Bowel dysfunction after treatment for rectal cancer

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REVIEW ARTICLE

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Abstract

Introduction. Rectal cancer is a common disease in Western populations. Improved treatment modalities have resulted in increased survival and tumour control. With increasing survival there is a growing need for knowledge about the long-term side effects and functional results after the treatment. *Aim.* To describe the long-term functional outcome in patients treated for rectal cancer through a systematic review of the current literature and to provide an outline of the promising developments within this area. *Results.* Standard resectional surgery with loss of the rectal reservoir function results in poor functional results in up to 50–60% of the patients. New methods of surgery including the construction of a neoreservoir and improvement of the technique for local excision have been developed to minimize the functional disturbances without compromising the oncological result. The addition of chemo and/or radiotherapy approximately doubles the risk of poor functional results. During the last decades the techniques for chemo/radiotherapy has been markedly improved with a positive impact on functional outcome. New methods for treatment of functional disturbances e.g. bowel irrigation and sacral nerve stimulation are currently under development. *Perspectives.* To improve the functional outcome in this growing patient population several approaches can be taken. The primary cancer treatment must be improved by minimizing the surgical trauma and optimizing the imaging and radiation techniques. Population screening should be considered in order to find the cancers at an earlier stage, hereby increasing the proportion of patients eligible for local excision without the need for chemo/irradiation. All patients recovering from rectal resection should be examined and registered systematically regarding their functional results and treatment should be offered to the severely affected patients. More studies are still needed to evaluate the efficacy of irrigation and nerve stimulation in this patient group.

Recent years' developments have resulted in improved survival and growing use of multimodality treatment for cancer. This has caused an increasing attention to the importance of knowledge on long-term side effects caused by the treatment. Knowledge of long-term side effects is essential to tailor treatment to each patient in order to achieve the right balance between optimizing tumour control and minimizing the side effects, and it is essential for providing sufficient information to the patients and the medical staff involved in the treatment and control. This knowledge is also crucial for the understanding of the underlying mechanisms and for the treatment of long-term side effects [1].

In light of this, Acta Oncologica held a multi disciplinary symposium in Oslo in the autumn 2006 discussing functional disturbances and side effects after treatment of cancer. This review on bowel dysfunction after treatment for rectal cancer was inspired by the symposium.

Functional disturbances constitute a major problem for many surviving rectal cancer patients. The majority of research in rectal cancer has been directed at improving survival, reducing local recurrence rate and increasing the number of patients receiving sphincter preserving resection. New surgical techniques, and the use of individualized pre-operative radio-chemotherapy have resulted in a markedly improved overall 5 year survival rate which is now about 70% [2]. With increasing survival, the long-term functional outcome is becoming more and more important. Studies have indicated that, following a traditional restorative resection, a large proportion of the surviving patients experience major bowel, urinary and sexual dysfunctions on a daily basis resulting in low quality of life [3–5]. The extent of these problems varies greatly with some patients

obtaining normal function after a postoperative recovery of a few months and others being severely disabled physically, mentally and socially for the rest of their lives.

In the present work the focus will be the long-term and often chronic disturbances in bowel function after treatment for rectal cancer.

Surgical treatment

Sphincter Preserving Resection (SPR)

Anterior resection with Total Mesorectal Excision (TME) is the golden standard for rectal cancer surgery. The resection is done Ad Modum Heald where the tumour and the mesorectum are excised by sharp dissection with preservation of the autonomic nerves of the pelvis [6]. Recently, laparoscopic techniques have been introduced but the advantages and limitations are still under investigation [7,8]. For tumours located 10 to 15 cm from the anal verge, a partial mesorectal resection (PME) dividing the mesorectum at least 5 cm distally from the tumour is preferable. Tumours located 5 to 10 cm from the anal verge are excised by a TME with a low anterior resection (LAR) and an ultralow anterior resection (UAR) is used on tumours located 3–5 cm from the anal verge, with a coloanal anastomosis at the dentate line.

Low Anterior Resection Syndrome

Traditional anterior resection with sphincter preservation often results in impaired functional results. Low anterior resection syndrome (LARS) is associated with the loss of the rectal reservoir function leading to urgency, frequent bowel movements and occasional faecal incontinence in a large group of the patients (see Table I) [3–5,9–14]. The functional disturbances are often most pronounced immedi-

ately after surgery, decrease during the post-operative months and reach a plateau approximately one year after surgery. Risk factors for developing LARS are low colorectal or ultra low coloanal anastomosis, end-to-end anastomosis, anastomotic leakage, acute or chronic inflammation and adjuvant radiotherapy, with the level of anastomosis the being most important factor [7].

