

Short- and Long-Term Results of Endoscopic Laser Therapy for Gastric Tumors

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Abstract: The efficacy of endoscopic laser irradiation for gastric tumors was evaluated on 130 patients. The patients consisted of 51 cases with advanced cancer, 30 with early cancer, 33 with adenoma and 16 with hyperplastic polyp. In 14 of 22 patients with advanced cancer complicated by stricture of the cardiac region, palliation of the stricture was successfully obtained by laser therapy. The survival rate of patients who obtained an effective improvement of the stricture was greater than that of the patients without palliation. Moreover, relief of the stricture enabled the patients to acquire a better quality of life. Significant tumor reduction by the laser did not affect the survival rate. As for early cancer, 12 of the 30 patients were cured by laser therapy. Adequate eradication of early cancer was possible in lesions of 10mm or less in diameter, which were confined to the mucosal layer with differentiated type of histology, and were without ulcer. The indication of curative laser irradiation should be restricted to highly selected patients, and careful follow-up study by repeated endoscopic examination is required. Adenomas were eradicated in 29 of 33 patients. However, cancer developed within a few years of the laser therapy in 3 of these, possibly indicating an adverse effect of the laser.

Recently in Japan, endoscopic mucosal resection (EMR) has become the preferred treatment for early cancer and adenoma. Laser therapy, however, is useful when EMR is impossible because of the location or size of lesions, and when the lesions remain after EMR.

Key Words: Endoscopic laser therapy, gastric cancer, gastric adenoma

Introduction

Lasers have numerous medical applications. Endoscopic laser therapy has become widespread in Japan since its introduction in 1978, and its main application has been the destruction of tumors in the gastrointestinal tract, and for hemostasis. Having passed through an era of "laser fever", a discreet assessment should be made on the efficacy of endoscopic laser therapy at present.

The aim of this study is to evaluate the short-and long-

term effects of laser therapy on gastric tumors, performed at four institutes over the past 8 years.

Patients and Methods

1. Patients

The series was comprised of 130 patients with gastric tumors, including cancer, adenoma and polyp, who received endoscopic laser irradiation between 1983 and 1990. There were 79 males and 51 females, with a mean age of 72.1 years (range 25 to 87). The patients consisted of 51 cases with advanced cancer, 30 with early cancer, 33 with adenoma and 16 with hyperplastic polyp (Table 1).

All of the patients with gastric cancer underwent staging to determine the resectability of the diseased stomach, and most were rejected for surgery on the basis of the investigative findings and/or other serious contraindications. Three patients with early cancer obstinately refused surgery in spite of relatively low risk. Thirteen patients with early cancer and 2 patients with advanced cancer underwent gastrectomy following laser irradiation.

Definitions and classifications of early gastric cancer were in accordance with the criteria of the Japanese Gastroenterological Endoscopy Society. The histological grading system of atypism in gastric biopsy (Group I to V) was applied according to the General Rules for the Gastric Cancer Study in Surgery and Pathology of Japanese Research Society for Gastric Cancer¹⁾. The depth of mural invasion of the cancer was determined by histological examination in surgical cases following irradiation or was assessed from radiologic and endoscopic findings before therapy in cases treated by laser irradiation only.

Table 1. Patients with Gastric Tumor Who Received Endoscopic Laser Therapy

Gastric Lesions		No. of Patients
Advanced cancer		
Borrmann	I	8
Borrmann	II	4
Borrmann	III	29
Borrmann	IV	10
Total		51
Early cancer		
Type	I	2
Type	IIa	10
Type	IIa + IIb	1
Type	IIc	16
Type	IIc + IIa	1
Total		30
Adenoma		
Group	II	1
Group	III	29
Group	IV	3
Total		33
Polyp		
Hyperplastic polyp		16
Total		130

2. Laser Irradiation

Nd: YAG laser (Moletron, Model 8,000) was used for coagulation of gastric tumors with a guide fiber through the working channel of a gastrofiberscope. A non-contact or contact method of laser irradiation was employed. In the non-contact method, the power range was set at 40 to 80 watts and the tip of the guide fiber was maintained at a distance of 5 to 10mm from the target lesions. In the contact method, the power range was set at 10 to 30 watts. Most cases with advanced cancer received additional chemotherapy with antineoplastic agents. In 2 patients with early cancer and 1 patient with Borrmann I type advanced cancer, antecedent polypectomy or strip biopsy²⁾ was performed before laser therapy.

