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Palliation of malignant dysphagia: an alternative to surgery

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This paper presents the results of palliative treatment of 474 patients with malignant dysphagia. Laser produces good relief of symptoms but requires frequent repetition. Self-expanding metal stents provide one-off relief of dysphagia but do have complications. A randomised trial of laser *versus* covered and uncovered metal stents has demonstrated improved relief of dysphagia of stents over laser, but highlighted the problems at the cardia when stents are used. Chemotherapy in patients with advanced adenocarcinoma using epirubicin, cisplatin and 5-fluorouracil produces a response in two-thirds of cases, with relief of dysphagia and possible increase in survival. A treatment plan for palliation of patients with malignant dysphagia is presented.

Although the results of surgery for malignant dysphagia have improved in the last decade, the majority of patients will be either unfit for surgery or have advanced disease at presentation *(1,2)*. Identification of such patients by CT scanning or endoluminal ultrasound *(3)* can avoid the high morbidity and mortality associated with purely palliative resection, where macroscopic disease clearance is not achieved. For these patients effective relief of dysphagia with the minimum of trauma is required.

Disappointment with the results of intubation led to the investigation of lasers and self-expanding metal stents to relieve dysphagia and chemotherapy to influence tumour growth.

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Patient data

A total of 474 patients was referred to the department of surgery at Guy's hospital in the 5 years before 1995. All were considered unsuitable for surgery owing to general infirmity or advanced disease. The median age of patients was 62 years (range 38–100 years); there were 294 males and 180 females. The median survival of all patients was 8 weeks from presentation (range < 1–200 weeks). Positive histology was obtained in all cases and all were endoscoped under sedation with midazolam 2–10 mg intravenously.

The severity of dysphagia was scored from 0–4 (0 normal swallowing, 1 some solids stick, 2 soft diet, 3 liquids only, 4 total dysphagia requiring intravenous fluids). The dysphagia grade (DG) at presentation was a median of 3 (range 1–4). Further data on patients are shown in Table I.

Of the 474 patients, 350 were treated primarily with the laser, 64 were treated with one of three types of self-expanding metal stents and 60 were entered into a randomised trial to compare laser with covered and uncovered expanding metal stents.

In addition, 48 patients with adenocarcinoma in the group treated with laser alone were entered into two Phase 2 studies into the effectiveness of cytotoxic chemotherapy.

In all cases, fully informed consent was obtained from all patients and ethical committee approval was obtained for the randomised trial of lasers and stents and for patients receiving chemotherapy.

Methods

Both laser treatment and insertion of self-expanding metal stents were performed under intravenous sedation with either midazolam (2–10 mg) or Diazemuls® (2–10 mg),

Table I. Tumour data

Histology	Adenocarcinoma	75%
	Squamous carcinoma	24%
	Undifferentiated	1%
Site	Involving the cardia	69%
	Upper/middle 2/3	31%
Length	Median 5 cm (range 1–20 cm)	

with the addition of fentanyl (50–100 μg) if necessary. Oxygen was given via nasal speculas and patients were monitored with pulse oximetry.

Laser treatment was undertaken using an NdYAG laser (Living Technology, Glasgow) using 50–70 joule pulses administered via a flexible gas-cooled quartz fibre. This was passed via one channel of an Olympus® 2T20 endoscope modified for laser use (Key Med, Southend-on-Sea). Between 2 and 10 000 joules were administered at one session and laser treatment was administered in a retrograde fashion. To facilitate passage of the endoscope into the stomach, pretreatment wire-guided dilatation was performed with a Celestin-type dilator in one-third of cases. Treatments were repeated at monthly intervals for life.

Insertion of self-expanding metal stents was performed under fluoroscopic control. An initial oesophagogram was performed in the upright position to demonstrate the site and length of the stricture. A guidewire was then passed followed by an Olbert® balloon catheter (Meadox, Caddington, England) which was gently dilated to 10 mm. This was withdrawn and the stent on its introducer placed across the stricture and released. Patients were kept nil by mouth overnight, when a check oesophagogram was performed. If the stent had migrated a further stent was placed, and if not fully dilated a balloon catheter was inserted and the stent fully expanded. Diet was then started.

