

Urologic and sexual morbidity following multimodality treatment for locally advanced primary and locally recurrent rectal cancer

G. H. H. Mannaerts^{*}, M. P. Schijven^{*}, A. Hendrikx[†], H. Martijn[‡], H. J. T. Rutten^{*} and T. Wiggers[¶]

Catharina Hospital, Departments of *Surgery, †Urology and ‡Radiotherapy, Eindhoven, The Netherlands and ¶University Hospital Rotterdam/Daniel den Hoed Cancer Center, Department of Surgical Oncology, Rotterdam, The Netherlands

Aims: In the treatment of patients with locally advanced primary or locally recurrent rectal cancer much attention is given to the oncological aspects. In long-term survivors, urogenital morbidity can have a large effect on the quality of life. This study evaluates the functional outcome after multimodality treatment in these patient groups.

Patients and methods: Between 1994 and August 1999, 55 patients with locally advanced primary and 66 patients with locally recurrent rectal cancer were treated with multimodality treatment: i.e. high-dose preoperative external beam radiation therapy, followed by extended surgery and intraoperative radiotherapy. The medical records of the 121 patients were reviewed. To assess long-term urogenital morbidity, all patients still alive, with a minimum follow-up of 4 months, were asked to fill out a questionnaire about their voiding and sexual function. Seventy-six of the 79 currently living patients (96%) returned the questionnaire (median FU 14 months, range 4–60).

Results: The questionnaire revealed identifiable voiding dysfunction as a new problem in 31% of the male and 58% of the female patients. In 42% of patients after locally advanced primary and 48% after locally recurrent rectal cancer treatment bladder dysfunction occurred. The preoperative ability to have an orgasm had disappeared in 50% of the male and 50% of the female patients, and in 45% of patients after locally advanced primary and in 57% after locally recurrent rectal cancer treatment rectal cancer treatment.

Conclusion: Multimodality treatment for locally advanced primary and recurrent rectal cancer results in acceptable urogenital dysfunction if weighed by the risk of uncontrolled tumour progression. Long-term voiding and sexual function is decreased in half of the patients. Preoperative counselling of these patients on treatment-related urogenital morbidity is important.

Key words: urologic; bladder dysfunction; sexual dysfunction; complications; IORT; radiotherapy; surgery; locally advanced; primary; recurrent; rectal cancer.

INTRODUCTION

Conventional low anterior and abdomino-perineal resection for rectal cancer is associated with local recurrence, sexual and voiding dysfunction.¹⁻³ The autonomous nerve-preserving total mesorectal excision (TME) technique has proven to reduce local recurrence rates from up to 35% to less than 10%, whilst preserving urogenital function.²⁻⁸

In locally advanced primary rectal carcinomas, TME may be insufficient to obtain a curative resection. As in

to the rectal compartment, due to severance of the fascial planes. anatomical Hence, extended circumferential margins are required to achieve a complete resection in both presentations of rectal cancer. Multimodality treatment, combining preoperative external beam radiation therapy (EBRT), with radical surgery, followed by intraoperative radiotherapy (IORT), results in cure in 46-62% of patients with locally advanced primary and in 19-21% of patients with locally recurrent rectal cancer.^{3,9–15} Multimodality treatment has its morbidity. Both radiotherapy and extended surgery can increase the probability of damage to the urogenital nerves and organs, which results in voiding and sexual dysfunction.^{1,16,17}

locally recurrent rectal cancer, the tumour is not confined

The purpose of this study is to assess the long-term urogenital outcome following multimodality treatment.

Correspondence to: H. J. T. Rutten, M.D., Ph.D., F.R.C.S., Department of Surgery, Catharina Hospital, Michelangelolaan 2, 5631EJ Eindhoven, The Netherlands. Tel: (+31) 402397155; Fax: (+31) 402443370; E-mail: harmr@iaehv.nl

PATIENTS AND METHODS

Patients

From February 1994 to August 1999, 121 patients underwent multimodality treatment in the Catharina Hospital and the Daniel den Hoed Cancer Center: 55 patients had locally advanced primary (32 males and 23 females), and 66 patients had locally recurrent rectal cancer (41 males and 25 females). The median overall age was 63 years (range 39–86).

The multimodality treatment consisted of high-dose preoperative radiotherapy (50.4 Gy or 30 Gy, if reirradiated), extended circumferential margin excision (ECME) and IORT (10-17.5 Gy).^{18,19} The IORT was delivered as intraoperative electron beam radiotherapy (IOERT) in the Catharina Hospital and as intraoperative high-dose rate brachytherapy (IOHDR) in the Daniel den Hoed Cancer Center. The specific details of the multimodality treatment are listed in Table 1.

Methods

All 121 patient records were reviewed for radiotherapy and surgical rectal treatment, and urological operative and postoperative complications caused by multimodality treatment. Scoring of late postoperative complications was stopped if a patient developed a local recurrence.