Damage to the sphincteric apparatus also contributes to the development of LARS. In LAR and UAR the sphincter muscles and/or the intrinsic rectal innervation may be compromised leading to disruption of the recto-sphincteric reflexes which causes decreased anal pressures [7]. In addition mechanical lesions to the internal sphincter may occur during the transanal introduction of the circular stapler [7,15].

Abdomino-Perineal Resection

All rectal cancers not suitable for sphincter-preserving surgery should be excised by abdominoperineal resection (APR) with removal of the entire distal rectum and anal canal including the sphincters and with the creation of a colostomy. The stoma is permanent and can markedly interfere with the patient's body image as well as physical and social functioning. It has therefore been suggested that sphincter-preserving surgery should be used whenever possible. Many studies have investigated the quality of life (QoL) after APR and sphincter-preserving surgery, but the results are inconclusive [16]. The majority of these studies conclude that the decrease in QoL caused by negative body image and impaired sexuality after APR is counterbalanced by impairment caused by diarrhoea and other bowel symptoms after SPR [17,18].

In general, APR patients have worse QoL than patients with a high anterior resection, but they have

Table I. Functional outcome after 12 months after LAR.

	Williamson et al. [5] N = 19	Machado et al. [12]† N = 43	Rasmussen et al. [13] N = 43	Ho et al. [14]* N = 87
Urgency	6%	53%		34.9%
Bowel frequency Defaecations/day Medium (range)	4 (1–7)	3.0 (2–4.9)	3 (1–10)	2.5 (0.3–8)
Incontinence				
gas			26%	12.6%
Liquid stool		29%‡	7%	10.3%
Solid stool			16%	5.8%
Use of pads	35%	18%		13.8%
Clustering of stools		44%		30.3%

*6 months after LAR.
†Side to end anastomosis.
‡Faecal/mucus leakage.

better QOL than patients with a low coloanal anastomosis.

Adjuvant and neo-adjuvant therapy

During the last decades, radiotherapy and chemo-irradiation have increased their role as adjuvant therapy in the treatment of rectal cancer. For years, radiotherapy has been a keystone in the treatment of locally advanced cancers reducing the risk of local recurrence in primarily resectable cancers and inducing tumour regression in primarily irresectable cancers, thus facilitating later radical surgery. Radiotherapy has been administered in many different regimens; pre- or postoperative, long- or short-course treatment. Randomised trials have shown that preoperative radiotherapy decreases local recurrence rates more than postoperative irradiation while also decreasing the side effects [2,19].

Irradiation to the pelvis can cause a large variety of symptoms, often divided into acute and chronic complications. The acute toxicity comprises diarrhoea, perineal dermatitis, anal incontinence and cystitis. These symptoms occur shortly after the beginning of radiation and often last 3–10 weeks. In few patients, the symptoms are so severe that treatment must be stopped and very rarely deaths have occurred [20]. Late toxicity develops several months after treatment. Depending on the irradiation field and dose given to surrounding tissues, the symptoms vary. Because of the anatomical proximity it can be difficult to completely avoid the irradiation of the small bowel that leads to small bowel toxicity. With modern irradiation techniques, the risk of severe small bowel toxicity is expected to be below 5% [21]. The most common symptoms of small bowel toxicity include diarrhoea, abdominal pain, nausea and vomiting. Less common but more severe symptoms include small bowel obstruction or stricture, bleeding, fistulation, necrosis, bowel perforation and risk of adhesions. It can also affect the absorptional function of the bowel, leading to malnourishment and weight loss [21].

Improving functional results

During the last decades, much has been done to improve the treatment for rectal cancer both with regards to improved survival and tumour control, and to improved functional outcome. The surgical techniques have been adjusted with more emphasis on sphincter and nerve sparing. Autonomic nerves should be preserved by visual identification and sparing of the superior and inferior hypogastric plexus [22]. Hereby the innervation of the sphinc-

teric apparatus is preserved and a better functional result is to be expected.

