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Low-power laser therapy for gastrointestinal neoplasia

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Abstract: The purpose of this study was to evaluate changes in the degree of neoplasia-induced stenosis and clinical symptoms before and after therapy with a contact low-power neodymium yttrium aluminum garnet (Nd:YAG) laser. Fifty patients with pathologically proven gastrointestinal (GI) neoplasia were studied; 21 with benign lesions and 29 with malignant tumors. The low-power contact Nd:YAG laser was applied toward the lesion, using an antegrade method as the scope was moved circumferentially and downward along the length of the lesions, step-by-step. The energy of the laser was 20 W, with a duration of 1 to 2 min for each shot. Either the tumor was eradicated completely, or the neoplasia-induced stenosis was recanalized by laser via the endoscope. All benign lesions were completely remitted by laser therapy. The clinical symptoms in the 29 patients with malignant GI neoplasia showed a significant improvement ($P < 0.001$; Wilcoxon matched-pairs signed-rank test, one-tailed) after laser therapy in comparison with the symptoms before treatment. Malignant GI stenosis treated by laser resulted in recanalization in 93.1% of the 29 patients. Unfortunately, in 1 patient with gastric cancer, the disease progressively worsened after treatment. One of 3 patients with early cancer of the stomach who received laser therapy was found to have distant metastasis 2 years later. A patient with esophageal cancer developed an esophagobronchial fistula that was not a direct complication of the laser effect. Four patients with malignancies died of cancer progression during the 2 years of follow-up. We conclude that the low-power contact laser is a safe, convenient method for the treatment of both benign and malignant tumors. Patients with advanced obstructive lesions have a better quality of life after laser therapy.

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Introduction

Surgical resection is usually the treatment of choice for gastrointestinal (GI) tumors. However, patients with advanced obstructive GI cancer, especially with lymph node or organ metastasis, are not good candidates for aggressive treatment, including surgery. A low survival rate has been noted for these patients, and the operative mortality increases with age.[1,2] An operation is not strongly indicated for small benign lesions in the GI tract. There are a number of suggested therapeutic indications for neodymium yttrium aluminum garnet (Nd:YAG) laser in the management of GI problems, including ulcer hemostasis, tumor removal, and recanalization of tumor obstruction. Endoscopic high-power laser therapy has had palliative effects by recanalizing tumor-induced stenosis[3–9] and curing small lesions. However, many disadvantages, such as chest discomfort or pain during laser treatment, and the high cost of the procedure, need to be resolved. The low-power contact laser was developed in 1983 and its primary outcomes have been encouraging.[10–13]

This study evaluated the changes in tumor size and clinical symptoms before and after therapy with a contact low-power Nd:YAG laser.

Patients and methods

Patients (Tables 1 and 2)

Fifty patients, 21 with benign lesions and 29 with malignant tumors, were recruited as study subjects. There were 10 men and 11 women in the group with benign lesions. The mean age in the benign lesion group

Table 1. Age, sex, and location of tumor in 50 patients with gastrointestinal tract tumor

	Benign (n = 21)	Malignant (n = 29)
Age (years), average	56.2	73.0
Range	20–86	58–86
Sex Men/women	10/11	22/7
Tumor location		
Esophagus		
Upper-third	2 (polyp,[a] 2)	1 (1)[d]
Middle-third	1 (polyp,[a] 1)	6 (6)[d]
Lower-third	8 (polyp,[a] 4; papillary, 3; stricture, 1)	7 (4)[d]
Stomach		
Cardia	1 (polyp,[a] 1)	6
Body	2 (polyp,[a] 1; leiomyoma, 1)	3
Body and antrum	1 (polyp,[a] 1)	1
Antrum	3 (polyp,[a] 2; leiomyoma, 1)	5
Duodenal bulb	2 (lymphoid hyperplasia, 2)	0
Rectum	1 (polyp,[a] 1)	0
Clinical features		
Abdominal discomfort or dyspepsia	20	3
Epigastric fullness or vomiting	1	6
Dysphagia	0	20[b]
Chest pain	0	16[c]
Laser energy used: total (Joules)	20510.0	241918.0
Average (Joules)	976.7	8342.0