Result

1. Advanced gastric cancer

The main aim of laser therapy for advanced cancer was improvement of the cancerous stricture of cardiac region in 22 patients (Table 2), and tumor reduction in 29 patients (Table 3). No complication was seen except for in one patient with continuous bleeding after the laser therapy which required operation.

Clinical efficacy as to the improvement of the cancerous stricture was evaluated as follows: effective; improvement of food passage for a duration of more than 2 weeks, and non-effective; no improvement of food passage, with no

Table 2. Background Characteristics of Patients Who Received Laser for Improvement of Stricture

Characteristics	effective group (n=14)	non-effective group (n=8)
Median age, yr	73.1 ± 12.4	67.8 ± 9.0
Sex		
Male	13	5
Female	1	3
Stage of disease		
~ III	6	2
IV	8	6
Gross appearance		
Localized type	2	0
Diffuse type	12	8
Size, mm	47.1 ± 7.3	51.4 ± 9.0
Histologic type		
Differentiated	4	2
Undifferentiated	8	6

Localized type: Borrmann I and II, Diffuse type: Borrmann III and IV. Differentiated: well and moderately differentiated adenocarcinoma, Undifferentiated: poorly differentiated adenocarcinoma and signet-ring cell carcinoma.

Table 3. Background Characteristics of Patients Who Received Laser for Tumor Reduction

Characteristics	effective group (n=8)	non-effective group (n=21)
Median age, yr	72.2 ± 9.6	68.2 ± 16.8
Sex		
Male	7	11
Female	1	10
Stage of disease		
~ III	4	6
IV	4	15
Gross appearance		
Localized type	5	5
Diffuse type	3	16
Size, mm	38.1 ± 11.9*	56.7 ± 29.6*
Histologic type		
Differentiated	8	9
Undifferentiated	0	12

significance: *, $p < 0.05$, **, $p < 0.01$

relief of the stricture. Laser therapy was effective in 14 of 22 patients. In those cases, relief of the stricture and passage of food were maintained for periods ranging from several months to 3 years after the initial irradiation (Fig. 1). As for tumor reduction, efficacy was evaluated as follows: effective; reduction in tumor volume of more than 50%, and non-effective; a reduction of less than 50%. Laser therapy for tumor reduction was effective in 8 patients and non-effective in 21.

To assess whether the prognosis was influenced by the outcome of the laser therapy, survival rates of the effective group and the non-effective group were statistically compared using the Kaplan-Meier method and the generalized Wilcoxon test. Characteristics of the patients of both groups were compared statistically by the chi-square test,

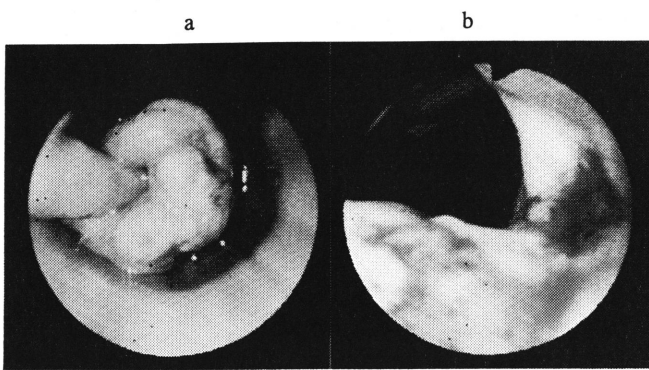


Fig. 1. a) Advanced gastric cancer complicated by stricture of the cardiac region.
b) Palliation of the stricture was obtained by repeated laser irradiation.

Fisher's exact test and student's t-test. In regard to improvement of the stricture, there was no significant difference in patients' age and sex distribution, stage of the disease, size and gross appearance of the lesion, or histological type, between the effective group (n=14) and the non-effective group (n=8) (Table 2). Survival rate in the effective group was greater than in the non-effective group (Fig. 2, $P < 0.05$; Kaplan-Meier method and generalized Wilcoxon test). Although statistically not significant, the former group included fewer stage IV cases (8 of 14 patients; 57.1%) than the latter (6 of 8 cases; 75.0%). Comparing only the stage IV patients, the difference in survival was not significant (Fig. 3).

