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Endoscopic treatment of early oesophageal or gastric cancer

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Abstract

***Background and Aims*—Endoscopic treatment has become increasingly popular in recent years as an alternative to surgical treatment with the hope of offering superior quality of life (QOL) for the patient. The results of endoscopic treatment of mucosal lesions of mostly early oesophageal or gastric cancer performed in 145 patients (155 lesions) over the past eight years were reviewed from the standpoint of QOL.**

***Results*—In 56 patients who underwent radical resection of the oesophageal mucosa, no serious complications and symptoms occurred, with epithelialisation completed within about a month. Patients also showed good results regarding dietary intake and performance status (PS), and all are currently alive without any sign of recurrence. One time fractionated endoscopic resection was carried out in about 40% of the 57 patients who underwent gastric mucosal resection. In these 57 patients, an artificial ulcer measuring 3 cm or more was formed, resulting in a favourable outcome after healing. An overwhelming proportion of these subjects had no symptoms and good PS after the treatment.**

***Conclusions*—The introduction of this method, endoscopic mucosal resection using a cap fitted panendoscope, is expected to permit additional indications for endoscopic treatment. Endoscopic Nd-YAG laser irradiation was applied mainly to early gastric cancer lesions (32 patients), usually for relative indications for endoscopic treatment. This procedure is safe and advantageous in that it requires no hospitalisation, permits fractionated irradiation, and secures good QOL.**

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Keywords: quality of life, oesophageal cancer, gastric cancer, endoscopic treatment, endoscopic mucosal resection.

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Endoscopic treatment has become increasingly popular in recent years as an alternative to surgical treatment in the hope of offering superior quality of life (QOL) for the patient by avoidance of a surgical procedure and its postoperative complaints.[1–3] Endoscopic treatment may achieve more widespread use if longterm results in a large number of patients prove to be favourable. In this study, the results of endoscopic treatment performed in patients mostly with early oesophageal or gastric cancer were reviewed with special reference to the postoperative course and the patient's QOL.

Methods

Indications for endoscopic treatment

Radical endoscopic treatment is indicated for cancer lesions confined within the mucosa and not accompanied by metastatic lymph nodes. All terms referring to oesophageal and gastric cancer used in this study were taken from the '*Guide lines for the Clinical and Pathologic Studies on Carcinoma of the Esophagus*'[4] and from the '*Japanese Classification of Gastric Carcinoma*'.[5]

A previous study that reviewed 235 cases of superficial oesophageal cancer[6] and 255 cases of early gastric cancer[7] surgically treated at our department showed that such mucosal lesions did not exceed about 2 cm in diameter or one third of the circumference of the oesophagus, with oesophageal lesions extending as far as the middle layer of the lamina propria mucosae in depth and those in the stomach being well differentiated lesions either of the protruded type, not exceeding 2 cm in diameter, or of the depressed type, not exceeding 1 cm in diameter. Therefore, we performed preoperative endoscopic assessment in which the histological type was confirmed in biopsy specimens and tumour size was measured by forceps. Endoscopic ultrasound was used for all cases to determine the depth of cancer invasion according to our diagnosis criteria.[8–10] Cases that were found to meet the above criteria upon such preoperative assessment were regarded as absolute indications for endoscopic treatment. Other cases of presumably early cancer in which surgery was impossible because of advanced age, serious complications or the patient's unwillingness to undergo surgery were regarded as relative indications.

Patients

As Table I shows, 155 consecutive lesions (145 patients) of the oesophagus and stomach were treated endoscopically at our department over the eight years from August 1987. Endoscopic mucosal resection was carried out for 122 lesions in 113 patients, usually using an electronic endoscope fitted with a transparent plastic cap (EMRC procedure).[11 12] In particular, a cap having a gutter around its tip has been used for recent cases, which permits prelooping of the snare inside the cap.[13]

TABLE I *Lesions in 145 subjects*

	Macroscopic type							
	I	*IIa*	*IIb*	*IIc*	*dysplasia*	*adenoma*	*carcinoid*	*Total*
	No of lesions (%)							
Oesophagus	2 (4)	5 (9)	9 (16)	31 (55)	9 (16)	–	–	56 (100)
Stomach	3 (4)	29 (44)	1 (2)	15 (22)	–	17 (26)	1 (2)	66 (100)
Stomach (Laser)	–	14 (42)	–	16 (49)	–	3 (9)	–	33 (100)

TABLE II *Clinicopathological profile (depth of cancer invasion)*

	Oesophagus No of lesions (%)	*Stomach No of lesions (%)*
Mucosal	43 (91)	45 (94)
middle layer	34	–
deep layer	9	–
Submucosal	4 (9)	3 (6)
shallower layer	4	2
deeper layer	0	1
Total	47 (100)	48 (100)

Nd-YAG laser irradiation was applied to 33 lesions in 32 patients, using a medical YAG laser system MC2100 (Technomedical International, Paris) by a non-contact method with continuous waves.

