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Review

Palliative Endoscopic Therapy of Rectal Carcinoma

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Curative surgery is not feasible in a considerable proportion of patients with rectal cancer because of extensive local spread or metastatic disease. However, most of these patients require palliative treatment to improve the symptoms of the disease, e.g. obstruction, pain and haemorrhage. Palliative surgery may be associated with a morbidity of 20–40% and a mortality of more than 10%. Endoscopic procedures can provide effective palliation with less complications. Before the development of lasers, endoscopic electrocoagulation and cryosurgery were used with some success. Currently, endoscopic Nd:YAG photocoagulation must be considered the treatment of choice in non-resectable rectal cancer. Laser therapy allows effective palliation in 85–95% of the patients, and generally, treatment-related complications occur in less than 10% of the patients and mortality is negligible. Transanal endoscopic resection may be effective in selected patients. New approaches to endoscopic palliation include photodynamic therapy (PDT) and implantation of self-expanding metal stents.

Key words: endoscopy, therapy, palliation, rectal cancer*Eur J Cancer*, Vol. 32A, No. 1, pp. 25–29, 1996

INTRODUCTION

CURATIVE SURGERY can be performed in approximately 50–60% of the patients with rectal cancer, while 30–40% of the patients are not candidates for aggressive surgery because of either distant metastases, extensive local tumour infiltration, poor general condition or refusal of the patient [1, 2]. These patients require palliative treatment to ameliorate the symptoms of their disease. The rationales for palliative treatment include improvement of bowel obstruction, relief of pain, therapy of haemorrhage and prevention of ileus.

Patients with advanced colorectal cancers not suitable for radical surgery may receive surgical or endoscopic palliation. Surgical procedures for palliative treatment of rectal carcinoma basically comprise limited resection; i.e. abdominoperineal resection and anterior resection or creation of a colostomy. However, even palliative local surgery is associated with a considerable morbidity and the figures for major procedures range between 30 and 45% [3, 4]. Mortality rates as high as 17% have been reported for patients with advanced rectal carcinoma undergoing surgery [4]. Even laparotomy for a colostomy or a bypass procedure without resection of the tumour may result in a mortality rate of up to 10% [5].

Consequently, endoscopic procedures such as Nd:YAG laser photocoagulation, electrocoagulation and cryotherapy have been used as an alternative to surgical treatment. More recently, endoscopic insertion of endoprosthesis and photodynamic ther-

apy (PDT) have been evaluated for the treatment of incurable patients with colorectal cancer.

LASER THERAPY

Endoscopic laser therapy has been increasingly used for palliation in patients with advanced metastatic or non-resectable rectal cancer. The favourable features of this technique appear to be simple application, low risk of complications and a reliable therapeutic effect. Moreover, in contrast to other local techniques, endoscopic laser irradiation can be carried out above the peritoneal reflection and without general anaesthesia as an outpatient procedure.

Generally, endoscopic laser treatment is applied using a Nd:YAG (neodymium yttrium aluminium garnet) laser at 60–100 W. Usually 2–6 treatment sessions of 30–90 min duration are required to maintain adequate recanalisation of obstructing tumours, while bleeding may be stopped by a single procedure. The timing of retreatment is assessed by monthly follow-up in the hospital by proctosigmoidoscopy. Follow-up and treatment can be performed on an outpatient basis which requires regular attendance in the hospital and bowel preparation by a small enema.

Consistently, success rates of 85–95% have been reported for laser palliation of advanced rectal cancer by various authors (Table 1). In a multicentre inquiry, involving seven international laser centres, Mathus-Vliegen and Tytgat investigated the role of laser photocoagulation for palliative treatment of colorectal cancer [6]. Good palliation was obtained in 89% of 181 patients. Endoscopic laser treatment resulted in a complication rate of

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Table 1. Results of representative studies using endoscopic laser therapy for palliation of rectal carcinoma

[Reference]	Year	n	Success (%)	Morbidity (%)	Mortality (%)
Mathus-Vliegen and Tytgat [6]	1986	181	89	9	1
Brunetaud <i>et al.</i> [38]	1987	85	85	0.1	0.1
Mandava <i>et al.</i> [39]	1990	27	85	15	0
Danecker <i>et al.</i> [37]	1991	37	84	2	5
Tacke <i>et al.</i> [9]	1993	37	95	0	0

9.4% and a treatment-related mortality of 1.1%. Laser photo-coagulation proved to be effective for haemostasis and recanalisation of obstructing tumours. Tumour response, complication rate and mortality were less favourable in 81 patients with obstructing tumours. The median survival was 10 months in this group, while patients presenting with bleeding survived 24 months on average.