[a] Polyp, polypoid lesions
[b] 14 patients with cancer in esophagus (upper-third, 1; middle-third, 6; lower-third, 7); 6 patients with cancer in stomach (cardia)
[c] 13 patients with esophageal cancer; 3 patients with gastric cancer
[d] 11 patients with squamous cell carcinoma of esophagus and another 3 patients with adenocarcinoma of esophagus (lower-third)

Table 2. Pathological findings in 50 patients with gastrointestinal tract tumors

	Benign n	Malignant n
Polypoid lesions[a]	13	0
Papillary tumor	3	0
Leiomyoma[b]	2	0
Benign stricture	1	0
Lymphoid hyperplasia	2	0
Squamous cell carcinoma	0	11
Adenocarcinoma	0	18[c]
Total	21	29

[a] Polypoid lesions
Esophagus, fibrovascular polyp, 1; granular cell tumors, 3; inflammatory fibroid polyp, 3
Stomach, hyperplastic polyp, 2; adenomatous polyp, 2; heterotopic pancreas, 1
Rectum, adenomatous polyp, 1
[b] Involved layer, submucosal layer; size, one was 2 mm in diameter, the other, 4 mm
[c] Including 3 patients with early cancer of the stomach and another 3 patients with adenocarcinoma of esophagus (lower-third)

was 56.2 years (range, 20 to 86 years). The types of benign lesions were: polypoid lesions in 13 patients, papillary tumors in 3, leiomyomas in 2, a benign stricture in 1, and lymphoid hyperplasia in 2. There were 22 men and 7 women in the malignant tumor group. Their mean age was 73 years (range, 58 to 86 years). All of the benign and malignant lesions were proven by pathological examinations. The benign lesions were located in the esophagus in 11 patients, the stomach in 7, the bulb of the duodenum in 2, and the rectum in 1.

The locations of 11 esophageal squamous cell cancers were in the upper-third of the esophagus in 1 patient, the middle-third in 6, and the lower-third in 4. Eighteen patients had adenocarcinoma (at the lower end of the esophagus in 3 patients, the cardia of the stomach in 6, the body of the stomach in 3, the body and antrum of the stomach in 1, and the antrum of the stomach in 5. The presenting symptoms on admission were abdominal discomfort or dyspepsia in 23 patients (20 with benign lesions; 3 with early cancers) and epigastric fullness or vomiting in 7 patients (1 with benign lesion; 6 with malignant tumors). Dysphagia was noted in 20 patients with malignant tumors (14 with tumors in the esophagus; 6 with tumors in the cardia of the stomach). Chest pain was the complaint in 16 patients with malignant tumors (13 with tumors in the esophagus; 3 with tumors in the cardia of stomach) (Table 1).

Methods

An upper panendoscope (GIF XQ-10 or GIF P-10; or a sigmoidoscope [ITS] from Olympus Tokyo, Japan) and

a neodymium yttrium aluminum garnet (Nd:YAG) laser machine (Messerschmitt-Bolkow-Blohm (MBB), Munich, Germany), were used. The contact laser probe used for tumor treatment was available from Japan. The laser power was directly applied as 20 W to the tumor, and the duration for each shot was 1 to 2 min. The laser power was delivered through a single flexible quartz fiber enclosed by a Teflon sheath. A water system helped to cool the fiber tip, remove debris, and reduce adherence of the contact probe. All treatments were accomplished in a single session. Destroyed tumor tissue was removed either with a biopsy forceps or by pushing it down to the stomach as much as possible if the lesion was from the esophagus. The patients were clearly informed of all treatment procedures by the endoscopist and consented to participate before enrolling in the study.