Neoreservoir

Patients receiving SPR benefit considerably by the creation of a neoreservoir, by markedly reducing the risk and severity of LARS [7]. Several surgical methods have been developed to address this problem: colonic J-pouch, end-to-side anastomosis a.m. Baker or coloplasty.

The colonic J-pouch is created by folding a short segment of the colon and making a side-to-side anastomosis between the two loops (Figure 1). This restores volume and improves rectal wall compliance and sensory function of the neorectum. A few randomised trials have been performed comparing functional results after colonic J-pouch and a straight end-to-end anastomosis, all showing significantly better functional outcome in the pouch group (see Table II) [23–27].

Different sizes of pouches have been explored, and though large pouches gave a higher reservoir capacity and rectal compliance, they also caused severe problems with evacuation. Small pouches resulted in less evacuational problems but increased urgency and stool frequency [7]. Time has shown that a colonic J-pouch of 6 cm is optimal with regard to functional results, but the size of the pouch may be customised for each patient taking into account their anal sphincteric function and the tendency to
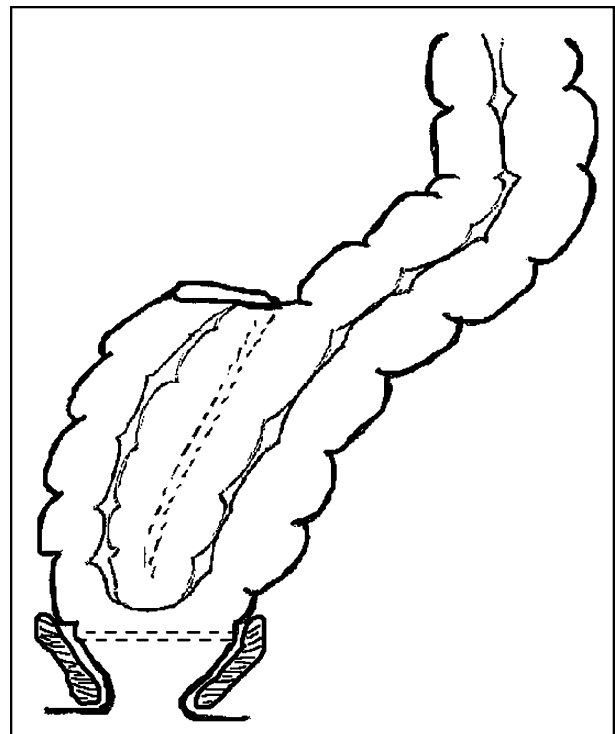

Figure 1. The colonic J-pouch.

Table II. Bowel function after colonic J-pouch and straight anastomosis.

	Bowel frequency Defaecations/day Medium (range)		Stool Clustering		Urgency		Incontinence			
							Gas		Faeces	
	J-P	Straight	J-P	Straight	J-P	Straight	J-P	Straight	J-P	Straight
Hallböök et al. [24]	2 (1.3–2.3)	3.5 (2.4–4.5)			7%*	45%*				
Ho et al. [25]			25%	37%	13%	26%	0%	16%	0%	5%
Dehni et al. [27]	1.6 (1–5)	2.8 (1–9)	30%	71%			45%	55%	13%†	12%†

* Never or Sometimes able to defer defecation for >30 min.
† Incontinence for faeces.

constipation/diarrhoea [3]. In patients where the pelvis is too narrow for a large colonic J-pouch, an end-to-end anastomosis combined with a coloplasty can be used. The coloplasty is formed by a 7–10 cm longitudinal incision which is closed transversally hereby creating a reservoir which is consequently connected to the rectal remnant by circular stapling (Figure 2). The result is a more voluminous neor-ectum with interrupted antegrade colonic peristalsis and therefore better faecal holding capacities [7,28,29]. A randomised study comparing colonic J-pouch and coloplasty showed no significant differences in functional results but a significantly higher risk of anastomotic leakage in the coloplasty group [30].

The anastomosis can also be achieved by an end-to-side anastomosis a.m. Baker in which a dilated distal blind end of the colon may increase the neorectal volume and change the motility patterns (Figure 3). The advantage of this technique is a faster surgical procedure, fewer stapler lines and therefore less risk of anastomotic leakage. Finally it is less bulky and thereby fits easier into a narrow pelvis. A Swedish randomised trial have investigated the functional outcome of the colonic J-pouch in comparison to end-to-side anastomosis, and found similar functional outcome except for a faster recovery in evacuation time, in favour of the pouch [12]. Another prospective randomized study also showed similar long-term functional outcome between colonic J-pouch and end-to-side anastomosis, with only minor differences in the recovery period [31].