As for tumor reduction, there was no difference in the characteristics of the effective group (n=8) and the non-effective group (n=21), with the exception of the size of the lesion ($p < 0.05$; T-test) and its histological type ($p < 0.01$); all 8 were of the differentiated type in the former, while 9 were of the differentiated type and 12 of the undifferentiated type in the latter group (Table 3). No differences in survival between the two groups were noted (Fig. 4).

2. Early Gastric Cancer

Thirty patients with early gastric cancer were treated by laser therapy (Table 4) with no serious complication.

Thirteen of 30 patients had an elevated type of early gastric cancer; 2 cases with type I, 8 with type IIa, 2 with aggregated type IIa and one case with IIa+IIb. Seventeen cases had a depressed type of early cancer; 16 cases with type IIc and one with type IIc+IIa.

Effects were evaluated on the basis of histological assessment of the resected stomach in the patients operated on after irradiation, and on autopsy specimens or biopsy specimens obtained by repeated follow-up endoscopy. The follow-up period of endoscopic examination ranged from 12 to 69 months, with a mean of 37.3 months.

In patients who had an operation or autopsy, a complete

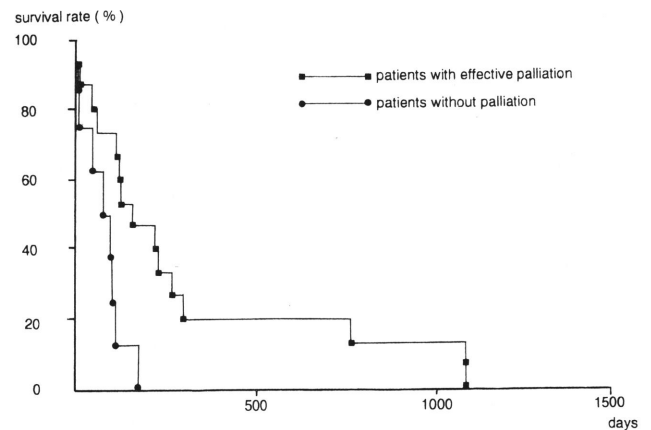


Fig. 2. Comparison of survival rates in patients who obtained effective palliation of cancerous stricture of the cardiac region and those without palliation. The former was significantly greater than the latter (Kaplan-Meier method and generalized Wilcoxon test: $p < 0.05$)

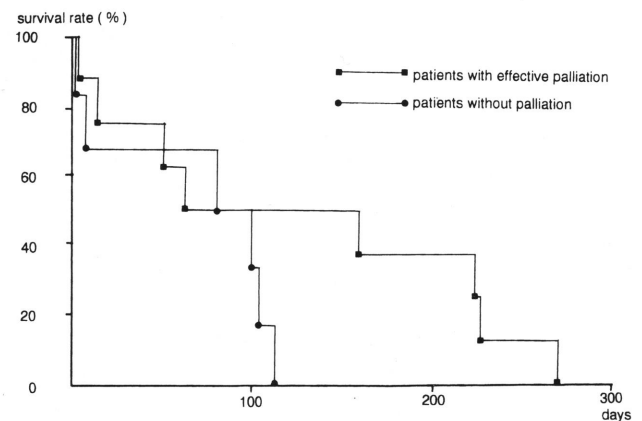


Fig. 3. Comparison of survival rates of patients with stage IV advanced cancer. There was no significant difference between the effective group and the non-effective group.

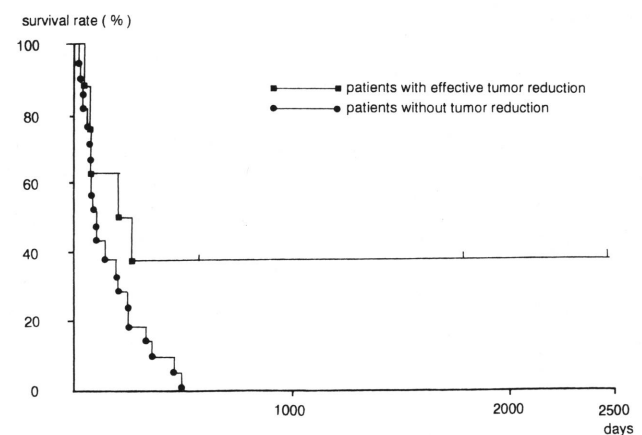


Fig. 4. Comparison of survival rates of advanced gastric cancer patients, between patients who obtained effective tumor reduction and those who did not. There was no significant difference.