The treatment was performed with the patient under topical anesthesia. The tumor location was visualized by endoscope. The laser catheter with a contact probe was inserted to reach the lesion by way of the biopsy channel of the endoscope, and then the laser therapy was carried out under direct vision. The laser treatment was started at the proximal portion of the tumor in a circumferential fashion, and then proceeded along in the direction of the tumor in an antegrade fashion, with the endoscopist proceeding carefully, step-by-step. The laser-guide probe was introduced into the narrowing lumen if the direction of the tumor was not apparent. The treatment was continued until either the small lesion was removed completely, or the narrow lumen was reopened sufficiently to permit passage of the endoscope via the stenotic tumor area. Endoscopic observation was needed for 5 to 7 days after the initial treatment, and determination of the necessity to repeat treatment depended on the therapeutic result achieved with the laser, shown during the 2 years of follow up.

A barium meal X-ray study and endoscopic examination for evaluation of the condition of the tumor, including tumor size, location, surrounding tissue, and the length and degree of the tumor stenosis, were conducted for each patient before and after laser treatment. The amelioration of the clinical symptoms of dysphagia was blindly graded, with a subjective scale from A to E, by modified classification from Sankar et al. report.[13] A patient was judged as grade A before or after treatment if the patient was able to eat a normal or solid diet without any complaints. Grade B was assigned if the patient was able to take a semiliquid diet well. Grade C meant the patient was able to eat thick liquid or fluid food without difficulty. If the patient was limited to drinking a liquid diet or water only, and if he or she had frequent vomiting, the dysphagia was judged to be grade D. Grade E meant that the patient's laser therapy was unsuccessful. The efficacy of laser therapy was evaluated by comparing the grading before and after laser therapy. Objective evaluation of the success of the treatment was accomplished in terms of the introduction of a large endoscope (over 9 mm in diameter) that passed through the narrow lumen smoothly, and/or in terms of alleviating or resolving the symptoms of clinical obstruction. Statistical analysis was performed by the Wilcoxon matched-pairs signed-rank test, one-tailed, and the McNemar χ^2 test, one tailed.

Results

All lesions in the benign lesion group resolved after treatment with the low-power laser. No patients developed hemorrhage, perforation, or recurrence. The malignant stenosis of the middle-third of the esophagus in 1 patient was more than 15 cm in length. The length of the stenosis of the other malignancies was 10 to 15 cm in 6 patients, 5 to 10 cm in 8 patients, and less than 5 cm in 14 patients (including 3 with early gastric cancers) (Table 3). Seven patients with esophageal cancer, 2 patients with cardia cancer of the stomach, and 3 patients with early cancer of the stomach (originally, 4 with grade A, 6 with grade B, and 2 with grade C) had a grade A response after laser therapy. A grade B response to laser therapy was found in 6 esophageal and 9

Table 3. Length involved by malignant stenosis in gastrointestinal tract

Length of stenosis (cm)	*n*	Percentage	Location						
			Esophagus			Stomach			
			(U/3	M/3	L/3)	(C	B	B&A	A)
<5	14	48.3	1	0	2	3	2	1	5
5–10	8	27.6	0	1	4	1	1	1	0
10–15	6	20.7	0	4	1	1	0	0	0
>15	1	3.4	0	1	0	0	0	0	0
Total	29	100.0							

U/3, upper-third; M/3, middle-third; L/3, lower-third; C, cardia; B, body; A, antrum

Table 4. Evaluation of clinical symptoms in patients treated by low-power laser therapy for GI malignant neoplasia

Before treatment *n*	Grade of symptoms	Grade after treatment* *n* (grade before treatment)
4	A	12 (A, 4; B, 6; C, 2)
9	B	15 (B, 2; C, 11; D, 2)
13	C	2 (B, 1; D, 1)
3	D	0
0	E	0

*Significant difference between before and after laser therapy, by Wilcoxson matched-pairs signed-rank test, one-tailed ($P < 0.001$)
A, The patient is able to eat a solid or normal diet
B, The patient is able to take a semiliquid diet smoothly
C, The patient is able to drink water or fluid food well
D, The patient has difficulty in swallowing a liquid diet and has frequent vomiting
E, The patient fails to swallow any food and has vomiting

Table 5. Evaluation of degree of malignant stenosis in GI tract before and after laser therapy

Degree of stenosis	*n*	Percentage
Stenotic lumen passible by endoscope		
Before treatment	19*	65.5
After treatment	27*	93.1
Stenotic lumen impassible by endoscope (lumen < 9 cm)		
Before treatment	10	34.5
After treatment	2	6.9