All oesophageal lesions corresponded to absolute indications and were treated by endoscopic mucosal resection. In contrast, until 1990, gastric lesions were treated by laser irradiation for either absolute or relative indications. From 1991 onward, cases of absolute indication have been treated by the EMRC, which, unlike laser therapy, permits recovery of resected specimens for histopathological examination, while laser therapy has been adopted for the treatment of cases of relative indication.

All subjects were observed endoscopically two weeks and one, three, six, and 12 months after treatment. Endoscopic biopsy has also been carried out annually or semiannually thereafter.

To determine changes in the patient's quality of life and degree of satisfaction after endoscopic treatment, all patients who survived were surveyed simultaneously on a single occasion via telephone or post after a median follow up period of 40 months (interquartile range, one year and eight months to five years and five months after endoscopic treatment). The patients self assessed their pretreatment and post-treatment conditions with regard to seven items: the presence and details of any symptoms, size and frequency of meals, working status (including housework), drug therapy, and performance status (PS) (PS; PS0=patient can undertake full time employment, PS1= patient's ability is reduced but can look after himself, PS2=patient is in bed more than 50% of daytime and requires help in his homelife, PS3=patient is totally bedridden and always requires help).[14] Data on the patients' pretreatment condition were also obtained from their medical records. The number of days required for the endoscopic procedures and the status of hospital visits after treatment were also examined.

Informed consent was obtained from all patients and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Results

Clinicopathological features (Table II)
Oesophageal mucosal resection was performed for 56 lesions in 56 patients. In cases of oesophageal cancer, histopathological examination showed that the cancer had infiltrated to either the middle layer or the deep layer of the lamina propria mucosae in 34 and nine cases, respectively, and to the submucosa in four cases. In addition, there were nine cases of mucosal dysplasia.

Gastric mucosal resection was carried out in 57 patients (66 lesions). Histopathologically, among early gastric cancers, there were 45 (94%) mucosal cancers and three submucosal cancers (infiltration reaching the shallower layer of the submucosa in two and the deeper layer in one). There were also 17 adenomas and one carcinoid.

Among 33 lesions in 32 patients who underwent endoscopic laser irradiation, the treatment was the first option in 24 lesions in 23 patients (15 lesions with an absolute indication, nine lesions with a relative indication). The other nine lesions were recurrences from residual malignancy after an endoscopic treatment, such as ethanol injection, performed at a different facility.

Extent and frequency of resection, dose, and frequency of irradiation (Table III)
EMRC of an oesophageal lesion provides a specimen 2-2.5 cm in diameter when the lesion is resected en bloc. This specimen corresponds to one third to one half of the circumference of oesophageal wall. Forty two (75%) lesions were dealt with by one time fractionated resection. Resection reaching or exceeding the semi-circumference accounted for 23 lesions, including a case in which the maximum resection reached 5 cm along the major axis and four fifths of the circumference.

Although EMRC of a gastric lesion also gives a specimen of similar size when en bloc resection is used, a substantial 26 (39%) of the total 66 lesions required one time fractionated resection. For these lesions, artificial ulcers measuring 3 cm or more were predominant, being formed in 19 lesions. Of the 66 lesions, 62 were completely resected en bloc or by the first or second fractionation. The remaining four lesions required a third fractionation. Thus, overall results of the EMRC procedure were favourable.

Laser irradiation was performed only once in 14 lesions, while the other 19 lesions were subjected to repeated irradiation applied on several different occasions, including six lesions subjected to five or more sessions. The total exposure dose was 2000 J or more in 17 lesions.

TABLE III *Frequency and extent of mucosal resection*

	Oesophagus No of lesions (%)		*Stomach No of lesions (%)*
Frequency			
en bloc	14 (25)		40 (61)
fractionated	42 (75)		26 (39)
Extent			
<1/2 circumference	33 (59)	<3 cm	47 (71)
>1/2 circumference	23 (41)	>3 cm	19 (29)

Course after treatment (Table IV)
All patients who underwent mucosal resection were hospitalised. All (54) patients with oesophageal lesions, excluding two with complications who will be described later, were discharged from the hospital within two weeks (minimum, three days). Fifty patients were asymptomatic postoperatively. Only six patients were symptomatic, having retrosternal pain, nausea, or epigastralgia. These symptoms required no analgesic agent, but antibiotic, antacid, and mucosa protecting drug treatment was given for a short period. Oral feeding was started on the following day or within three days. Endoscopic examination revealed that artificial ulcers were usually epithelialised within about a month.