Analysis of long-term urogenital morbidity was by means of a structured questionnaire, sent to all surviving patients. Questions were paralleled and repeated. The first set reflected the function in the period six months before multimodality treatment, and the second the current function after multimodality treatment. Followup was at least four months, as most postoperative morbidity is reversible in this period.^{16,20-22} Voiding function was measured by the following variables: bladder hypotonia, lower urinary tract symptoms (LUTS: including hesitancy, weak stream, dribbling and nocturia), urgency and incontinence. Sexual function was measured by the following variables: sexual activity, experience of pain or discomfort during intercourse, erection, ejaculation and orgasm. Quality of orgasm and erectile function were assessed using a variable analogue scale (VAS). All sexual questions could also be answered by 'sexually inactive'.

The response rate was 96% (76/79). Groups consisted of 37 (49%) locally advanced primary (male-female: 22–15) and 39 (51%) locally recurrent patients (male-female: 24–15). Median time between the operation and the questionnaire was 14 months (range 4–60 months). Patients who returned the questionnaire but who had currently or previously received an ileum conduit (n = 10) were excluded for questions concerning urological dysfunction but not for sexual dysfunction. Patients indicating 'sexually inactive' (n = 8) were excluded from the analysis on sexual dysfunction.
 Table I
 Patient and treatment characteristics

	Loo adva	ally nced	Loca	Locally recurrent			
	prir No.	nary (%)	No.	(%)			
Total number	55	(45)	66	(55)			
Age (years)							
Median	64		61				
Range	36–86		39–82				
Sex							
Male	32	(26)	41	(34)			
Female	23	(19)	25	(21)			
Prior treatment							
Irradiation	-		25	(38)			
Mean (Gy)	-		50.4				
Range (Gy)	-		25–66				
Surgical procedure							
Low anterior res.	-		40	(61)			
Abdominoperin. res.	-		23	(35)			
Exenteration	-		3	(4)			
lleum conduit	-		3	(4)			
Multimodality							
treatment							
Irradiation (n)*	55	(100)	48	(73)			
Median (Gy)	50.4		50				
Range (Gy)	25–61		16–50.4				
Surgical procedure							
Low anterior res.	15	(27)	7	(11)			
Abdominoperin. res.	20	(36)	21	(32)			
Abdominosacral res.	12	(22)	26	(39)			
Exenteration	8	(15)	12	(18)			
lleum conduit	4	(7)	9	(12)			
Radicality resection		. ,		. ,			
Neg. margins	45	(82)	31	(47)			
Microsc. pos.	6	(10)	19	(29)			
Macrosc. pos.	4	(8)	16	(24)			
marg.				()			
IORT**							
IOERT (n)	45	(82)	49	(74)			
10 Gy	38	(66)	24	(33)			
, 12.5 Gy	I	(2)	_				
15 Gy	6	(10)	17	(23)			
17.5 Gy	2	(4)	13	(18)			
IOHDR		()					
10 Gy	10	(18)	17	(26)			

* Seven patients in the locally recurrent group received 30 Gy reirradiation.

** Two locally advanced primary and five locally

recurrent patients received two IORT applications.

Statistical comparisons of occurrence of urogential complications and dysfunction were performed using the T-test, Z-test, Npar-tests, Fisher's Exact test, Wilcoxon test or McNemar test for repeated measures situations

Table 2	Operative and	Dostoperative	complications

	Locally advanced		Loo recu	ally rrent
	No.	nary (%)	No.	(%)
Operative complications		. ,		
Bladder losion		(2)	2	(5)
	;	(2)	2	(3)
Lirethra lesion	_	(2)	2	(3)
Immediate postop, complicatio	-		•	(2)
Voiding difficulties	21	(39)	23	(35)
Hypotonia	15	(37)	20	(30)
Chronic hypotonia	7	(27)	11	(17)
Temporary hypot	, 8	(15)	8	(17)
Preevistent hypot	_	(13)	1	(12)
Lirgency/urge_incont	6	(11)	i	(2)
Chronic hypotonia	_	(11)	i	(2)
	4	(7)	_	(2)
Preevistent urgency	2	(7)	_	
Stress incontinence	_	(1)	2	(3)
Chronic stress inc	_		ī	(2)
Temporary stress inc	_		i	(2)
Urinary tract infection	10	(18)	10	(15)
Leading to sepsis	3	(5)	2	(3)
Urogenital fistula	2	(4)	6	(9)
Vesico-cutaneous fist.	Ī	(2)	_	(.)
Vesico-rectal fistula	_	(-)	1	(2)
Vesico-vaginal fistula	_		i	(2)
Uretero-cutaneous fist.	_		i	(2)
Uretero-vagina fistula	_		i	(2)
Recto-vaginal fistula	_		1	(2)
lleum conduit fistula	I	(2)	I	(2)
Hydronephrosis	I	(2)	I	(2)
Unilateral	_	()	I	(2)
Bilateral	1	(2)	_	~ /
Late postop. complications		()		
Ureter fibrosis	_		2	(3)
Radiation cystitis	-		I	(2)

in individual persons, when appropriate. The following variables were analysed: primary vs recurrent, sex, age (≤ 60 or >60 years), and type of surgery (low anterior resection vs other resection types). *P* values less than 0.05 were considered statistically significant.