*$P < 0.05$ by χ^2 test, one-tailed, which compared findings before and after treatment

gastric cancer patients (originally, 2 with grade B, 11 with grade C, and 2 with grade D). Two patients, 1 with esophageal cancer with grade B and 1 with stomach cancer with grade D had grade C responses to laser therapy (Table 4). Although the tumors in 4 grade-A patients and 2 grade-B patients showed no change in grade after laser therapy, the patients' symptoms were greatly alleviated after treatment.

Two of 3 patients with grade A early gastric cancer (1 body, 1 antrum) achieved complete remission during 2 years of follow-up after laser therapy. Nodal metastasis was found in another patient during an operation 2 years later, and that patient's condition declined, with final death of the disease. Two-thirds (66.7%) of patients with grade B tumors ($n = 6$) progressed to a grade A response, showing an improvement of one grade. Unfortunately, one patient with a grade B tumor showed a worsening of one grade, to grade C (11.1%). Two of 13 patients in grade C (15.4%) progressed to grade A, with an improvement of two grades, after laser therapy. Eleven patients in grade C (84.6%) progressed to a grade B response, a one-grade improvement. Two-thirds of patients with grade D tumors (66.7%) progressed to a grade B response, a two-grade improvement. One-third of patients with grade D tumors (33.3%) progressed to a grade C response, with a one-grade improvement. There were no patients with failure to respond (grade E) after laser therapy.

Although the degree of improvement was not equally distributed among the tumor grades (22 [76%] improved, 6 [21%] showed no change, and 1 worsened, the clinical symptoms showed a significant improvement ($P < 0.001$) after laser therapy in comparison with symptoms before therapy (Table 4). In 27 patients with malignant stenosis (93.1%), the endoscope passed through the stenotic lumen after treatment, a significant difference compared with passage in 19 patients before treatment ($P < 0.05$) (Table 5). Of the 2 other patients with malignant stenosis (6.9%), 1 had grade D, with one grade of symptomatic improvement and 1 had grade B, with one grade of worsening after treatment. In 10 patients, the stenotic lumen was less than 9 mm in diameter and was impassable by the endoscope before laser treatment.

One patient with squamous cell carcinoma in the upper-third of the esophagus had a grade B response after laser therapy, but developed an esophagobronchial fistula during follow-up. His condition was good under conservative management. A patient with antral cancer of the stomach developed a high fever after treatment that may have been secondary to transient bacteremia during the laser procedure. Four patients, including two with a grade D response, died of the cancer itself. There were no instances of perforation or hemorrhage during or after laser management. The average laser energy used for the treatment of these lesions was 977 joules in the benign lesion group and 8342 joules in the malignant tumor group.

Discussion

In our study, all benign lesions of the GI tract achieved complete remission after laser treatment with the low-power contact method. A surgical operation for a small lesion may entail some problems, such as adhesions and intestinal obstruction. Van Stolk et al.[14] and Sander and Posel[15] reported that was possible to remove polypoid or sessile lesions of the GI tract with a heat probe, a bicap probe, or a hot or snare polypectomy. High-power laser is able to provide a good result for small lesions, but a risk of damage to normal tissues surrounding the target lesion may exist because of the high-power laser effect. High cure rates for benign colon adenomas have been reported with laser therapy in many studies.[16–19] Endoscopic treatment of asymptomatic non-neoplastic stenosis is one indication for high-power laser therapy. Kiefhaber[18] and Sander and Posel[20] have shown that the high-power laser is effective in opening strictures of

the GI tract caused by scarring or inflammation. The effectiveness depends on the location, extent, and cause of the stricture. Incomplete removal of adenomas or polypoid lesions by snare polypectomy or surgical local excision is an indication for laser therapy. Relief of the symptoms of extensive lesions in elderly patients is another purpose of endoscopic laser treatment. A patient with a benign pyloric ulcer stricture in our series had an excellent response to low-power laser treatment. The above excellent outcome showed the same effect as that shown in other reports.[10–13]