Three types of stent were used, an uncovered Strecker® nitinol stent (Boston Scientific, St Albans), a polyurethane covered Wallstent® (Schneider Bulach, Switzerland), and a polyethylene covered Gianturco® stent (William Cook, Europe).

Two Phase 2 studies of chemotherapy were undertaken in patients undergoing laser treatment; involving in 14 patients 5-flourouracil and folinic acid (FA/5-FU) and in 34 patients epirubicin, cisplatin and continuous 5-flourouracil (ECF) administered via a minipump and Hickman catheter. Doses for the drugs used were:

FA/5-FU—Folinic acid 200 mg/m^2 over 2 h. 5-Fluorouracil 400 mg/m^2—bolus followed by 400 mg/m^2 over 22 h. This was repeated every 14 days.

ECF—Epirubicin 50 mg/m^2 bolus, cisplatin 60 mg/m^2 bolus, both repeated every 3 weeks. 5-Fluorouracil 200 mg/m^2 continuous intravenous infusion via a Hickman catheter and minipump.

Response was determined after six cycles of FA/5-FU and three cycles of ECF using WHO criteria *(4)*.

Results

The results for the 350 patients treated with laser alone are shown in Fig 1. The improvement in swallowing from a median of 3 before treatment to 2 after treatment and then to 1 for the remainder of life is significant at $P<0.001$ up to 8 months and $P<0.05$ at 10 months (Wilcoxon rank sum test for paired values *versus* pretreatment). The pattern of swallowing in patients was one of good swallowing with occasional lapses responding to laser in two-thirds, a gradual deterioration in swallowing in one-quarter and a poor result requiring early intubation in the others.

Overall in this group, only 48% of patients survived longer than 2 months, reflecting the policy of helping as many patients as possible.

There were seven deaths directly attributable to laser therapy (2%). This was the result of perforation in five cases, three of which were a result of dilatation and recognised at the time and treated conservatively and two recognised 24 h later in patients who had not had dilatation and were attributable to the laser. The remaining two cases were the result of haemorrhage. Oesophageal perforation is the most common complication of laser therapy and is the result of pre-laser dilatation. The incidence of perforation was 6% of patients and 2% of treatments. Early recognition and aggressive conservative management with intravenous fluids, antibiotics, H_2 receptor antagonists and enteral feeding via a nasogastric tube resulted in 20 of the recognised 23 patients with perforations surviving (87%).

In earlier reports involving the first 200 patients, attempts were made to predict outcome of laser treatment by preoperative assessment of tumour length, histology, site and dysphagia grade at presentation *(5,6)*. A summary is shown in Table II.

The only factor which related to outcome was dysphagia grade at presentation (Fig. 2); those with

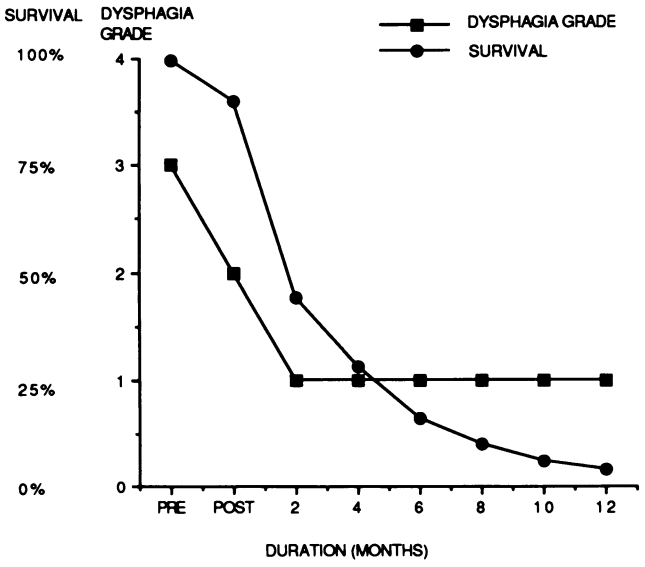

Figure 1. Survival and dysphagia grade for the 350 patients treated with laser alone.