In conclusion, all three types of neoreservoir results in comparable functional results. Both the coloplasty and the end-to-side anastomosis have the advantage of being less bulky. However, the coloplasty has a higher risk of anastomotic leakage, and has therefore in our opinion no place in standard surgery. In Scandinavia today, the preferred neor-ectal construction is the end-to-side anastomosis
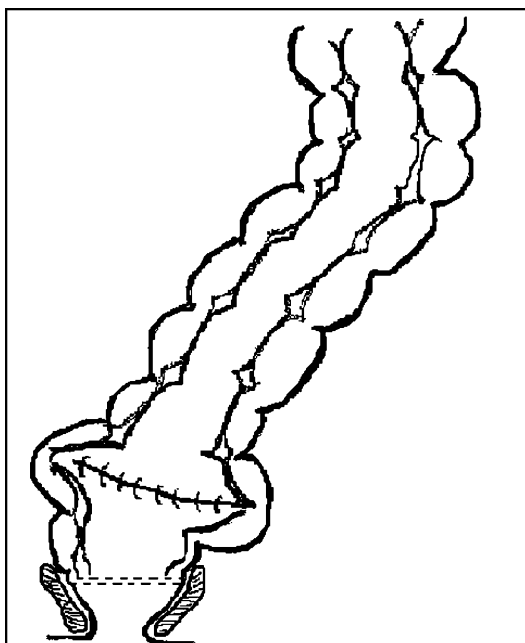

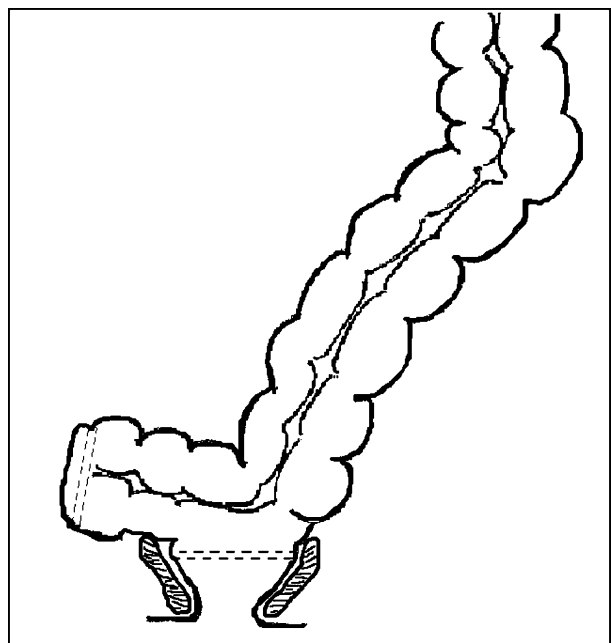Figure 2. The coloplasty.

Figure 3. The end-to-side anastomosis.

since it decreases time of surgery and lessens the number of stapler lines whereby it reduces the risk of leakage.

Both the descending and the sigmoid colon can be used for the anastomosis with or without a pouch [3]. When using the sigmoid colon, mobilisation of the left colonic flexure is not mandatory. Using the descending colon always requires mobilisation of the left colonic flexure to obtain adequate length and gives higher risk of splenic lesions and damaging of autonomic nerves in front of the aorta. The wall of the descending colon is regularly thinner and more indolent while the sigmoid is often diseased with diverticulae and thickened by muscular hypertrophy and is therefore less compliant. One study compared the use of sigmoid and descending colon in ultra-low colonic J-pouch and found no significant differences in functional outcome in the two groups [32]. Still there is a general consensus that in case of multiple diverticulae in the sigmoid, the descending colon is used for the anastomosis [32].

Perineal Colostomy

Especially among the young and active patients, a permanent abdominal colostomy is considered a mutilating procedure. A new surgical approach with construction of a perineal colostomy (PC) has been developed and is still being adjusted. The technique has been combined with smooth muscleplasty to create a pseudo-continent function (pseudo-continent perineal colostomy PCPC), and recently a total anorectal reconstruction with single or double dynamic graciloplasty has been developed. This creation of a neosphincter is a complicated surgical procedure and the morbidity is high [33]. All patients with a perineal colostomy require lifelong colonic irrigation to regulate stool evacuation [34]. This method has proven to obtain acceptable continence and a satisfying QoL by improving the patients' body image and may in the future become an acceptable alternative to a permanent abdominal colostomy [35–37].