Overall comparable survival rates have been found for patients undergoing palliative surgery and patients receiving laser therapy [6,7]. Nonetheless, it should be remembered that endoscopic laser treatment can occasionally induce complete destruction of the malignancy. In a series of 272 patients receiving Nd:YAG laser therapy for palliation rectal cancer, negative biopsies were obtained in 37 patients at the end of the treatment [8]. After a mean follow-up of 37 months, the calculated actuarial 4 year survival was 79%.

Most data on endoscopic palliation are based on retrospective studies and only sporadic comparative studies have been performed to investigate the value of laser therapy and alternative palliative procedures. Tacke and colleagues accomplished good palliative results in 35 of 37 patients (95%) by endoscopic laser therapy, while colostomy was required in only 2 patients due to tumour progression [9]. No relevant morbidity or mortality was observed related to endoscopic treatment. Palliative surgery induced effective palliation in 41 of 42 patients (98%). Although only limited procedures were performed, surgical treatment was associated with a morbidity of 7% and a mortality of 2%.

In times of limited resources, the costs for palliative treatment may become more important for the choice of the therapeutic approach. It must be considered that surgery generally provides definitive treatment in colorectal cancer, while repeated sessions may be necessary with laser treatment. Nonetheless, it has been found that the expenses for laser treatment are significantly lower compared with surgery. Mellow and associates calculated lifetime charges of \$22 000 for surgically treated patients and \$12 000 for laser-treated patients with advanced disease [10].

Presently Nd:YAG laser therapy is considered the treatment of choice for endoscopic palliation of rectal malignancy.

ELECTROCOAGULATION

Electrocoagulation has been widely used for the treatment of small rectal carcinomas below the peritoneal reflection. The coagulation is applied either in the contact technique to fulgurate the surface of the tumour or by interstitial placement of the electrode to destroy deeper parts of the malignancy. Tumour destruction equivalent to laser vaporisation requires multiple treatment sessions with hospitalisation and general or at least regional anaesthesia [11]. Overall, a success rate with respect to sufficient palliation between 77 and 90% has been reported for electrocoagulation by most groups [11–13]. However, Hughes

and colleagues observed only poor palliation in the majority of patients treated by electrosurgery, although multiple treatments were performed in most patients [14].

Compared with Nd:Yag laser therapy, the depth of tissue necrosis is much less controlled, especially using the interstitial application technique. Consequently, serious complications including haemorrhage, rectal stenosis and perforation with subsequent septicaemia occur in up to 28% of the patients [15]. Therefore, in the last few years, other local techniques have been favoured for palliation of advanced rectal cancer.

CRYOTHERAPY

Cryotherapy involves the use of an endoscopic cryoprobe which is cooled down to a temperature of -190°C by a liquid nitrogen cooling generator. After 30–60 s, contact with the cryoprobe tumour tissue is frozen reaching temperatures between -15 and -20° . This results in necrosis to a depth of 4–8 mm. Generally, 2–3 repetitions are required before beneficial effects of the therapy occur [16].

Endoscopic cryotherapy has been evaluated in large series of patients for palliation of obstructing rectal cancer. In a series of 213 patients treated by cryotherapy, Geissler and colleagues achieved satisfactory palliation in 109 patients (51%). In spite of cryotherapy, permanent tumour progression was noted in 76 patients (28%) and 28 of these patients subsequently required a colostomy. Overall, serious complications, including fistulae, septicaemia and major haemorrhage, occurred in 18% of the patients [17]. In a recent study on 182 patients, marked reduction of the tumour size or sometimes complete eradication of malignancy were induced in 70% of the patients [18]. Satisfactory palliation with respect to obstruction was provided in most patients, while most other symptoms were not relieved sufficiently. Pain and mucus discharge were improved in less than 50% of the cases, while major haemorrhage was controlled in only 56%. Stenosis due to extensive scarring developed in 13 patients (10%) and finally colostomy had to be performed in 14 patients. In three major studies with more than 500 patients, a complication rate of 15–17% has been reported uniformly [5, 19, 20]. In one of these studies, 22% of the patients finally required colostomy due to malignant stenosis, stricture formation or perforation [20].