Complications occurred in five cases (bleeding in two, perforation in one, stenosis in two). Four cases were healed by conservative treatment. One of the stenotic cases was treated by oesophageal resection through right thoracotomy, followed by reconstruction with the gastric tube. The course after surgery has been uneventful. There were few subjective symptoms in the case of perforation. The patient was observed for two weeks while taking fasting therapy. Oral intake was started after the closure was confirmed with an endoscopic examination on the 14th postoperative day, and the patient was discharged on the 18th day.

The mean period of hospitalisation was five days among patients with gastric lesions. Most patients, even those having an artificial ulcer measuring 3 cm or more in diameter, were asymptomatic; only five patients complained of a burning sensation or constriction in the epigastrium. Only nine patients had complications (muscle resection without perforation in three, bleeding in six). Pressure by the cap or endoscopic clipping achieved haemostasis in all these cases, permitting conservative treatment.

Among 32 patients to whom laser irradiation was applied, most, 24 (73%), could be treated at our outpatient clinic. There were no complications or postoperative symptoms in any of the patients, excluding one who had epigastralgia and another who had back pain. No bleeding or perforation occurred afterwards. Regardless of whether mucosal resection or laser irradiation was performed, patients with a gastric lesion usually started to have meals the day after treatment. No analgesics were necessary. Treatment with H_2 receptor antagonist, antipepsin, antacid, and mucosa protecting agents was given until the ulcer was epithelialised.

TABLE IV *Complications and symptoms*

	Oesophagus No of patients	*Stomach No of patients*	*Stomach (laser) No of patients*
Complications	5	9	0
bleeding	2	6	–
muscle resection	–	3	–
perforation	1	–	–
stenosis	2	–	–
Symptoms			
asymptomatic	50	52	30
symptomatic	6	5	2

TABLE V *Prognosis and performance status (PS)*

	Oesophagus No of patients	*Stomach No of patients*	*Stomach (laser) No of patients*
Total	56	57	32
Alive	53	56	27
Follow up period (median period) (IQR*)	5m–6y2m (39m) (1y7m–4y11m)	6m–4y9m (32m) (1y4m–3y10m)	4m–8y2m (53m) (2y2m–6y5m)
Residual cancer or recurrence			
(–)	53	54	24
(+)	–	2†	3
Died of other diseases	3	1	5
PS 0–1	51	56	21
2–3	2	–	6

m=month(s), y=year(s). *=interquartile range, †=residual cancer.

Prognosis (Table V)
To date, the 56 patients with oesophageal lesions treated by endoscopic mucosal resection have been followed up for six years and two months at maximum (median period; three years and three months). Radiotherapy was applied to a case of cancer that had infiltrated into the shallower layer of the submucosa, while the other three cases of the same depth (in one of the three there was accompanying advanced cancer of another organ) and nine cases of cancer that had infiltrated into the deep layer of the lamina propria mucosae have been followed up without the need for additional treatment. Three patients died of other diseases. The other 53 patients are all alive, showing no recurrence. There were no changes in PS in 51 (96%) patients after treatment, classified as scale 0–1. The poor PS of scale 2 or 3 seen in only two patients was attributable to other diseases such as cerebrovascular disturbance and renal failure. Dietary intake after treatment was normal as assessed by the questionnaire.

The 57 patients with gastric lesions treated by mucosal resection have been followed up for four years and nine months at maximum (median period; two years and eight months). All patients except for one who died of other causes are currently alive. Histopathological examination showed residual cancer due to horizontally incomplete resection of the mucosal layer in two patients (as shown in the middle column of Table V), both of whom were given additional single irradiation of Nd-YAG laser within 50 days after the mucosal resection. In one patient, proximal gastrectomy was combined because of vertical infiltration of cancer into the deeper layer of the submucosa. Histopathological examination of the resected specimen, however, showed no residual cancer or metastatic lymph nodes. The other two cases of submucosal cancer, both involving

only the shallower layer of the submucosa, had no lymphatic permeation or vascular invasion. These cases are now being followed up. All cases including these have shown no recurrence. PS and dietary conditions after treatment were as favourable as those before treatment in all patients including the one who underwent gastrectomy. Apart from the two patients with oesophageal lesions who showed poor postoperative PS of scale 2 or 3, all patients with oesophageal and gastric lesions were restored to the same level of working status as they had before treatment, and no longterm drug therapy related to our procedure was given in any of the patients.