Table II. Prediction of outcome of laser treatment

Variable	*Survival*	*Relief of dysphagia*
Length (less or greater than 5 cm)	No effect	No effect
Histology (adeno/squam)*	No effect	No effect
Site (Upper 2/3, lower 1/3)	No effect	No effect
Severity of dysphagia at presentation	Negative effect	No effect

*Adenocarcinoma/squamous cell carcinoma

Table III. Distribution of self-expanding metal stents

	No of patients	*No of stents*
Gianturco	5	5
Strecker	19	22
Wallstent	40	54

severe dysphagia—DG 3/4 survived significantly less than those with good swallowing, DG 1/2 ($P<0.001$, Mann–Whitney U test).

The distribution of stents in the initial 64 patients treated with self-expanding metal stents is shown in Table III. Patients received more than one stent if tumour length exceeded the stent length or migration occurred. Technical success in placement of the stent was achieved in all cases with an improvement in dysphagia grade from a median of 3 to 1 ($P<0.001$ Wilcoxon rank sum test for paired values). Twelve patients had oesophageal perforations or tracheo-oesophageal fistulas and all were sealed.

Complications include recurrent dysphagia (15.5%), Table IV; one patient had both a bolus obstruction and, later, ingrowth. Other complications include aspiration of gastric contents (9%), delayed pneumonia (5%), haemorrhage (3%) and a mortality of 5% owing to haemorrhage and aspiration pneumonia.

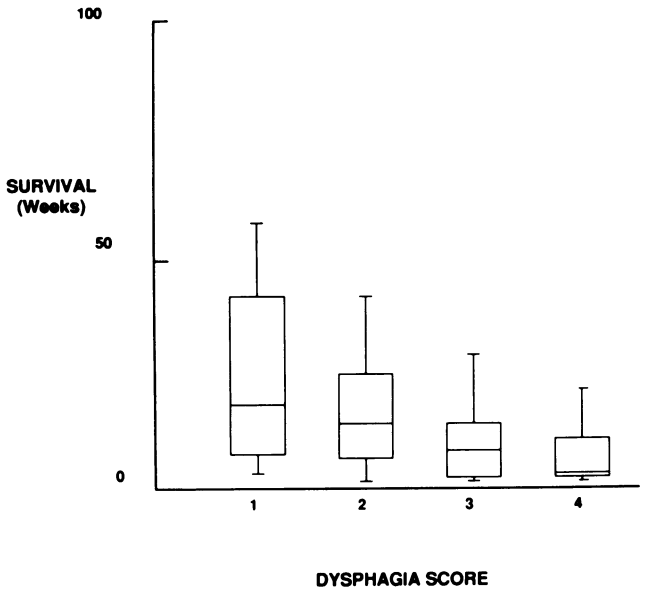

Figure 2. Association between dysphagia grade at presentation and survival for patients with adenocarcinoma *(6)*.

Table IV. Recurrent dysphagia (10 cases)

Cause	*n*	*Type of stent*	*n*
Complete migration	4	G	2 (40%)
		S	1 (5.5%)
		W	1 (2.5%)
Overgrowth	3	S	1 (5.5%)
		W	2 (5%)
Ingrowth	2	S	2 (11%)
Bolus obstruction	2	S	1 (5.5%)
		W	1 (2.5%)

*One patient had both a bolus obstruction and later ingrowth
G, Gianturco; S, Strecker; W, Wallstent

All cases of recurrent dysphagia, with the exception of migration, were treated successfully with endoscopy and laser.