Table 4. Early Gastric Cancer Treated with Laser Therapy

Case No.	Type	Size (mm)	Depth of invasion	Ulcer	Histological type	Outcome	Follow-up period
1	I	22	m	-	diff.	disappeared	48 months
2	IIa	5	m	-	diff.	disappeared	48 months
3	IIa	9	m	-	diff.	disappeared	operation
4	IIa	9	m	-	diff.	disappeared	40 months
5	IIa	10	m	-	diff.	disappeared	operation
6	IIa	10	m	-	diff.	disappeared	autopsy at 72 mo.
7	IIa	15	sm	-	diff.	disappeared	50 months
8	agg-IIa	30	m	-	diff.	disappeared	24 months
9	IIc	7	m	-	diff.	disappeared	42 months
10	IIc	10	m	-	diff.	disappeared	41 months
11	IIc	10	m	-	diff.	disappeared	30 months
12	IIc	10	m	+	diff.	disappeared	19 months
13	I	35	m	-	diff.	remained	operation
14	IIa	6	m	-	diff.	remained	operation
15	IIa	20	sm	-	diff.	recurred	12 months
16	IIa + IIb	25	m	-	diff.	remained	operation
17	agg-IIa	25	m	-	diff.	remained	operation
18	IIc	5	m	-	diff.	remained	operation
19	IIc	10	m	+	diff.	remained	operation
20	IIc	15	m	+	undif.	remained	operation
21	IIc	17	m	+	undif.	remained	operation
22	IIc	20	m	+	diff.	remained	18 months
23	IIc	25	m	-	diff.	remained	operation
24	IIc	10	sm	+	undif.	remained	operation
25	IIc + IIa	10	sm	+	diff.	recurred	69 months
26	IIc	15	sm	+	diff.	remained	operation
27	IIc	15	sm	+	diff.	remained	died at 72 mo.
28	IIc	15	sm	-	diff.	remained	operation
29	IIc	15	sm	+	diff.	remained	died at 12 mo.
30	IIc	20	sm	+	diff.	remained	18 months

agg-IIa: aggregated IIa, m: mucosal layer, sm: submucosal layer diff.: differentiated type, undif. undifferentiated type

disappearance of cancer was confirmed by histological examination of the resected stomach in 2 patients (Cases 3 and 5) and on the autopsy specimen in 1 patient (Case 6) with type IIa intramucosal cancer.

Residual cancer after irradiation was found histologically in the resected stomach in 4 patients with an elevated type of early gastric cancer (cases 13, 14, 16 and 17) and in 8 patients with a depressed type (case 18-21, 23, 24, 26 and 28). In cases with intramucosal cancer, only a small part of the cancer remained in the mucosal layer, either at the edge of the irradiated area or close to the lesion; the former, as a result of misrecognition of the tumor margin, and the latter, indicating the presence of endoscopically invisible microscopic satellite lesions. In cases with cancer invading the submucosal layer, the remaining cancer was seen either or both in the submucosal layer beneath the irradiated area and/or in the adjacent mucosal and submucosal layer.

In patients who received follow-up endoscopic study, five patients with an elevated type (Cases 1, 2, 4, 7, 8) and 4 with a depressed type (cases 9-12) with intramucosal can-

cer showed no recurrence (Fig. 5). One patient with type IIa cancer, invading the submucosal layer, showed recurrence 12 months after the initial irradiation (case 12). Five patients with a depressed type showed no disappearance of the lesion, or recurrence of the lesion soon after cessation

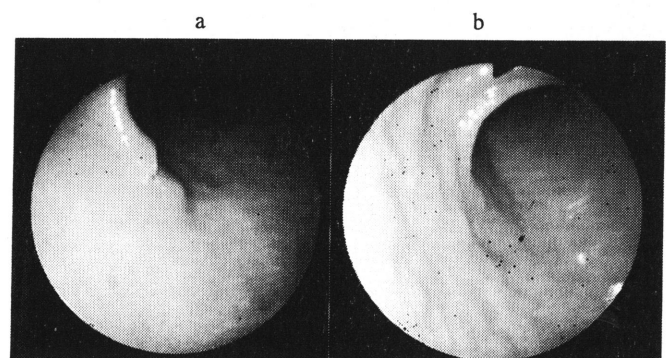


Fig. 5. a) Early gastric cancer of IIc type.
b) The lesion was completely eradicated by laser therapy.

of the laser therapy (cases 22, 25, 27, 29 and 30). One patient of these died of advanced cancer 72 months after the initial irradiation (case 27) and another patient of respiratory failure 12 months after the initial irradiation (case 29). Four patients were all alive in February 1991. Twelve of 30 patients were successfully cured by laser therapy (Table 4).