Patients with tumours involving the sphincter have so far all been candidates for APR. With recent developments, some of these patients might be eligible for chemoradiation followed by a local excision, whereby the anal canal and the bowel continuity are preserved.

Curative management by rectum-conserving methods

Smaller rectal tumours can be curatively treated by non-resectable methods, hereby avoiding the detrimental effects of resectional surgery. This can be done as a local excision from within the lumen by a transanal excision (TE) or transanal endoscopic

microsurgery (TEM) depending on the height of the tumour with tumours located within 5 cm from the dentate line amenable for TE, while tumours located higher than this require a TEM [38]. The tumour is visualised either by anal retraction or by insertion of a specialised resectoscope. In both cases, the tumour is removed with a circumferential margin of 1–2 cm with a full-wall incision, which can be closed transversely with sutures. Tumours located as high as 20 cm posteriorly can be excised by this technique [38]. The major problem with local excision is the inability to assess the occurrence of microscopic spreading of the disease since regional lymph nodes cannot be excised [39]. So far imaging techniques cannot reliably detect metastases in regional lymph nodes [39]. In many centres TE/TEM is recommended for T1 tumours without high risk features (poorly differentiated carcinoma, deep submucosal invasion, lymphovascular invasion and lesions in the lower third of the rectum) [40]. With careful selection of patients, TEM can achieve similar oncological outcome to TME while limiting mortality and morbidity [41]. The incidence of defaecational disorders after TEM is significantly lower than after TME [42].

Local excision can be combined with neoadjuvant therapy to eradicate any nodal disease, hereby decreasing the risk of local recurrence [39,43]. An Italian study showed comparable results between TEM and TME after neoadjuvant chemoradiation in treatment of T2 cancers with regards to probability of failure and survival with a median follow-up period of 56 months [44].

Chemo and radiotherapy

The combination of chemo/radiotherapy and surgery is a major cause of poor functional result. A large number of patients are given chemo/radiotherapy to prevent a few cases of locally recurrent cancer. Patient selection with regards to risk of recurrence is essential to find the patients most likely to benefit from this treatment, hereby minimizing the number of patients receiving chemo/irradiation [45–47].

The technique for radiotherapy has improved markedly over the last decades. Imaging techniques (CT and MRI) are used for 3D dose planning. The use of new techniques for dynamic radiation with tighter margins restrict the irradiation volume to the target volume, hereby maintaining the efficacy on the tumour and minimising the side effects by minimising the radiation dose given to the surrounding tissues. Due to these new techniques, the anal sphincters have recently been excluded from the radiation field when possible in the hope of decreasing the risk of anal incontinence. Through the use of

postoperative radiotherapy, the neorectum is irradiated and this causes frequent and severe side effects with increased number of stools, urgency of defecation, faecal incontinence and frequent use of pads [48]. With preoperative radiotherapy, the irradiated rectum and sigmoid colon are removed during surgery, hereby decreasing the risk of developing severe side effects in these segments of the gut.

A Danish prospective, randomized multicenter study of postoperative radiotherapy showed a significant median delay in time to local recurrence in radiated patients compared with non-radiated patients [49]. A study performed 14 years later in the surviving patients showed a long-term detrimental effect on anorectal function with high stool frequency, faecal urgency and faecal incontinence in patients receiving postoperative radiation [50]. By use of rectal impedance planimetry it was shown that the addition of radiotherapy had induced rigidity of the rectum with reduced reservoir capacity and a weakened, less sensitive anal sphincter causing major anal dysfunction [48].

In Sweden, two large randomized prospective trials including 1 406 patients were performed between 1980 and 1993 evaluating short course preoperative radiotherapy in rectal cancers (see Table III). In 2002, the 252 patients that were still alive were asked to participate in a study investigating QoL and medical history, and of these 139 patients were interviewed and examined by anorectal examination by sigmoidoscopy and anorectal physiological testing. The investigators found significantly more late complications including faecal and urinary incontinence in patients treated with adjuvant radiotherapy in comparison to non-radiated patients [51]. Another Swedish study followed-up on a randomized study including 1 147 patients randomly assigned to preoperative irradiation or surgery alone. The patients without recurrence were matched against the Swedish Hospital Discharge Register to identify patients admitted to hospital after the primary treatment of the rectal cancer. They found an increase in the occurrence of bowel obstruction,

nausea and abdominal pain in radiated patients [52]. A large Dutch study including 597 patients randomized to surgery with or without short course preoperative radiotherapy showed a significant increase in long-term bowel dysfunction following radiotherapy with a faecal incontinence rate of 38% in the non-radiated group and 62% in the radiated group [53]. In all studies mentioned, the sphincteric structures were included in the irradiation fields.