Overall, cryosurgery appears to be inferior to other ablative endoscopic techniques because of poorer treatment results and higher risk of complications.

ENDOSCOPIC TRANSANAL RESECTION

Excellent long-term outcome has been obtained using endoscopic transanal resection for benign tumours or early rectal carcinoma thus avoiding major surgery [21]. This minimally invasive technique has been also evaluated for palliation of rectal

carcinoma in patients with advanced disease or with poor medical condition [22].

General or at least spinal anaesthesia is required for the procedure. Transanal endoscopic resection is performed with a resectoscope and cutting loops, using a similar technique to prostate resection. However, application of this method is limited by the rigidity and the length of the resectoscope. Consequently, tumours above 20 cm are not accessible. Moreover, endoscopic transanal resection is only feasible if there is enough residual lumen to pass the resectoscope to the cephalad border of the tumour. The depth of resection can be judged by the appearance of the muscular bowel layers or the perirectal fat.

There are now sufficient data to justify the use of endoscopic transanal resection in the palliation of selected patients with advanced rectal malignancy (Table 2). In a recent series of 49 patients, symptomatic relief was achieved in 74% patients with advanced rectal cancer [23]. However, in approximately 50% of the cases, more than one procedure was required to receive and maintain satisfactory palliation. The morbidity in this series was 19% and the mortality rate 5%. Berry and associates presented encouraging results in 81 patients undergoing 137 transanal resections [24]. In 31 patients, the indication was palliative. The commonest symptoms, i.e. change of bowel habit and rectal bleeding, was markedly improved in 77 and 66% of the patients, respectively. It is remarkable that faecal incontinence was improved in 50% of the patients. Multiple resections were necessary in 36% of the patients at 3–4 monthly intervals. The most frequent complication was haemorrhage followed by intraperitoneal perforation, resulting in a complication rate of 15%. Only 4 procedure-related deaths corresponding to a mortality of 5% were noted. In conclusion, endoscopic transanal resection gives acceptable results in the palliation-selected patients with advanced rectal cancer.

STENT IMPLANTATION

Although endoscopic implantation of stents is a generally accepted method for the treatment of malignant oesophageal and biliary strictures, there is only limited experience with this technique in rectal cancer [25, 26]. Recently, encouraging results have been reported for the treatment of stenotic rectal or sigmoid carcinoma by endoscopic implantation of a prosthesis [27–29]. In contrast to most endoscopic procedures which require repeated treatment sessions after initial recanalisation, rectal endoprosthesis may prevent obstruction until death. Technically endoscopic implantation of a stent is a simple procedure that can be completed within 20–30 min (Figure 1a,b).

Spinelli and colleagues recently presented results of endoscopic palliation of 6 patients with obstructing rectal carcinoma by self-expanding mesh stents. In all patients, recanalisation was