Factors relating to outcome are shown in Table 5. Residual cancer was seen in 5 of 13 patients (38.5%) with an elevated type, but in 13 of 17 patients (76.5%) with a depressed type. Among the patients with a depressed type, the residual rate was much higher in IIc cases with ulceration than in those without ulceration. The residual rate was 35.7% (5 of 14 lesions) in lesions of up to 10mm in diameter, while it was 81.3% (13 of 16 lesions) in lesions of 11 mm or more in diameter. It was 47.6% (10 of 21 lesions) in cases of intramucosal cancer, and 88.9% (8 of 9 lesions) in cases of cancer invading the submucosal layer. 55.6% (15 of 27 patients) with a differentiated type of adenocarcinoma (well and moderately differentiated adenocarcinoma) showed residual lesions. In contrast, all 3 cases with an undifferentiated type (poorly differentiated adenocarcinoma and signet-ring cell carcinoma) had remnant foci of cancer.

Table 5. Factors Relating to Outcome

Factor	No. of cases	Residual cancer	
		No.	%
Gross appearance			
elevated type	13	5	38.5
depressed type	17	13	76.5
(without ulcer)	(6)	(3)	(50.0)
(with ulcer)	(11)	(10)	(90.9)
Size of lesion			
~10mm	14	5	35.7
11~20mm	10	9	90.0
21~ mm	6	4	66.7
Depth of invasion			
m	21	10	47.6
sm	9	8	88.9
Histologic type			
differentiated	27	15	55.6
undifferentiated	3	3	100.0

3. Gastric adenoma

Thirty-three patients with gastric adenoma were treated by laser endoscopy (Table 1). This series consisted of one patient with a Group II lesion, 29 patients with Group III lesions and 3 with Group IV lesions. All lesions were eradicated by laser therapy with the exception of 3 Group III lesion cases, in which cancer developed 1-3 years after irradiation, and in another Group III patient, who is still undergoing laser therapy, whose lesion shows aggregated

multiple nodular appearance. For that patient, it was difficult to eliminate the lesion completely because the tumor margin was obscure.

4. Gastric polyp

Sixteen hyperplastic polyps in 16 patients were treated and eradicated by laser therapy (Table 1).

Discussion

The aims of endoscopic laser therapy for advanced gastric cancer are to improve local symptoms and the patient's quality of life with minimal morbidity and mortality. ND; YAG laser has been used for improvement of stricture and tumor reduction. It has proved to be sufficiently useful for the relief of cardiac stricture^{3,4}. In this study, in patients with advanced cancer complicated by the cardiac stricture, ND: YAG laser provided successful palliation in 63.6%. Our experience is in agreement with that of other groups who have reported success rates in similar patients, although our figure was slightly lower than the others. Saifuku et al⁴ reported that 87% of patients with stricture showed an improvement in food passage and prolongation of survival as a result of laser therapy. In our study, survival rates were compared to evaluate whether the outcome of laser therapy for palliation of the stricture had influence on the prognosis. Survival was greater in patients with successful palliation than in those without palliation. This difference, however, was not great, because the p-value was between 0.01 and 0.05. In addition, comparison between those patients with stage IV disease alone revealed no significant difference. Nevertheless, symptomatic palliation was maintained by repeated treatment in a considerable number of patients and we are convinced that the laser therapy provided a better quality of life in those cases. In contrast, the outcome of the therapy in regard to tumor reduction did not affect the prognosis, although there were statistical differences in some of the characteristics of the two groups. However, one patient with Borrmann I type advanced cancer who showed a marked regression of the tumor still survives 5 years after the laser therapy. Our results, and the experience of others, indicate that endoscopic laser therapy generally provides good palliation by debulking tumors and recanalizing the lumen and is easy to repeat.

The efficacy of laser therapy in early gastric cancer has been described by many authors and curative rates of 43-84% have been reported in the literature^{5,6,7}. Our experience showed a relatively lower curative rate. In our study, 40.0% of early gastric cancer was curable by laser therapy. In cases of intramucosal cancer with a differentiated type of histology, and those of 10mm or less in size, the curative rate was 72.7%. Of those cases, the

curative rate was 83.3% in patients with IIa type lesions, 75.0% in those with IIc type lesions without ulceration, and 50.0% in those with IIc lesions with ulcer.