An alternative strategy is to use long-course preoperative radiotherapy administering smaller fractions to a higher dose over 5–6 weeks followed by surgery 4–6 weeks later. This approach has been used in an effort to increase local control and to downstage the primarily irresectable cancers. The effect of long-course irradiation is enhanced when combined with chemotherapy[54,55]. Several chemotherapeutical drugs are known to have a radio sensitizing effect besides the conventional cytotoxic effect [45,56]. This combination has been proved to result in a 73.3–84% conversion rate for primarily irresectable cancers and to decrease the risk of local recurrence [57,58].

Preoperative compared to postoperative chemoradiation shows the same overall survival rates but a significant reduction in local recurrence rate and treatment morbidity [19,59]. The addition of chemotherapy to irradiation increases the risk of severe acute toxicity especially diarrhoea [20]. The Polish Colorectal Study Group compared preoperative long-course chemoradiation with short-course radiation. They found no differences in survival, local control or late toxicity between the two groups with a median follow up of 48 months [60]. Approx. 12–13 months after surgery the patients' QoL and anorectal and sexual functioning were investigated through questionnaires and showed no significant differences [61]. No systematic studies have investigated the long-term functional outcome of chemoradiation, and no studies have evaluated the effect of short-course vs. long-course radiotherapy on functional outcome.

Table III. Long term side effects of preoperative short course radiotherapy.

Study	Treatment	Surgery	Surgery+RT	P-values
Pollack et al. [51]	Faecal incontinence	26%	57%	p = 0.013
RCT. $n = 252$ ptt	Diarrhoea	9%	30%	p = 0.002
Birgisson et al. [52]	Bowel obstruction	1*	1.88*	p = 0.02
RCT. $n = 1147$ ptt	Nausea	1*	4.04*	p = 0.03
	Abdominal pain	1*	1.92*	p = 0.01
Peeters et al. [53]	Faecal incontinence	38%	62%	p < 0.001
RCT. $n = 597$ ptt	Use of pads	33%	56%	p < 0.001
	Anal blood loss	3%	11%	p = 0.004
	Mucus loss	15%	27%	p = 0.005

*RR (Relative risk).

Neoadjuvant chemoradiation without surgery can lead to complete pathological response in some patients. Few studies have indicated a complete response rate of 10–25% with marked effect on survival and local recurrence [59]. A controversial Brazilian study suggests that complete responders could be treated by chemoradiation alone [62]. What currently limits this approach is the problem of identifying the complete responders. This has so far been done postoperatively by examining the excised tumour and comparing it to the preoperative clinical staging. The standard imaging techniques for staging of the tumour are unreliable after chemoradiation. Transanal ultra sound, usually considered the most accurate method for staging T1 and T2 rectal tumours, has difficulties distinguishing between residual tumour and post-irradiation fibrosis [63,64]. MRI has also proven inaccurate in re-staging rectal cancers after chemoradiation [65]. Recent studies indicate that F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) more accurately assesses the treatment response and stages the irradiated cancers [59,66]. More research is needed to verify these findings before complete responders accurately can be identified and be spared the detrimental effects of resectional surgery.

Contact radiotherapy and brachytherapy are both methods for endocavitary irradiation with delivery of high dose irradiation to the tumour but low dose to the normal surrounding tissues. Local control has been achieved in 85–90% of patients with T1N0 tumours by endocavitary irradiation alone. By combining it with external beam irradiation, local control can be achieved in 80% of T2 tumours and 60% of T3 tumours [67].

Treatment modalities for bowel dysfunction

Conservative management

To date, most functional disturbances are treated with conservative therapy including dietary advice, fibres, laxatives, Loperamide and suppositories, although the evidence for these regimens has never been provided. A large group of patients obtain unsatisfactory results, and this group may require more invasive therapy in order to obtain good functional outcome and high quality of life.