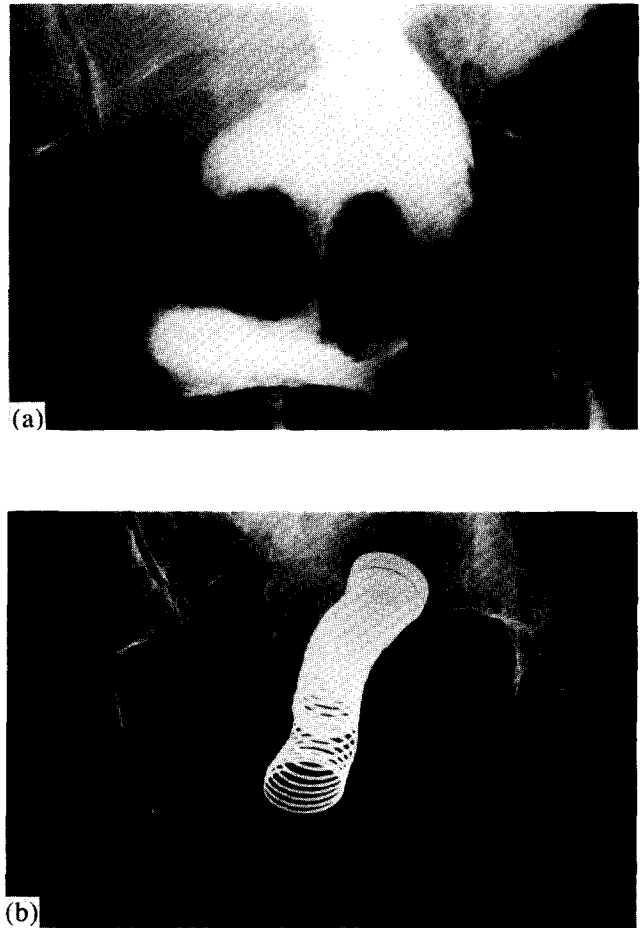


Figure 1. (a) Contrast enema showing a rectal stenosis caused by an advanced carcinoma. (b) Correct position of a self-expanding metal stent is documented by a plain X-ray. The stent is fully expanded thus maintaining a lumen of 2 cm.

achieved by the prosthesis [27]. Dohmoto and associates treated 10 patients with rectal stenosis by implantation of plastic tubes ($n = 8$) or self-expanding metal stents ($n = 2$). All patients experienced a significant relief of obstructing symptoms resulting in normal defaecation. No serious complications were observed related to the endoscopic procedure. Dislocation of the prosthesis occurred in 3 patients with plastic tubes, two of which successfully underwent reimplantation [28].

These preliminary encouraging results and the absence of serious complication justify further application of this technique. Further evaluation of the procedure will be necessary to establish the clinical value of this technique. Future studies will have to

Table 2. Results of endoscopic transanal resection for palliation of advanced rectal cancer

[Reference]	Year	<i>n</i>	Success (%)	Complications (%)	Mortality (%)
Ottrey <i>et al.</i> [22]	1986	14	71	26	7
Kurz <i>et al.</i> [44]	1988	15	80	13	0
Berry <i>et al.</i> [24]	1990	31	63	15	5
Wetherall <i>et al.</i> [21]	1993	7	71	14	0
Dickinson <i>et al.</i> [23]	1993	49	74	19	5
Fischer [45]	1994	31	80	12	0

consider the efficacy of the method with respect to the resulting quality of life as well as the costs of this treatment.

PHOTODYNAMIC THERAPY

Thermal laser treatment has been widely used for palliation of rectal malignancy by vaporisation and coagulation of the tumour. The major disadvantage of this technique appears to be the risk of perforation by colonic wall necrosis and the occurrence of severe scarring resulting in stricture formation.

Photodynamic therapy (PDT) is a new method of laser therapy which involves the activation of an intravenously applied photosensitising drug. Photosensitisers tend to accumulate in tumours and are activated at laser energy levels which do not cause damage to normal tissues. Therefore, PDT provides the opportunity for selective eradication of rectal cancer [30].

In contrast to Nd:YAG laser treatment, photodynamic therapy carries only a small risk of perforation. It has been demonstrated that the collagen layer of the colonic wall remains intact even if full thickness necrosis is caused by the treatment. Moreover, the colon affected by photodynamic therapy heals predominantly by regeneration without substantial risk of scarring [31].

So far, this new technique has been applied mainly to inoperable patients with advanced cancers. Nevertheless, complete remission of the local tumour has been reported in 35% of cases and partial remission has been achieved in 44% (Table 3). The success of treatment has demonstrated a significant correlation to tumour size. Total eradication of the tumour has only been possible in small tumours. In advanced cancers, PDT has induced a reduction of the tumour size and has been associated with a substantial relief of chronic tumour-related pain [32]. This effect may be useful in improving the quality of life of inoperable patients. Recently, Kashtan and coworkers conducted a pilot study to determine the efficacy of PDT in the palliation of advanced cancer [33]. Significant clinical improvement and radiological response to the treatment was observed in 5 of the 6 patients. There was no major complication, even at the maximum light doses.