The 32 patients treated by laser irradiation have been followed up for eight years and two months at maximum (median period; four years and five months). Twenty four patients have had no residual cancer or recurrence of disease, while recurrence from residual cancer was found in three patients (one of them had had a relative indication). Two of the three patients underwent gastrectomy. Both had undergone endoscopic treatment at different facilities before coming to our hospital, where laser irradiation was unsuccessfully applied to residual cancer. The remaining patient is still receiving laser therapy. This patient is currently also taking anti-ulcer drug therapy. Eight patients, including the two who underwent gastrectomy, resigned from work because of poor health. Five other patients died of other diseases. PS was rated as 0–1 in 21 patients, and 2 and 3 in three patients each. Dietary intake and frequency of meals were similar before and after laser irradiation for all but four patients: three with a PS scale of 3 and one with a scale of 2.

Discussion

On the basis of numerous surgical data, favourable postoperative outcome in terms of survival is currently expected in cases of early oesophageal and early gastric cancers.[15–17] In an effort to obtain a better QOL for the patient, less invasive treatment has become more commonly adopted for such cancers when there is a low possibility of accompanying metastatic lymph nodes.[18 19]

Endoscopic treatment is one such treatment option in gastrointestinal oncology, and its therapeutic efficacy is now being evaluated from various perspectives, including that of QOL.

Although we refer to QOL in general terms, what one person finds acceptable another may not. For this reason, the 'quality' of the patient's life is usually assessed by doctor(s) in terms of given items for checking the patient's daily life. In this study, we tried to assess changes in the patient's quality of life and degree of contentment in a simple and objective manner, focusing our attention on three main items – that is, symptoms, meals, and work – while also taking into account PS, medication, and duration of treatment.

The QOL of patients who have undergone surgery for gastric cancer has been studied by Habu *et al*,[20] who compared the postoperative life among patients in relation to the type of operation (distal gastrectomy, total gastrectomy), presence/absence of combined resection, extent of lymph node dissection, and presence/absence of thoracotomy. According to their report, poor results were characteristic of patients who underwent total gastrectomy, combined resection, and group 2 lymph node dissection. They also concluded that resolution of complaints such as heart burn, abdominal pain, diarrhoea, oesophageal regurgitation, a sensation of postprandial fullness, palpitation, excessive gas, and fatigability was significant in improving the patient's QOL.

In addition, focusing attention on the surgical results in elderly patients in their 70s or older, Habu *et al*[14] investigated their postoperative lives and found that, although combined resection of other organs or group 2 or more extensive lymph node dissection was comparatively rare in these elderly patients, the postoperative employment rate was considerably reduced even when there was no sign of recurrence, with 40% of patients who had been working before surgery retiring after surgery. Patients with a PS of 0 accounted for 79% of the total preoperatively, but only 56% postoperatively, a significant decrease.

Interestingly, the rate of those who retired from their jobs reached 9% even in their 145 patients under 70s, 65% of whom were at histological stage I. In contrast, no patients retired from work after EMRC and six of 32 resigned from work because of poor health after laser therapy.

Furthermore, endoscopic treatment of early gastric cancer[21–23] is expected to fully restore the patient's PS and QOL to the preoperative levels. Such treatment is ideal for this group of patients when properly indicated.

The mean period of hospitalisation in recent patients with oesophageal lesions was eight days when endoscopic mucosal resection was performed under topical anaesthesia. Although mucosa protecting and antacid agents were always given, the overwhelming majority had no postoperative symptoms, which obviated the use of any sedative or analgesic agent. The level of PS and dietary intake were also favourable.

In patients with gastric lesions, despite the fact that the artificial ulcer measured 3 cm or more in about 29% of all such patients, postoperative symptoms such as epigastric pain were found in just five patients, although H_2 receptor antagonists, antipepsin, and antacid agents were usually given. PS and dietary intake have also been as favourable as in patients with oesophageal lesions.

Recently, laser therapy has been frequently applied in cases of early gastric cancer in which surgery is not possible for some reason, rather than in cases of absolute indication aimed at cure. The greatest advantages of this therapy are its ability to reach the deeper layer of the submucosa and its effectiveness in haemostasis, which make complications extremely rare and enable divided and repeated irradiation to be performed in an outpatient clinic.

We have carried out laser irradiation in 33 lesions, and encountered no serious complications in any patient. Postoperative symptoms were present in only two patients, resulting in favourable QOL.

Indications for endoscopic treatment of early oesophageal and early gastric cancers are now being established on the basis of data obtained through clinicopathological studies of patients with such cancer who have been surgically resected.[6 7] Indeed, this treatment, when carried out with full informed consent, results in a favourable healing process and good QOL (in terms of PS, dietary intake, work, and drug therapy), with an extremely low incidence of postoperative complaints. The non-invasive nature of this treatment leads us to expect that it will be indicated more extensively as a first choice treatment for these cancers, securing a favourable prognosis at least over the period of follow up in this study.

In view of the fact that thoracotomy is not without risk, this method is of particularly great significance for patients with oesophageal lesions, serving both as a total biopsy procedure and an early cancer treatment.

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