RESULTS

Locally advanced primary rectal cancer

The various operative and postoperative complications are summarized in Table 2. Postoperative voiding difficulties, requiring prolonged catheterizations and medication, were observed in 21 patients (39%). Fifteen of them had bladder hypotonia, which was temporary (<4 months) in eight patients. The remaining six patients had urgency or urge incontinence, which was temporarily in four and preexistent in two. The results of the questionnaire concerning preoperative vs current urogenital functionality are listed in Table 3. Three percent had preoperative voiding dysfunction vs 44% postoperatively (P=0.000). Bladder hypotonia requiring catheterizations (atonic bladder) was observed in 0% preoperatively vs 19% postoperatively (P=0.03). Hypotonia, not requiring catheterizations, was preoperatively observed in 3% vs 41% postoperatively (P=0.000). LUTS were observed in 6% preoperatively vs 50% postoperatively (P=0.000). Urgency was experienced by 6% preoperatively vs 58% postoperatively (P=0.000). Six percent used incontinence pads preoperatively vs 41% postoperatively (P=0.001).

Seventy-nine percent of the primary patients were sexually active preoperatively vs 32% postoperatively (P=0.000). Ninety-seven percent were able to experience orgasm preoperatively vs 53% postoperatively (P=0.000). The mean quality of orgasm, as indicated on a 5-cm analogue scale, was reduced from 60% to 28% (P=0.000). Pain or discomfort during intercourse was experienced in 13% preoperatively vs 40% postoperatively (P=0.1). The ability to have spontaneous erections was reported by 100% preoperatively vs 44% postoperatively (P = 0.002). The mean quality of erectile function, as indicated on a 5-cm analogue scale, had reduced from 66% to 14% (P = 0.000). The ability to ejaculate had decreased from 95% preoperatively to 24% postoperatively (P = 0.000).

Locally recurrent rectal cancer

Postoperative voiding difficulties, requiring prolonged catheterizations and medication, were observed in 23 patients (35%). Twenty of them had bladder hypotonia, which was temporary (<4 months) in eight and preexistent in one patient. Another patient developed urge incontinence. The remaining two patients had stress incontinence, which was temporary in one.

The questionnaire revealed that 22% of the locally recurrent patients had preoperative voiding dysfunction vs 56% postoperatively (P = 0.001). Bladder hypotonia requiring catheterizations was observed not preoperatively vs 9% postoperatively (P = 0.3). Bladder not requiring catheterizations, hypotonia, was preoperatively observed in 9% vs 34% postoperatively (P=0.008). LUTS were observed in 38% preoperatively vs 78% postoperatively (P = 0.001). Urgency was experienced by 28% preoperatively vs 66% postoperatively (P = 0.002). Twenty-six percent used incontinence pads preoperatively vs 52% postoperatively (P = 0.02).

Sixty-eight percent of the locally recurrent patients were sexually active preoperatively vs 32% postoperatively (P = 0.000). Seventy-two percent were able to experience orgasm preoperatively vs 31% postoperatively (P = 0.000). The mean quality of orgasm, as indicated on a 5-cm analogue scale, was reduced

	Locally advanced primary rectal cancer				Locally recurrent rectal cancer					
	Preope	erative	Postop	erative P value		Preoperative		Postoperative		P value
	n .	%	n	%		n .	%	n .	%	
Voiding dysfunction	1/34	3	15/34	44	0.000	7/32	22	18/32	56	0.001
Hypotone bladder requiring catheterization	0/32	0	6/32	19	0.03	0/33	0	3/33	9	0.3
Hypotone bladder not requiring catheterization	1/32	3	13/32	41	0.000	3/32	9	11/32	34	0.008
LUTS	2/34	6	17/34	50	0.000	12/32	38	25/32	78	0.001
Urgency	2/31	6	18/31	58	0.000	9/32	28	21/32	66	0.002
Incontinence	2/32	6	13/32	41	0.001	8/3 I	26	16/31	52	0.02
Sexual activity	27/34	79	11/34	32	0.000	23/34	68	11/34	32	0.000
Ability to have orgasm	29/30	97	16/30	53	0.000	23/32	72	10/32	31	0.000
Experience of pain/discomfort during intercourse	2/15	13	6/15	40	0.1	1/12	8	5/12	42	0.1
Ability to achieve normal erection	18/18	100	8/18	44	0.002	15/19	79	7/19	37	0.008
Ability to ejaculate	20/21	95	5/21	24	0.000	14/20	70	2/20	10	0.000
Quality of orgasm (mean on 5 cm VAS)	3.0	60	1.4	28	0.000	2.5	50	1.1	22	0.000
Quality of erection (mean on 5 cm VAS)	3.3	66	0.7	14	0.000	2.7	54	0.5	10	0.000

Table 3 Questionnaire urogenital dysfunction in locally advanced primary and locally recurrent rectal cancer