PDT has proved to be a safe modality for the treatment of colorectal cancers [34]. There have been no severe complications except two cases of haemorrhage [31]. Skin photosensitisation is prevented by avoiding bright sunlight for some weeks.

The application of PDT may be most suitable for the treatment of small tumours or for sterilisation of areas containing microscopic residual tumour, particularly in resection margins. In

large tumours, it might be feasible to use photodynamic therapy after debulking surgery or Nd:YAG laser irradiation.

CONCLUSION

By definition, palliative therapy of colorectal cancer is performed in patients with non-resectable metastases or with locally advanced malignancy where complete excision is not possible.

In the past, surgery was the only palliative treatment option for quick and effective management of advanced rectal cancer, either by limited resection or faecal diversion using a colostomy. If feasible, palliative resection of rectal cancer may provide good relief of local symptoms. However, the mortality rate of such procedures may be as high as 17%, and there is not sufficient evidence that palliative resection prolongs survival [4]. Although a colostomy can improve the symptoms of obstruction and prevent ileus, it does not control bleeding or relieve pain. Indeed, the presence of a stoma may violate the quality of life in patients with limited life expectancy.

Local methods have been increasingly used in patients with non-resectable disease or fatal medical conditions to ameliorate distressing symptoms of colorectal cancer without major surgery or a stoma. Radiotherapy can produce local palliation in 60–70% of the patients if higher doses are used, but the response is slow and the complications increase with dose [35, 36].

Endoscopic procedures, including laser photoablation, transanal endoscopic resection, electrocoagulation and cryotherapy, warrant more rapid and reliable tumour destruction. Cryotherapy with liquid nitrogen and electrocoagulation are only applicable to very low rectal lesions. Furthermore, tissue damage caused by these techniques is difficult to control which results in a considerable complication rate. Transanal endoscopic resection can be performed for rectal tumours up to 20 cm, but requires general or at least spinal anaesthesia. The results obtained are somewhat better than those of cryotherapy or electrocoagulation.

In contrast to other endoscopic techniques, Nd:YAG laser vaporisation represents an effective method for local tumour eradication that can be applied to rectal and colonic tumours. Favourable response rates with successful palliation in 85–95% of the patients have been consistently reported [9, 37]. Generally, the complication rates are below 10% and the mortality rates below 2% [6]. Currently, endoscopic laser treatment is considered the treatment of choice in patients unsuitable for palliative resection.

There is recent evidence that PDT and endoscopic stent implantation may be suitable for palliative treatment of advanced

Table 3. Therapeutic results of photodynamic therapy in advanced rectal cancer

[Reference]	Year	n	CR	PR	NR	Maximum follow-up (months)
Spinelli <i>et al.</i> [40]	1984	3	0	3	0	13
Gatenby <i>et al.</i> [41]	1987	5	0	5	0	22
Jin <i>et al.</i> [42]	1989	10	1	7	2	51
Barr <i>et al.</i> [31]	1990	10	2	6	2	28
Herrera <i>et al.</i> [32]	1990	22	12	7	3	36
Patrice <i>et al.</i> [43]	1990	21	10	3	8	32
Total		71	25 (35%)	31 (44%)	15 (21%)	

CR, complete response; PR, partial response; NR, no response.

rectal cancer [28, 33]. Yet there is only limited experience with these procedures and further more comprehensive studies will be required to establish their clinical value.

Generally, endoscopic treatment is a safe procedure with low morbidity and mortality. Furthermore no general anaesthesia is required for endoscopic palliation which makes outpatient treatment possible. These factors can be important determinants to the quality of life in cancer patients with limited life expectancy, and provide support for the use of endoscopic treatment as a palliative measure.

Although local surgical and endoscopic procedures will be beneficial for patients with obstruction or bleeding, cachexia as well as pain from plexus infiltration and loss of sphincter function will remain unaffected. Consequently, a multidisciplinary approach including radiotherapy and chemotherapy should be considered in incurable patients with a reasonable life expectancy.

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