Histological study on the resected stomach after laser therapy revealed that cancer was not completely eradicated for the following reasons: (1) misjudgement of tumor margin, (2) misrecognition of the surrounding IIb lesion, (3) failure to find microscopic satellite lesions which are invisible by endoscopic and gross observation. These factors seem to be unsolvable even by endoscopy using the dye-spraying method. Only careful endoscopic follow-up study can resolve the problems.

The literature^{3,9)} and our experience indicate that laser irradiation usually achieves a cure in cases of early gastric cancer, if the histology is differentiated and the lesion is confined to the mucosal layer, without lymphnode metastasis. To satisfy these conditions, it is necessary to find lesions while they are as small as possible and to make an accurate diagnosis of the depth of cancer invasion. At present in Japan, with the progress in endoscopic technique, detection of small or minute gastric cancer is no longer uncommon. Recently, endoscopic ultrasonography (EUS) has been introduced to evaluate the depth of cancerous invasion; accuracy of the diagnosis, however, remains 70-80% with this method^{9,10)}. Endoscopic mucosal resection provides more accurate information of the mural invasion by means of histological examination of the resected specimen. Detection of small lymphnode metastasis is extremely difficult even when using EUS in addition to CT and MRI. Oguro et al⁹⁾ reported that lymphnode metastasis was not seen in the lesions of intramucosal well-differentiated adenocarcinoma of type I, type IIa, type IIb lesions, or of type IIa + IIc lesions of 20mm and less in size; and stated that the lesions are good candidates for laser therapy, with the complete eradication of early gastric cancer possible in such cases. However, Ezaki¹¹⁾ reported two extremely rare cases of differentiated intramucosal gastric cancer, of 5mm in size, with gross appearance of IIb and IIc respectively, which showed lymphnode metastasis. Indication for the therapy for the curative treatment of early gastric cancer should be restricted to highly selected patients, whose operative risks are thought to be fair. Our experience, and the literature, suggest that an indication in such cases is as follows: (1) gross appearance; I, IIa and IIc without ulcer, (2) size; 10mm or less, (3) depth of invasion; confinement to mucosal layer, and (4) histologic type: differentiated. In high risk patients, the indication can be extended to some extent.

Gastric adenoma was successfully eradicated in 29 out of 33 patients in this study. Three cases with Group III lesions developed cancer within a few years of the therapy. An adverse effect of laser irradiation has been reported in the literature, in which the author described two cases with atypical cell nests which developed cancer, and one case with IIa + IIc type early cancer which grew rapidly to

advanced cancer soon after laser therapy. He advocated familiarity with this effect when using laser. In the above mentioned 3 cases in our study, however, we cannot be sure whether the original lesions included foci of carcinoma or developed into carcinoma later. Group III lesions have been the source of much controversy. According to Takemoto¹²⁾, the final diagnosis based on strip biopsy specimen was carcinoma for 70.5% of group III lesions and 91.7% of group IV lesions.

As for gastric polyps, snare polypectomy is greatly superior to laser therapy, and therefore its efficacy is not discussed here.

The two main disadvantages of the laser in the treatment of early gastric cancer and adenoma are their high price and the lack of total histology of the tumors. A solution to both problems is an endoscopic mucosal resection (EMR)^{12,13,14)}. Histological evaluation of total lesions is possible by means of this therapy, which makes an accurate diagnosis of cancer invasion and atypism of border-line lesions. The number of patients undergoing laser therapy for early cancer and adenoma has been declining over the past three years at our institutes, since we prefer mucosal resection to the laser. Laser irradiation, however, is recommended if the size of lesions is larger than 10mm and if piecemeal resection is required¹⁵⁾. Furthermore, the laser is useful for the eradication of residual lesions after a mucosectomy.

Conclusion

Endoscopic laser therapy appears to be the most effective therapy for advanced gastric cancers with cancerous stricture of the cardiac region. Successful palliation of the stricture provided prolongation of survival rates and a better quality of life. The laser is also effective in eradicating tumor tissue in patients with intramucosal cancer, who are poor surgical risks.

Recently, EMR has become the procedure of preference for treatment of early gastric cancer and borderline lesions. Laser therapy is recommended, however, when this approach is impossible or when tumor tissue is not completely eradicated by EMR.

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