The high migration rate seen with the Gianturco stent and the degree of pain experienced by patients led to our abandoning its further use. It was decided, therefore, that a randomised trial should involve laser alone, the uncovered Strecker stent and the covered Wallstent.

To date, 60 patients have been randomised. Entry criteria included all patients with malignant dysphagia unsuitable for surgery who were suitable for all three modes of treatment. Dysphagia grade was the same in each group (median 3, range 1–4). A summary of the results is shown in Table V and Fig 3.

The improvement in dysphagia seen with the laser was significantly worse than that seen with either stent (Kruskall Wallis analysis of variance 11.38, $P=0.003$). The high incidence in migration seen with the Wallstent occurred only when the stent crossed the cardio-oesophageal junction, where the incidence was 50%. Complete migration of the stent into the stomach occurred in only two of the eight cases, but the apparent difference in migration between the two types of stent was significant (χ^2 analysis with Yates' correction factor $=6.1$, $P<0.02$). Gastro-oesophageal reflux was only a problem in stents crossing the cardia and was present in 22% of such cases.

The cause of mortality (5%) was haemorrhage in two cases and aspiration pneumonia in one case.

The results of the two Phase 2 studies of chemotherapy

Table V. Summary of results

	Laser	*Strecker*	*Wallstent*
No of patients	18	19	23
Improvement in DG (median and range)	1 (0–2)	2 (0–4)	2 (−1–3)
Perforation	1	0	0
Migration	0	0	8
Recurrent dysphagia	2	5	1
Gastro-oesophageal reflux	0	4	2
Mortality	1	0	2

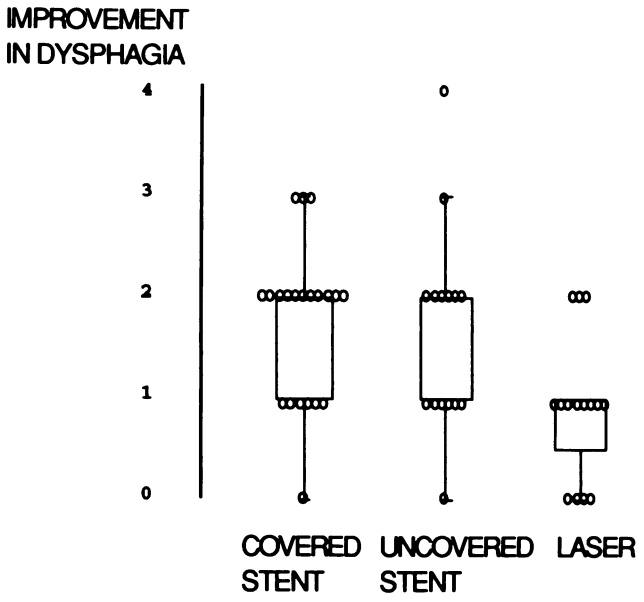

Figure 3. Improvement in dysphagia achieved by patients treated with laser, covered Wallstent and uncovered Strecker stent.

(7,8) in malignant dysphagia are shown in Fig. 4 and Fig. 5. The two groups of patients have been compared with the first 30 patients treated with laser alone in the series of 350 who survived at least 2 months from presentation. Their fitness and disease stage was similar to those receiving chemotherapy. The factors compared were the frequency of laser treatment to maintain good swallowing,

