2001; 74:891-900.

4. Weigel TL, Frumiento C, Gaumintz E. Endoluminal palliation for dysphagia secondary to esophageal carcinoma. Surg Clin North Am 2002; 82:747-61.

5. Rozanes I, Poyanli A, Acunas 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.

6. Raijman I, Siddique I, Ajani J, Lynch P. Palliation of malignant dysphagia and fistulae with coated expandable metal stents: experience with 101 patients. Gastrointest Endosc 1998; 48:172-9.

7. Tan BS, Mason RC, Adam A. Minimally invasive therapy for advanced oesophageal malignancy. Clin Radiol 1996; 51:828-36.

8. Hramiec JE, O'Shea MA, Quinlan RM. Expandable metallic esophageal stents in benign disease: a cause for concern. Surg Laparosc Endosc 1998; 8:40-3.

9. Z-stent Product Label. Abstract.

10. Ultraflex stent product label. Abstract.

11. Wallstent II product label. Abstract.

12. Acunas B, Poyanli A, Rozanes I. Intervention in gastrointestinal tract: the treatment of esophageal, gastroduodenal and colorectal obstructions with metallic stents. Eur J Radiol 2002; 42:240-8.

13. Leiper K, Morris AI. Treatment of oesophago-gastric tumours. Endoscopy 2002; 34:139-45.

14. Petruzziello L, Costamagna G. Stenting in esophageal strictures. Dig Dis 2002; 20:154-66.

15. Wang MQ, Sze DY, Wang ZP, Wang ZQ, Gao YA, Dake MD. Delayed complications after esophageal stent placement for treatment of malignant esophageal obstructions and esophagorespiratory fistulas. J Vasc Interv Radiol 2001; 12:465-74.

16. Christie NA, Buenaventura PO, Fernando HC, Nguyen NT, Weigel TL, Ferson PF, et al. Results of expandable metal stents for malignant esophageal obstruction in 100 patients: short-term and long-term follow-up. Ann Thorac Surg 2001; 71:1797-801; discussion 1801-2.

17. Golder M, Tekkis PP, Kennedy C, Lath S, Toye R, Steger AC. Chest pain following oesophageal stenting for malignant dysphagia. Clin Radiol 2001; 56:202-5.

18. Siersema PD, Hop WC, van Blankenstein M, van Tilburg AJ, Bac DJ, Homs MY, et al. 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; 54:145-53.

19. Dorta G, Binek J, Blum AL, Buhler H, Felley CP, Koelz HR, et al. Comparison between esophageal Wallstent and Ultraflex stents in the treatment of malignant stenoses of the esophagus and cardia. Endoscopy 1997; 29:149-54.

20. Ludwig D, Dehne A, Burmester E, Wiedemann GJ, Stange EF. Treatment of unresectable carcinoma of the esophagus or the gastroesophageal junction by mesh stents with or without radiochemotherapy. Int J Oncol 1998; 13:583-8.

21. Raltz SL, Kozarek RA. Do age, gender, or tumor location affect outcomes when using metallic stents in the palliative treatment of esophageal carcinoma? Gastroenterol Nurs 1999; 22:249-53.

22. De Palma GD, Sivero L, Galloro G, Siciliano S, Pigna F, Catanzano C. [The palliation of dysphagia secondary to esophageal-cardial carcinoma with self-expandable metal prostheses. The authors' personal experience with 92 patients]. Minerva Chir 1999; 54:213-8.

23. Decker P, Ulrich A, Decker D, Hirner A. [Palliative therapy of esophageal carcinoma]. Zentralbl Chir 1998; 123:697-702.

24. Kozarek RA, Ball TJ, Brandabur JJ, Patterson DJ, Low D, Hill L, et al. Expandable versus conventional esophageal prostheses: easier insertion may not preclude subsequent stent-related problems. Gastrointest Endosc 1996; 43:204-8.

25. Adam A, Ellul J, Watkinson AF, Tan BS, Morgan RA, Saunders MP, et al. Palliation of inoperable esophageal carcinoma: a prospective randomized trial of laser therapy and stent placement. Radiology 1997; 202:344-8.

26. 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; 48:383-8.

27. Siersema PD, Schrauwen SL, van Blankenstein M, Steyerberg EW, van der Gaast A, Tilanus HW, et al. Self-expanding metal stents for complicated and recurrent esophagogastric cancer. Gastrointest Endosc 2001; 54:579-86.