 Table 4
 Questionnaire urogenital dysfunction in males and females

	Male					Female				
	Preoperative		Postop	erative	P value	Preoperative		Postoperative		P value
	n	%	n	%		n	%	n	%	
Voiding dysfunction	6/38	16	16/38	42	0.02	2/28	7	17/28	61	0.000
Hypotone bladder requiring catheterization	0/38	0	4/38	П	0.1	0/27	0	5/27	19	0.06
Hypotone bladder not requiring catheterization	4/36	П	13/36	36	0.04	0/28	0	11/28	39	0.01
LUTS	8/38	21	24/38	63	0.000	6/28	21	18/28	64	0.000
Urgency	4/36	11	19/36	52	0.000	7/27	26	20/27	74	0.000
Incontinence	2/36	6	9/36	25	0.04	8/27	30	20/27	74	0.000
Sexual activity	33/41	80	15/41	37	0.000	17/27	63	7/27	26	0.002
Ability to have orgasm	36/40	90	18/40	45	0.000	16/22	73	8/22	36	0.008
Experience of pain/discomfort during intercourse	1/18	6	6/18	33	0.06	2/9	22	5/9	56	0.3
Quality of orgasm (mean on 5 cm VAS)	2.8	56	1.2	24	0.000	2.7	54	1.4	28	0.000

from 50% to 22% (P=0.000). Pain or discomfort during intercourse was experienced in 8% preoperatively vs 42% postoperatively (P=0.1).

The ability to get spontaneous erection was reported by 79% preoperatively vs 37% postoperatively (P = 0.008). The mean quality of erectile function, as indicated on a 5-cm analogue scale, had reduced from 54% to 10% (P = 0.000). The ability to ejaculate had decreased from 70% preoperatively to 10% postoperatively (P = 0.000).

Males vs females (Table 4)

The questionnaire revealed that 16% of male patients had preoperative voiding dysfunction vs 42% postoperatively

(P=0.02). In female patients these figures were 7% and 61% (P=0.02). Postoperative long-term voiding dysfunction was higher in females.

Interest in sexual activity decreased in males from 80% to 37% (P = 0.000) and in females from 63% to 26% (P = 0.002). Both preoperative and postoperative sexual dysfunction was higher in women.

Multivariate analysis

Higher age (>60 years) significantly reduced the ability to have orgasm postoperatively (P=0.046), as well as the ability to have sexual intercourse (P=0.04). Females experienced a significantly higher frequency of bladder

hypotonia (P=0.02) and had a significantly increased voiding frequency to prevent incontinence in comparison with males (P=0.01). The number of patients was too small to show significant differences in urogenital morbidity between the locally advanced primary and the locally recurrent group, nor between the different types of resection.

From the 66 patients, without an ileum conduit who returned the questionnaire, eight had voiding dysfunction preoperatively, of which five experienced direct postoperative voiding dysfunction. Of the remaining 58 patients, 25 developed voiding dysfunction as a new complaint, of which 13 had direct postoperative voiding dysfunction, and 33 patients developed no long-term voiding dysfunction, although eight of them had experienced direct postoperative voiding dysfunction. Direct postoperative voiding dysfunction was found to predispose significantly for long-term voiding dysfunction (P = 0.04).

DISCUSSION

Multimodality treatment, using preoperative high-dose EBRT, extended surgery and IORT, improves the outcome in both locally advanced primary and locally recurrent rectal cancer.^{18,19} Cure is the main goal in these patients and treatment-related morbidity is of less importance. This is reflected by the lack of data reported on morbidity after multimodality treatment. Two reports have described general complications after IORT-containing multimodality treatment for rectal cancer,^{23,24} while others briefly summarize these side effects. However, the outcome of multimodality treatment can only be placed into proper perspective if treatment-related morbidity is also taken into consideration. The probability of cure is less than the chance for urogenital morbidity.

Wound infections, neuropathy of the legs and buttocks, and urogenital morbidity are the most frequent and important treatment-related sequellae. Wound infections and delayed closures resolve in time. Neuropathy is not a frequent complication after multimodality treatment, is often not severe and is in most cases self-limiting.^{18,19} Urogenital morbidity, however, is a frequently observed problem in patients after multimodality treatment and is often irreversible. It is therefore more important than the literature shows and in fact may constitute a major problem.

Voiding problems according to the literature consist of difficulty in emptying the bladder, hypotonia, urgency, incontinence, and urinary tract infection.^{20,22,25–29} Sexual complications consist of erection and ejaculation disturbances in male patients and dyspareunia and decreased lubrication in female patients.³⁰

Damage to the urogenital system can be caused by radiotherapy but more likely by surgery.^{30,31} This is caused by the limited access to the lesser pelvis, the close

relation of the nerves responsible for voiding and sexual function to the resection planes, and the aim of complete resection, as this is the most important prognostic oncological factor.^{18,19} The incidence of urinary and sexual dysfunction rises with more radical operations.^{17,31} The dissection will even be more complicated in locally recurrent rectal cancer patients, due to distortion of fascial borders and fibrotic reaction caused by previous surgery and irradiation. In some cases, the urogenital system may already be damaged. It is therefore of utmost importance to use gentle sharp dissection and to have a detailed knowledge of the pelvic and perineal anatomy. Some phases in the operation predispose for iatrogenic injury. Most important urogenital nerves that can be harmed during the dissection are:

- (1) The parasympathetic sacral splanchnic nerves (nervi erigentes), which run from the sacral nerve plexus (level S2–S4) ventrally and laterally to the inferior hypogastric plexus and from there to the bladder/ prostate, largely control micturition by controlling the musculus detrusor vesiculae and control erection in men, may be damaged directly during dissection on the anterolateral aspect of the lower rectum anteriorly to the fascia of Denonvilliers.^{1,32–35} Partial damage will result in a decreased detrusor pressure at micturition (hypotonia) and complete denervation results in impaired bladder emptying (atonic or neurogenic bladder).
- (2) The sympathetic hypogastric nerves, which run from the superior hypogastric plexus (level L3-S1) caudally and laterally (parallel with the ureters and the internal iliac vessels) to the inferior hypogastric plexus, can be damaged at the origin of the inferior mesenteric artery; or laterally to the rectum close to the middle rectal arteries at the promontory nearby the iliac vessels and around the ureter;32,35 or when the posterior wall of the prostatic capsule is dissected.³⁶ Damage to the sympathetic nerves influences bladder control by a diminished proximal urethral pressure and incompetent bladder neck,²² which results in a loss of controlling the urine when bladder pressure rises, thus resulting in increased frequency of and urgency.⁷ sympathetic micturition The hypogastric nerves also control ejaculation.³⁷
- (3) The inferior hypogastric plexus, which contains both sympathetic pelvic splanchnic and parasympathetic hypogastric nerves, is located at the side of the lateral ligament where the visceral dorsal fascia (fascia recti) changes in the parietal dorsal fascia or fascia sacralis. This is the danger point of harming the plexus,^{1,34} and therefore the lateral ligament should if possible be cut close to the mesorectum leaving pelvic plexus undamaged on the lateral pelvic wall. Whenever possible, we attempt to preserve at least one set of both nerves.
- (4) The somatic pudendal nerves (deriving from S2–S4),

which can delay urination by contraction of the external bladder sphincter, can suddenly compensate for increase of intraabdominal pressure (i.e. coughing) and can propel the seed by contraction of the ischiocavernous and bulbospongiosus muscles, are most vulnerable in the presacral space and ischiorectal fossa.⁷

Apart from direct injury, neuropathy of the urogenital nerves can be caused by traction on the lower rectum during mobilization, which might explain the improvement of the voiding dysfunction in many patients in the months following the operation.³⁴

Postoperative urogenital dysfunction may also be caused by several non-neurogenic reasons: inflammatory changes in the perivesical tissues,³⁸ altered perineal anatomy,^{25,28,30} immobilization, the recumbent posture, failure of perineal relaxation caused by pain, failure to open the bladder-neck due to stress-induced sympathetic overactivity, bladder distension and reduced contractility as a result of high intravenous fluid loads, or bladder sedation due to residual effects of anaesthetic agents are not infrequent. These factors may explain the transient nature of symptoms encountered in many patients.¹⁶

External beam radiotherapy has a negative effect on the peripheral nerves, most probably as a result of damage to the capillaries of the neurovascular bundles, and may also result in a decline of smooth muscle content, diffuse fibrosis and mucosal irritation, which can cause a loss of bladder compliance, vasculogenic impotence in men, and dyspareunia in women.^{30,39} Further damage can be caused by IORT, since peripheral nerves are the main dose-limiting structures for IORT.^{23,40,41} The use of small radiation fields, carefully fractionated doses, exclusion of bowel and bladder, and dose titration with the time interval between initial treatment and recurrence of disease all seem necessary to prevent damage to the peripheral nerves.⁴²

Postoperative urinary retention is a troublesome, though often temporary, complication after rectal resection and is usually related to outlet obstruction.^{20,43} Proper bladder drainage in the postoperative period is essential, because prolonged bladder distension will extend the problem. All patients, except those who had an ileum conduit constructed, therefore received a supra-pubic bladder catheter. This has the advantage of assessing the micturition capability, without repeated removal and placement of catheters and avoids the complication of urethral stricture. If micturition fails, pharmacological treatment may be started to improve bladder hypotonia. Long-term observation shows a declining incidence of bladder dysfunction.¹⁷ Therefore, any indication for early postoperative surgical intervention, like a transurethral resection of the prostate in cases of urethral sphincter obstruction, hardly exists, and may, especially if the pudendal nerves are damaged, lead to incontinence.16,44