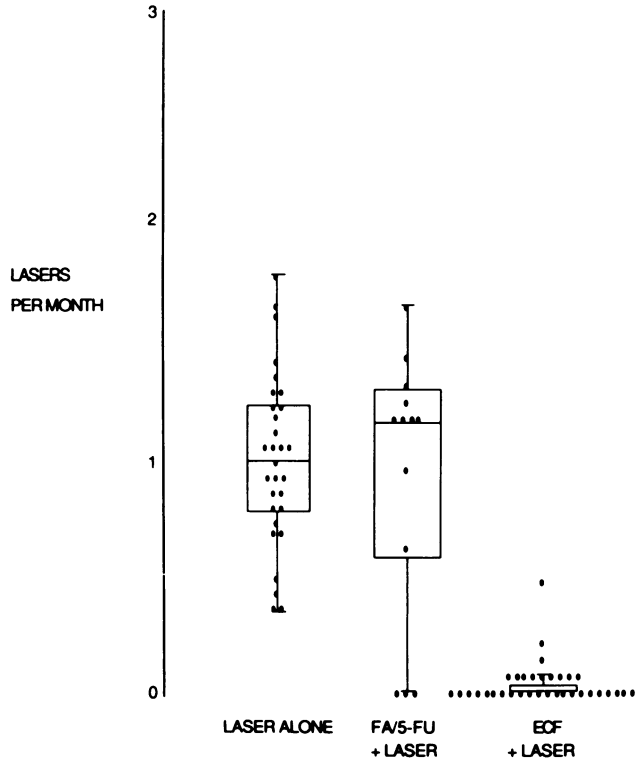

Figure 4. Frequency of laser treatment required to maintain good swallowing in patients treated with laser alone, FA/5-FU and ECF.

and survival. Side-effects of the chemotherapy were low, with the majority of treatment cycles free from side-effects. Assessment of response was made by repeat endoscopy and CT scan. No response was seen in patients treated with FA/5-FU, but a 61% response was seen in patients treated with ECF. This was mirrored by a significant reduction in need for laser to maintain swallowing ($P < 0.001$ Mann–Whitney U test, ECF *versus* laser alone and FA/5-FU), and an increase in survival for ECF patients compared with laser alone and FA/5-FU ($P = 0.001$ log rank χ^2 test $= 10.61$).

Discussion

For patients with malignant dysphagia, the most important aspect in palliation is to improve swallowing. Although resection is the best means of achieving this in fit patients with small tumours, palliative resection carries a high morbidity and mortality with survival measured in months *(1,2)*. The most common non-surgical methods of relieving dysphagia is intubation with a plastic tube which will enable a soft diet to be swallowed, but this has a significant procedural mortality *(9)*. These results confirm that laser can achieve good swallowing, at least as good as a tube, with minimal complications. Randomised trials comparing the two techniques *(10,11)* bear out the improved swallowing after laser treatment but highlight the need for repeat treatments. Attempts to predict response to laser treatment and direct patients straight to intubation as described were unsuccessful. The impression of this series confirms that of others *(10,11)* that the laser is best for small polypoid intraluminal tumours and intubation for mural and extramural disease. As most patients have tumours exhibiting both luminal and mural components, our practice was to treat with laser first and only intubate laser failures.

Early results from the use of self-expanding metal stents suggested a methods by which the good swallowing of the laser could be achieved with a one-off procedure performed under sedation *(12)*. Our early results appeared to confirm this and the results from the randomised trial have shown better relief of dysphagia with both types of stent, but not without problems. The problem area is the cardia where most cases of malignant dysphagia occur. Current designs of covered stent have an unacceptable rate of migration and uncovered stents suffer from ingrowth. This can, however, easily be remedied by the use of laser. Another aspect of stenting is cost. Each stent costs in the region of £900 compared with £30–£50 for a plastic tube. In a randomised trial comparing stents with intubation, this difference in cost was more than compensated for by a reduction in morbidity and mortality *(12)*. From the present study, it appears that optimum management will be achieved by a combination of all modalities, laser and stent.