28. O'Sullivan GJ, Grundy A. Palliation of malignant dysphagia with expanding metallic stents. J Vasc Interv Radiol 1999; 10:346-51.

29. 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; 94:270-2.

30. Vakil N, Bethge N. Metal stents for malignant esophageal obstruction. Am J Gastroenterol 1996; 91:2471-6.

31. Konigsrainer A, Riedmann B, De Vries A, Ofner D, Spechtenhauser B, Aigner F, et al. Expandable metal stents versus laser combined with radiotherapy for palliation of unresectable esophageal cancer: a prospective randomized trial. Hepatogastroenterology 2000; 47:724-7.

32. Gukovsky-Reicher S. Expandable Metal Esophageal Stents: Efficacy and Safety. Review of Current Literature Data and of 53 Stents Placed at Harbour-UCLA Medical Center. Medscape General Medicine (www.medscape.com/viewarticle/423508_1) 2002; Abstract.

33. Bethge N, Sommer A, Vakil N. A prospective trial of self-expanding metal stents in the palliation of malignant esophageal strictures near the upper esophageal sphincter. Gastrointest Endosc 1997; 45:300-3.

34. Angueira CE, Kadakia SC. Esophageal stents for inoperable esophageal cancer: which to use? Am J Gastroenterol 1997; 92:373-6.

35. McManus K, Khan I, McGuigan J. Self-expanding oesophageal stents: strategies for re-intervention. Endoscopy 2001; 33:601-4.

36. O'Donnell CA, Fullarton GM, Watt E, Lennon K, Murray GD, Moss JG. Randomized clinical trial comparing self-expanding metallic stents with plastic endoprostheses in the palliation of oesophageal cancer. Br J Surg 2002; 89:985-92.

37. Sihvo EI, Pentikainen T, Luostarinen ME, Ramo OJ, Salo JA. Inoperable adenocarcinoma of the oesophagogastric junction: a comparative clinical study of laser coagulation versus self-expanding metallic stents with special reference to cost analysis. Eur J Surg Oncol 2002; 28:711-5.

38. 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; 80:394-7.

39. Osugi H, Lee S, Higashino M, Tokuhara T, Kaseno S, Takada N, et al. Usefulness of self-expandable metallic stent with an antireflux mechanism as a palliation for malignant strictures at the gastroesophageal junction. Surg Endosc 2002; 16:1478-82.

40. 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; 225:359-65.

41. Dua KS. Antireflux stents in tumors of the cardia. Am J Med 2001; 111 Suppl 8A:190S-196S.

42. Macdonald S, Edwards RD, Moss JG. Patient tolerance of cervical esophageal metallic stents. J Vasc Interv Radiol 2000; 11:891-8.

43. Conio M, Caroli-Bosc F, Demarquay JF, Sorbi D, Maes B, Delmont J, et al. Self-expanding metal stents in the palliation of neoplasms of the cervical esophagus. Hepatogastroenterology 1999; 46:272-7.

44. Gislason GT, Pasricha PJ. Crossing the upper limit: esophageal stenting in the proximal esophagus. Dysphagia 1997; 12:84-5.

45. May A, Ell C. Palliative treatment of malignant esophagorespiratory fistulas with Gianturco-Z stents. A prospective clinical trial and review of the literature on covered metal stents. Am J Gastroenterol 1998; 93:532-5.

46. Tomaselli F, Maier A, Sankin O, Woltsche M, Pinter H, Smolle-Juttner FM. Successful endoscopical sealing of malignant esophageotracheal fistulae by using a covered self-expandable stenting system. Eur J Cardiothorac Surg 2001; 20:734-8.

47. Dumonceau JM . Esophageal fistula sealing: choice of stent, practical management, and cost. Gastrointestinal Endoscopy 1999; 49:70-78. Abstract.

48. Mason R. Palliation of malignant dysphagia: an alternative to surgery. Ann R Coll Surg Engl 1996;

78:457-62.

49. 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; 54:549-57.

50. Crott R. The cost of an upper gastroduodenal endoscopy: an activity-based approach. Can. J. Gastroenterol. 2002; 16:473-482. Abstract.

51. 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; 10:653-7.

52. Nicholson DA, Haycox A, Kay CL, Rate A, Attwood S, Bancewicz J. The cost effectiveness of metal oesophageal stenting in malignant disease compared with conventional therapy. Clin Radiol 1999; 54:212-5.