In this study, 36% (44/121) of all patients had direct postoperative voiding dysfunction requiring medical treatment, which was temporary in more than half of them (Table 3). Long-term voiding dysfunction was significantly related to direct postoperative voiding dysfunction (P = 0.04). Other reports have not identified such a relation. The questionnaire on late morbidity revealed voiding dysfunction in 31% (10/32) of the male and 58% (15/26) of the female patients, who had normal preoperative bladder function (Table 4). This was respectively 42% (14/33) after treatment of primary and 48% (12/25) after treatment of locally recurrent rectal cancer (Table 3). Other studies show a wide range of voiding dysfunction rates between 7 to 73%, depending on radicality of resection and the attention paid on autonomous nerve-preserving surgery.^{4-6,8,16,17,20,25-28,30,31,37,} ^{45,46} An atonic bladder occurred between 9 to 19% in the different groups in this study, which is comparable to the reported rates ranging between 0 and $59\%.^{\rm 8,16,20,}$ ^{26-30,45} Havenga, who used a similar questionnaire for urogenital morbidity in patients with TME for primary mobile rectal cancer, revealed a postoperative voiding dysfunction ranging between 27-37%, no atonic bladder, and an incontinence rate of 5-30% in male and female groups with normal preoperative voiding function.³⁰ In this study, in which both sexes had a significant reduction of normal voiding function, 20% (7/34) of the males and 63% (12/19) of the females developed incontinence as a new complaint. Furthermore, females experienced a significantly higher difficulty emptying their bladder than males (P = 0.02) and females deliberately urinated more frequently to prevent leakage than males (P = 0.01). This may be associated with the larger bladder capacity but shorter length of the urethra in women.³⁰

It is known that sexual dysfunction is a common problem after rectal resection and more frequent after larger resections.³⁵ After abdominosacral resection, sexual function is still normal if the S3 nerve root is severed bilaterally.⁴⁷ However, unilateral damage of S2 nerve root leads to loss of sensation in the penis or the labia and weakens erection.^{33,47} After conventional operations, permanent, complete or partial erectile dysfunction is reported to occur in 5-65% of patients^{8,30,} ^{46,48-51} and loss of the ability to ejaculate is reported in 12-69%.^{4,8,30,46,48-51} In the study of Havenga, using a similar questionnaire to analyse sexual dysfunction after TME surgery for mobile rectal cancer, 4% of the males and 2% of the females lost the ability to achieve $orgasm.^{30}$ ln this study, sexual function was also significantly influenced by the multimodality treatment. In 50% (18/36) of the male and 50% (8/16) of the female patients, and in 45% (13/29) of patients after primary and 57% (13/23) after recurrent rectal cancer treatment, the preoperative ability to have an orgasm had disappeared. The ability to achieve both erection and ejaculation was also significantly reduced in males of all groups in this study. An increase of pain or discomfort during intercourse was both observed in males and females. But the numbers were too low to draw conclusions.

Comparable to other studies,^{30,46} age had a large influence on sexual activity after surgery. Higher age (>60 years) significantly reduced the ability to have an orgasm (P=0.046), as well as the ability to have sexual intercourse (P=0.04) postoperatively. Sexual dysfunction due to autonomous nerve damage is a major problem in men after rectal surgery because of subsequent erectile and ejaculation disturbance. However, exact evaluation of sexual function in elderly men, who may find it embarrassing to discuss declining potency, is difficult. Fortunately, new pharmaceutical drugs to improve potential function have become available.

CONCLUSION

Multimodality treatment for locally advanced primary and locally recurrent rectal cancer can be accomplished with acceptable urogenital morbidity, weighed by the risks of uncontrolled tumour growth. Most urinary complications are not potentially life-threatening and become less severe in time following proper management. However, long-term voiding and sexual function is reduced in half of the patients, who had a normal function preoperatively. The main causes of voiding and sexual dysfunction after rectal surgery are most probably due to damage of the autonomic nerves supplying the urogenital organs. Completeness of the tumour resection remains the main goal of the treatment, though, sharp nerve-sparing dissection is often still possible and is essential to maintain proper urogenital function. Preoperative EBRT and IORT can have a magnifying effect on urological complications. Preoperative information to the patient about treatmentrelated urogenital morbidity is important. Results of this study have prompted us to incorporate this information preoperative counselling. Furthermore, in the communication between the rectal surgeon and the urologist should be optimal to assess any occurring problems properly.

ACKNOWLEDGEMENTS

The authors thank the following referring and cooperating surgeons, urologists, and radiotherapists: I. P. T. van Bebber, M.D., Ph.D., M. H. M. Bender, M.D., C. L. O. van Berlo, M.D., Ph.D., P. R. M. de Bevere, M.D., S. J. Brenninkmeijer, M.D., S. Bouwer, M.D., E. J. Carol, M.D., Ph.D., F. A. A. M. Croiset van Uchelen, M.D., Ph.D., C. D. van Duyn, M.D., Ph.D., W. F. M. van Erp, M.D., Ph.D., W. A. H. Gelderman, M.D., Ph.D., G. P. Gerritsen, M.D., K. Havenga, M.D., Ph.D., J. J. Jakimowicz, M.D., Ph.D., F.R.C.S., E. G. M. Leerkotte, M.D., F. G. J. Laudy, M.D., A. van Linge, M.D., J. W. A. van Luijt, M.D., E. J. T. H. Luiten, M.D., M. G. Luiting, M.D., F. Marechal, M.D.,

G. Niessen, M.D., Ph.D., J. S. K. Nuytinck, M.D., Ph.D., S. B. Oei, M.D., H. J. M. Oostvogel, M.D., Ph.D., P. H. M. Reemst, M.D., J. F. M. Reinders, M.D., Ph.D., J. A. M. Reinen, M.D., Ph.D., O. J. Repelaer van Driel, M.D., Ph.D., R. M. H. Roumen, M.D., Ph.D., J. R. M. van der Sijp, M.D., Ph.D., Th. J. van Straaten, M.D., Ph.D., B. H. M. Storck, M.D., L. J. A. Strobbe, M.D., C. D. G. W. Verheij, M.D., G. Verspui, M.D., Ph.D., E. Vrijhof, M.D., J. W. D. de Waard, M.D.