The good results achieved in the management of oesophageal perforation by covered stents when compared with conservative management as described *(13,14)*

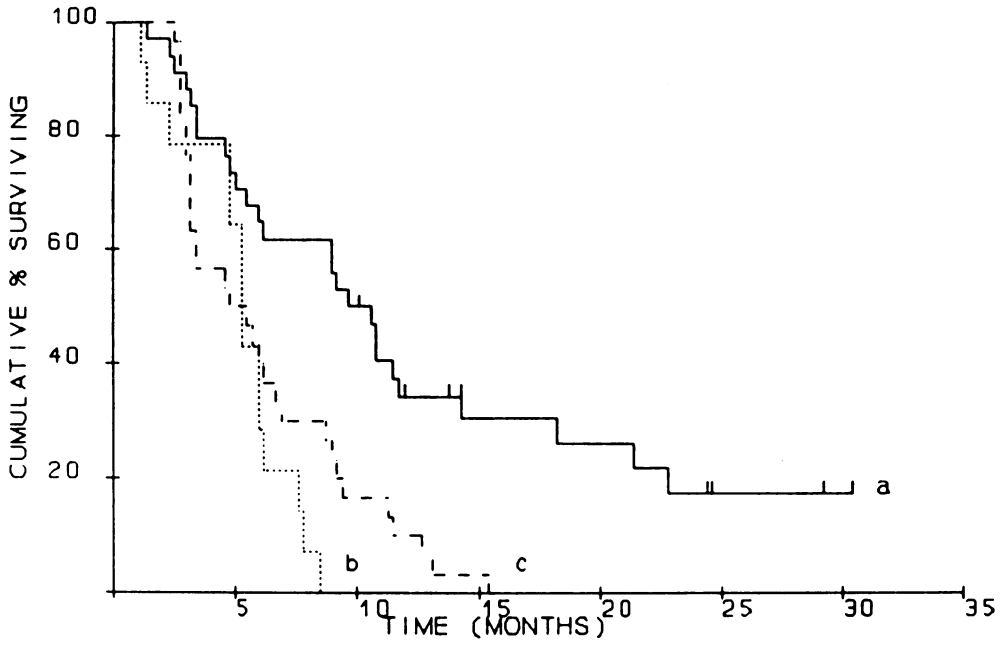

Figure 5. Survival for patients treated with laser alone (c), FA/5-FU (b), and ECF (a).

has led to this becoming our routine practice for treating this complication.

Having improved dysphagia, the next objective is to determine whether tumour growth can be retarded by chemotherapy. Other workers using radiotherapy have demonstrated that this can reduce the need for lasers to maintain swallowing and may have some survival benefit *(15)*. In this series, it appears that treatment with ECF, but not FA/5-FU, achieves both relief of dysphagia and prolonged survival. In this series, patients who responded needed no repeat laser treatment until their disease relapsed. This confirms the results of others who described some complete responders using combination chemoradiotherapy *(16)*. This opens the possibility of downstaging disease with chemotherapy, and converting inoperable into operable disease. We have so far operated on five patients who have had complete remission on repeat CT scanning and endoscopy with complete histological remission in two.

From the experience gained in the treatment of these 474 patients, we have constructed a treatment plan for the management of malignant dysphagia. This is shown in Fig. 6. Such plans are intended for guidance only and will no doubt frequently be modified in the future.