Bowel irrigation

Patients with an abdominal colostomy often complain of odour, flatus and peri-stomal skin conditions caused by stomal incontinence. Many of these patients can improve their function significantly by colostomy irrigation.

Colostomy irrigation can be done through retrograde irrigation with instillation of lukewarm water into the lumen of the gut by a catheter inserted through the stoma, or through antegrade irrigation with instillation through an appendicostomy. Studies have shown that up to 92–97% of patients with abdominal colostomies may achieve continence with retrograde colostomy irrigation hereby improving their physical wellbeing and QoL [68,69]. The technique is time consuming and requires thorough instruction and training. Even after correct irrigation, episodes with faecal discharge between washouts can occur [68].

Patients with a perineal colostomy require lifelong colonic irrigation to obtain acceptable functional results [35,37]. This is usually done as a retrograde colonic irrigation, but newer approaches include cecal access for antegrade irrigation sometimes in shape of an appendicostomy, a cecal flap conduit or an ileal tubularisation. Retrograde irrigation has proved efficient resulting in faecal continence in 71% of these patients [34]. The newer approach with antegrade irrigation through an appendicostomy or cecal access (Malone procedure) in perineal stoma patients has been shown to improve the continence rate to 84.6% [35].

Retrograde transanal irrigation has proven valuable in relieving continence disturbances in a variety of patients including rectal cancer patients [70,71]. The technique is similar to the colostomy irrigation except the catheter is inserted through the anal canal. In patients with defecation disturbances after low anterior resection, retrograde transanal irrigation proved efficient in up to 79% of patients in small series [72,73].

Antegrade irrigation through an appendicostomy has been investigated and has proven to be safe and efficient in patients suffering from defaecational disturbances where it induces highly effective emptying of the large bowel even in patients with severe constipation [74–76].

Nerve stimulation

Sacral Nerve Stimulation (SNS) is a new method for relieving defaecational disturbances. It has been tested on a variety of patients suffering from faecal incontinence due to sphincteric injury, neuronal damage and idiopathic incontinence and studies have shown that up to 80% of patients experience markedly improved function after implantation of the stimulator [77,78].

Before the implantation of a permanent stimulator (the SNS), an external stimulator is implanted for testing the correct position and the functional results. This is obtained by Percutaneous Nerve

Evaluation (PNE) with implantation of a small electrode into a sacral. The electrode is tested and if a significant reduction in incontinence episodes occurs, a permanent stimulator is implanted. The mode of action of SNS is unknown since it has no or only minor measurable effect on anal manometry and rectal volume tolerability. It has been hypothesized that the effect is due to modulation of the anorectal and/or colorectal motility, but this remains to be investigated [77]. Only few studies have investigated the use of SNS in rectal cancer patients, but they have shown positive effects [79,80]. The procedure of implantation and testing the device is uncomplicated and safe, which makes the method interesting for future studies in bowel disturbances after the treatment for rectal cancer.

Future Perspectives

Treatment for rectal cancer is in rapid development. Much research has been done improving survival and tumour control, and during the last decade functional outcome has been gaining more attention. In order to improve and treat the functional outcome several approaches can be chosen:

Improving primary cancer treatment:

1. Finding the tumours earlier by population screening, hereby increasing the number of patients eligible for non-resectional surgery without the need for neoadjuvant treatment.
2. Lessen the surgical trauma by optimizing the surgical procedures with minimal nerve and sphincter damage.
3. Optimizing the radiation techniques to ensure maximal irradiation of the tumour with minimal irradiation of the surrounding tissues.
4. Improving imaging techniques including MRI and CT for better detection of regional lymph node metastases and hereby correctly N-staging the tumours for better selection of patients eligible for local excision.
5. Improving imaging techniques for identifying complete responders to chemoradiation, hereby sparing them the surgery.
6. The use of molecular markers to identify the tumours sensitive to adjuvant therapy hereby limiting the risk of over treatment.

Improving secondary treatment of functional problems:

1. Prospective evaluations of functional deficits in all patients using validated questionnaires to improve knowledge of incidence and severity of the problems.
2. Better understanding of the impact of the functional problems on the patients' QoL.
3. Prospective randomised trials evaluating all aspects of treatment, including conservative bowel management and newer treatment modalities such as TAI and SNS/PNE, to achieve high level of evidence for the efficacy of treatment.

Acknowledgements

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