REFERENCES

- Havenga K, DeRuiter MC, Enker WA, Welvaart K. Anatomical basis of autonomic nerve preserving total mesorectal excision for rectal cancer. Br J Surg 1996; 83: 384–8.
- Huber FT, Stepan R, Zimmermann F, Fink U, Molls M, Siewert JR. Locally advanced rectal cancer: Resection and intraoperative radiotherapy using the flab method combined with preoperative or postoperative radiochemotherapy. *Dis Colon Rectum* 1996; 39: 774–9.
- Farouk R, Nelson H, Gunderson L. Aggressive treatment for locally advanced irresectable rectal cancer. Br J Surg 1997; 84: 741–9.
- Enker WE. Potency, cure, and local control in the operative treatment of rectal cancer. Arch Surg 1992; 127: 1396–402.
- 5. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986; 1: 1479–82.
- MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet 1993; 341: 457–60.
- Akker JW. Histological verification of the laterale ligament. An anatomical study concerning the autonomic nerve preserving total mesorectal excision. Thesis. University of Utrecht, Dept. of Anatomy, The Netherlands, 1997.
- Nesbakken A, Nygaard K, Bull-Njaa T, Carlsen E, Eri LM. Bladder and sexual dysfunction after mesorectal excision for rectal cancer. Br J Surg 2000; 87: 206–10.
- Kim HK, Jessup JM, Beard CJ, et al. Locally advanced rectal carcinoma: pelvic control and morbidity following preoperative radiation therapy, resection, and intraoperative radiation therapy. Int J Radiat Oncol Biol Phys 1997; 38: 777–83.
- Gunderson LL, Nelson H, Martenson JA, et al. Locally advanced primary coporectal cancer: intraoperative electron and external beam irradiation ± 5-FU. Int J Radiat Oncol Biol Phys 1997; 37: 601–14.
- Willett CG, Shellito PC, Tepper JE, Eliseio R, Convery K, Wood WC. Intraoperative electron beam radiation therapy for primary locally advanced rectal and rectosigmoid carcinoma. J Clin Oncol 1991; 9: 843–9.
- Suzuki K, Gunderson LL, Devine RM, et al. Intraoperative irradiation after palliative surgery for locally recurrent rectal cancer. Cancer 1995; 75: 939–52.
- Willett CG, Shellito PC, Tepper JE, Eliseo R, Convery K, Wood WC. Intraoperative electron beam radiation therapy for recurrent locally advanced rectal or rectosigmoid carcinoma. *Cancer* 1991; 67: 1504–8.
- Hashiguchi Y, Sekine T, Sakamoto H, et al. Intraoperative irradiation after surgery for locally recurrent rectal cancer. Dis Colon Rect 1999; 42: 886–95.
- Gunderson LL, Nelson H, Martenson JA, et al. Intraoperative electron beam and external beam irradiation with or without 5fluorouracil and maximum surgical resection for previously unirradiated, locally recurrent colorectal cancer. Dis Colon Rect 1996; 39: 1379–95.
- Leveckis J, Boucher NR, Parys BT, Reed MWR, Shorthouse AJ, Anderson JB. Bladder and erectile dysfunction before and after rectal surgery for cancer. Br J Urol 1995; 76: 752-6.
- Kinn AC, Ohman U. Bladder and sexual function after surgery for rectal cancer. Dis Colon Rect 1986; 29: 43–8.
- Mannaerts GHH, Martijn H, Crommelin MA, et al. Intraoperative electron beam radiation therapy for locally recurrent rectal carcinoma. Int J Radiat Oncol Biol Phys 1999; 45: 297–308.