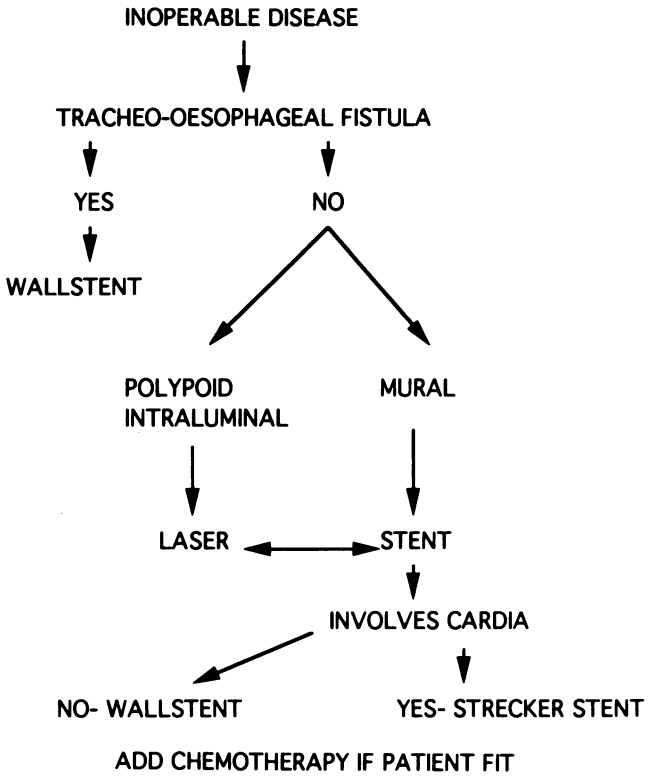

Figure 6. Treatment plan for patients with inoperable malignant dysphagia.

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References

1 Earlam R, Chunha-Melo JR. Oesophageal squamous cell carcinoma: 1, A critical review of surgery. *Br J Surg* 1980; **67**: 381–90.

2 Muller JM, Erasmi H, Stelzner M *et al.* Surgical therapy of oesophageal carcinoma. *Br J Surg* 1990; **70**: 845–57.

3 Rankin S, Mason R. Staging of oesophageal carcinoma. *Clin Radiol* 1992; **46**: 373–7.

4 Miller AB, Hoogstraten B, Staquet M *et al.* Reporting results of cancer treatment. *Cancer* 1981; **47**: 207–14.

5 Mason RC, Bright N, McColl I. Palliation of malignant dysphagia with laser therapy: predictability of results. *Br J Surg* 1991; **78**: 1346–7.

6 Derodra JK, Hale PR, Mason RC. Inoperable oesophageal cancer: factors affecting outcome. *Gullet* 1992; **2**: 163–6.

7 Highly MS, Hill ME, Ziras N *et al.* High dose folinic acid with 5-fluorouracil bolus and continuous infusion in the treatment of advanced gastric and oesophageal adenocarcinoma. *Br J Cancer* 1993; **67**: 407–8.

8 Highley MS, Parnis FX, Trotter GA *et al.* Combination chemotherapy with epirubicin, cisplatin and 5-fluorouracil for the palliation of advanced gastric and oesophageal adenocarcinoma. *Br J Surg* 1994; **81**: 1763–5.

9 Bown SG. Palliation of malignant dysphagia: surgery, radiotherapy, laser, intubation alone or in combination. *Gut* 1991; **32**: 841–4.

10 Loizou LA, Grigg D, Atkinson M *et al.* A prospective comparison of laser therapy and intubation in endoscopic palliation for malignant dysphagia. *Gastroenterology* 1991; **100**: 1303–10.

11 Alderson D, Wright PD. Laser recanalization versus endoscopic intubation in the palliation of a malignant dysphagia. *Br J Surg* 1990; **77**: 1151–3.

12 Knyrim K, Wagner HJ, Bethge N *et al.* A controlled trial of an expansile metal stent for palliation of oesophageal obstruction due to inoperable cancer. *N Engl J Med* 1993; **329**: 1302–7.

13 Tyrrell MR, Trotter GA, Adam A *et al.* The incidence and management of laser associated oesophageal perforation. *Br J Surg* 1995; **82**: 1257–8.

14 Watkinson A, Ellul J, Entwistle M *et al.* Plastic-covered metallic endoprostheses in the management of oesophageal perforation in patients with oesophageal carcinoma. *Clin Radiol* 1995; **50**: 304–9.

15 Sargeant IR, Loizou La, Tobias JS *et al.* Radiation enhancement of laser palliation for malignant dysphagia: a pilot study. *Gut* 1992; **33**: 1597–1601.

16 Gill PG, Jamieson GG, Denham J *et al.* Treatment of adenocarcinoma of the cardia with synchronous chemotherapy and radiotherapy. *Br J Surg* 1990; **77**: 1020–3.

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