Electrical surgery or high-power lasers can destroy tumors in order to reopen obstructed lumens in advanced late-stage GI cancer, which, in turn, improves the patient's nutritional status. The effective rate of palliative treatment of malignant stenosis varies from 80% to 100%.[1–9,19–24] The degree of penetration and the course of destruction of GI tumors by high-power non-contact laser or electrical surgery cannot be precisely predicted.[10–13,25] The preliminary outcome of laser treatment with the low-power contact method has been, encouragingly, as effective as that of high-power laser treatment, with a low risk of complications. Low-power energy used with a contact probe can prevent the disadvantage of non-contact high-power laser therapy and electrical surgery.[10–13]

About 20% of patients complain of chest pain with a burning sensation during or after high-power laser therapy.[1,4,9,19] Our study and other reports[10,25] found that patients had less pain with a low-power contact laser. Acute perforation was a severe complication in 4% of patients receiving high-power laser therapy.[1,17,24] This complication was found much more frequently in patients who had received radiotherapy before laser management. Hemorrhage or fistula formation is not a common complication with high-power laser.[1,7,19,26] A patient with antral cancer in our series developed a high fever for 2 days after low-power laser treatment. This may have been associated with transient bacteremia during the laser procedure.[27]

Laser therapy is best applied to a mass protruding from the lumen of the GI tract or at the high cervical level in esophageal cancer.[1,9] During the follow-up period, one of our patients with cancer in the upper-third of the esophagus developed an esophagobronchial fistula which was not directly caused by the laser effect. Once the patient was found to have the esophagobronchial fistula, laser therapy was not indicated.

In our series, two patients with grade B tumors had the same grading response after laser therapy. Another patient with a grade B tumor declined to a grade C response. A patient with a grade D tumor was upgraded to a grade C response. It was not easy to perform laser therapy in these four patients with submucosal tumor, because of the approach technique. With a submucosal tumor it is also difficult to differentiate extrinsic compression from neighboring organs. If the angle of orientation of the lumen misses the protruding mass, or if the tumor segment is too long, or if patients are uncooperative, the response to laser therapy may be limited, or the therapy may even fail.[1,17,28] All three of our patients with early cancer of the stomach (one in the body, two in the antrum) had an excellent response to low-power laser therapy (100%). Two of them (66.7%) had complete remission. But one patient with cancer in the antrum developed distant metastasis 2 years later, although an endoscopic ultrasound examination had been conducted before the laser therapy. Early cancer of the stomach or esophagus may be cured if the cancer is detected as early as possible and there is no lymphatic tissue involvement.[1,12,17,21,29] Laser therapy seemed to have been effective in our patients with malignancies, with 93.1% of these patients showing clinical endoscopic improvement.

The depth of necrotic tissue produced by laser penetration can be precisely predicted by endoscopic ultrasound. Careful control of all parameters can provide the safe ablation of early cancer with a low-power contact laser and endoscope.[30–34] Photodynamic therapy (PDT) with an argon laser is another choice for treating small GI cancers. However, PDT can ablate small tumors (up to 1- to 2-cm thick) partly because red light can penetrate only a few millimeters of tissue. Another problem is the risk of delayed hemorrhage following partial necrosis of large lesions. If the main bulk of a cancer is removed by surgery, PDT may be helpful in destroying any small areas of remaining cancer.[35] Endoscopic mucosal resection (EMR) is another valuable method for treating both early gastric and esophageal cancers.[28] A metallic stent can have a palliative effect for malignant esophageal stenosis, but migration of the stent and reflux of gastric juice are still problems. The effect of the low-power contact laser combined with either EMR for early or small cancers, or metallic stent palliation for advanced obstructive GI cancers requires further evaluation.

If the patient is old, has a recurrent tumor, has a stricture after treatment, has severe cardiopulmonary problems, or refuses surgery, low-power laser palliation is indicated for advanced GI cancer with obstruction. The low-power contact laser appears to be safe and convenient, and may provide another choice of treatment for the cure of small tumors or the relief of the stenosis of a malignancy.

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