- Mannaerts GHH, Martijn H, Crommelin MA, Dries W, Repelaer van Driel OJ, Rutten HJT. Feasibility and first results of multimodality treatment, combing EBRT, extensive surgery and IOERT in locally advanced primary rectal cancer. Int J Radiat Oncol Biol Phys 2000; 47: 425–33.
- Fowler JT. The incidence and consequence of damage to the parasympatic nerve supply to the bladder after abdominoperineal resection of the rectum for carcinoma. Br J Urol 1978; 50: 95–8.
- 21. Banerjee AK. Sexual dysfunction after surgery for rectal cancer. Lancet 1999; **353**: 1900–2.
- Blaivas JG, Barbalias GA. Characteristics of neural injury after abdominoperineal resection. J Urol 1983; 129: 84–7.
- Tepper JÉ, Gunderson LL, Orlow E, et al. Complications of intraoperative radiation therapy. Int J Radiat Oncol Biol Phys 1984; 10: 1831-9.
- Noyes R, Weiss SM, Krall JM, et al. Surgical complications of intraoperative radiation therapy: The radiation therapy oncology group experience. J Surg Oncol 1992; 50: 209–15.
- Kirkegaard P, Hjortrup A, Sanders S. Bladder dysfunction after low anterior resection for mid-rectal cancer. Am J Surg 1981; 141: 266–8.
- Neal DE, Williams NS, Johnston D. A prospective study of bladder function before and after sphincter-saving resections for low carcinoma of the rectum. Br J Urol 1981; 53: 558–62.
- Gerstenberg TC, Nielsen N, Clausen S, Blaabjberg J, Lindenberg J. Bladder function after abdominoperineal resection of the rectum for anorectal cancer: urodynamic investigation before and after operation in consecutive series. Ann Surg 1980; 191: 81–6.
- Eickenberg H-U, Amin M, Klompus W, Lich R. Urologic complications following abdominoperineal resection. J Urol 1976; 115: 180–2.
- Baumrucker GO, Shaw JW. Urological complications following abdominoperineal resection of the rectum. Arch Surg 1953; 67: 502–13.
- Havenga K, Enker WE, McDermott K, Cohen AM, Minsky BD, Guillem J. Male and female sexual and urinary function after total mesorectal excision for carcinoma of the rectum. J Am Coll Surg 1996; 182: 495–502.
- Hojo K, Vernava AM III, Sugihara K, Katumata K. Preservation of urine voiding and sexual functioning after rectal cancer surgery. Dis Colon Rect 1991; 34: 532–9.
- Church JM, Raudkivi PJ, Hill GL. The surgical anatomy of the rectum: a review with particular relevance to the hazards of rectal mobilisation. Int J Colorect Dis 1987; 2: 158–66.
- Stener B, Gunterberg B. High amputation of the sacrum for extirpation of tumors: principles and technique. Spine 1978; 3: 351–66.

- Mundy AR. An anatomical explanation for bladder dysfunction following rectal and uterine surgery. Br J Urol 1982; 54: 501–4.
- Hellstrom P. Urinary and sexual dysfunction after rectosigmoid surgery. Ann Chir Gyn 1988; 77: 51-6.
- 36. Duthie HL. The rectum and anal canal. Clin Gastroenterol 1979; 8: 443-54.
- Masui H, Ike H, Yamaguchi S, Oki S, Shimada H. Male sexual function after autonamic nerve preserving operation for rectal cancer. Dis Colon Rect 1996; 39: 1140-5.
- Campbell MF. Urologic complications of anorectal and colon surgery. Am J Proctol 1961; 12: 43–51.
- Hall SJ, Basile G, Bertero EB, de las Morenas A, Goldstein J. Extensive corporeal fibrosis after penile irradiation. J Urol 1995; 153: 372–7.
- Kinsella TJ, Sindelar WF, Deluca AM, et al. Tolerance of peripheral nerve to intraoperative radiotherapy (IORT): clinical and experimental studies. Int J Radiat Oncol Biol Phys 1985; 11: 1579–85.
- Kinsella TJ, Deluca AM, Barnes M, Anderson W, Terrill R, Sindelar WF. Threshold dose for peripheral neuropathy following intraoperative radiotherapy (IORT) in a large animal model. Int J Radiat Oncol Biol Phys 1991; 20: 697–701.
- Mohiuddin M, Marks GM, Lingareddy V, Marks J. Curative surgical resection following reirradiation for recurrent rectal cancer. Int J Radiat Oncol Biol Phys 1997; 39: 643–9.
- Duijn van J. Urological deviation after abdomino-perineal resection for rectal cancer. Neth J Med 1973; 117: 1925–32.
- McGuire EJ. Urodynamic evaluation after abdominoperineal resection and lumbar vertebral disk herniation. Urology 1975; 6: 63-70.
- Rankin JT. Urological complications of rectal surgery. Br J Urol 1969; 41: 655–9.
- Danzi M, Ferulano GP, Abate S, Califano G. Male sexual function after abdominoperineal resection for rectal cancer. *Dis Colon Rect* 1983; 26: 665–8.
- Wanebo HJ, Marcove RC. Abdominal sarcal resection of locally recurrent rectal cancer. Ann Surg 1981; 194: 458–71.
- Santangelo ML, Romano G, Sassaroli C. Sexual function after resection for rectal cancer. Am J Surg 1987; 154: 502–4.
- Balslev I, Harling H. Sexual dysfunction following operation for carcinoma of the rectum. Dis Colon Rect 1983; 26: 785-8.
- McDonald PJ, Heald RJ. A survey of postoperative function after rectal anastomosis with circular stapling devices. Br J Surg 1983; 70: 727–9.
- Williams NS, Johnston D. The quality of life after rectal excision for low rectal cancer. Br J Surg 1983; 70: 460-2.

Accepted for publication 6 December 2000