ORIGINAL CONTRIBUTION

Measuring Sexual and Urinary Outcomes in Women after Rectal Cancer Excision

P. P. Tekkis, M.D.[1,2] • J. A. Cornish, M.R.C.S.[2] • F. H. Remzi, M.D.[1]
H. S. Tilney, M.R.C.S.[2] • S. A. Strong, M.D.[1] • J. M. Church, M.D.[1]
I. C. Lavery, M.D.[1] • V. W. Fazio, M.D.[1]

1 Department of Colorectal Surgery, Cleveland Clinic Foundation, Cleveland, Ohio
2 Imperial College London, Department of Biosurgery and Surgical Technology, St. Mary's Hospital, London, United Kingdom

PURPOSE: This study was designed to investigate sexual and urinary dysfunction in women who underwent rectal cancer excision, and the influence of tumor and treatment variables on long-term outcomes.

METHODS: Data were prospectively collected on 295 women who underwent rectal cancer excision at a tertiary referral colorectal center from 1998 to 2006. Sexual and urinary function was assessed preoperatively and at intervals up to five years after surgery. Functional outcomes were assessed by using univariate and multivariate regression analysis, chi-squared test for trend, or Kruskal-Wallis test.

RESULTS: The mean age of the patients was 60.9 years. Anterior resection was performed in 222 patients (75.2 percent) and abdominoperineal resection in 73 patients (24.7 percent). Patients who underwent abdominoperineal resection were less sexually active (25 *vs.* 50 percent; $P = 0.02$) and had a lower frequency of intercourse than anterior resection patients at one year after surgery (anterior resection, 3 (0–5) (median interquartile range); abdominoperineal resection 0 (0–4); $P = 0.029$). The frequency of intercourse improved over time for abdominoperineal resection (4 months, 0 (0–0) median interquartile range; 5 years, 3 (0.25–4) median interquartile range; $P = 0.028$). Abdominoperineal resection was associated with increased dyspareunia (odds ratio, 5.75; 95 percent confidence interval (CI), 1.87–17.6; $P = 0.002$), urinary urgency (odds ratio, 8.52; 95 percent CI, 2.81–25.8; $P < 0.001$), incontinence (odds ratio, 2.41; 95 percent CI, 1.11–5.26; $P = 0.026$), poor stream (odds ratio, 5.64, 95 percent CI, 2.55–12.5; $P \leq 0.001$), and urinary retention (odds ratio, 11.7; 95 percent CI, 4.15–32.9; $P < 0.001$). Women who underwent radiotherapy had a 4.68-fold increase in dyspareunia (95 percent CI, 1.84–11.9; $P = 0.001$). Intra-abdominal sepsis was associated with decreased ability to achieve arousal (odds ratio, 0.085; 95 percent CI, 0.008–0.958; $P = 0.046$).

CONCLUSIONS: Abdominoperineal resection, radiotherapy, intra-abdominal sepsis, and age 65 years or older are associated with significant impairments in female urinary and sexual outcomes after rectal cancer excision. Sexual and urinary outcomes should be considered when planning treatment for patients with rectal cancer.

KEY WORDS: Rectal cancer; Sexual function; Urinary function; Anterior resection; Abdominoperineal resection.

Female sexual and urinary dysfunction are recognized complications of both anterior resection (AR) and abdominoperineal excision (APR) for rectal cancer. Although the effects of radical rectal excision on male sexual and urinary function have been well described,[1] substantially less evidence has been published about the impact on similar outcomes in women.[2,3] Furthermore, many studies include patients who have undergone neoadjuvant therapy, making it difficult to determine the impact of surgical operation alone on female sexual and urinary function.[3–5]

Potential explanations for the apparent paucity of evidence include difficulties in the measurement of changes in sexual function over time in women compared with men. The primary focus on male sexual function has been erectile function and retrograde ejaculation, whereas female sexual

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Address of correspondence: Paris Tekkis, M.D., F.R.C.S., Imperial College, Department of Biosurgery and Surgical Technology, St. Mary's Hospital, 10th Floor QEQM Wing, Praed Street, London W2 1NY, United Kingdom. E-mail: p.tekkis@imperial.ac.uk

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function is poorly defined.[6] Most studies assess female sexual function in relation to sexual activity,[3–5,7–10] and other studies report dyspareunia,[3,5] loss of libido,[9] and decreased ability to achieve orgasm[5,7] after rectal cancer excision. Symptoms of urinary dysfunction after AR and APR have been reported to include difficulties in voiding,[5] urinary incontinence,[9] increased frequency of voiding,[4] and the effects of the hypotonic bladder.[10]

The primary goal of the study was to compare the effect of nonrestorative (APR) *vs.* sphincter-preserving (AR) surgery on sexual and urinary function over time for women who underwent rectal cancer excision. The secondary goal was to identify risk factors independently associated with sexual and urinary dysfunction, allowing both patients and clinicians a better understanding of the implications of their treatment options.

METHODS

Data Source

Female patients who underwent rectal cancer excision from 1998 to 2006 were identified from the Institutional Review Board (IRB) approved colorectal cancer database of the Cleveland Clinic Foundation, Cleveland, Ohio. The study has been deemed IRB exempt. Although the database included patients from 1976 onward, prospectively collected functional data were only available from the period beginning 1998. Functional outcomes were recorded at eight time intervals; preoperatively, four months, eight months, one year, two years, three years, four years, and five years after surgery. A dedicated database officer validated the data by requesting duplicate information from patient charts.

Inclusion and Exclusion Criteria

Prospective data on all female patients younger than aged 80 years who underwent AR or APR for rectal cancer (tumors within 15 cm of the anal verge) was included. Patients with Stage IV rectal cancer (metastatic disease) were excluded. All operations were performed by experienced staff surgeons in a practice of high-volume rectal cancer surgery using routine nerve-sparing total mesorectal excision technique as described in previous reports from this institution.[11–13]

Study Design

This was a nonrandomized, observational, comparative study based on a retrospective analysis of prospectively collected data comparing outcomes between women who underwent AR *vs.* APR for rectal cancer.

Study Primary End Points and Definitions

The primary end point of the study was sexual and urinary dysfunction after oncologic resection for rectal cancer in women. Assessment of female sexual function was undertaken across the following domains: 1) whether the patient was sexually active; 2) ability to achieve arousal; 3) ability to attain orgasm; 4) frequency of sexual intercourse per month; and 5) presence of dyspareunia. The domains assessed in relation to urinary function were symptoms of 1) urinary urgency, 2) urinary incontinence, 3) nocturia, 4) poor urinary stream, 5) straining to pass urine, and in addition 6) the incidence of urinary retention, and 7) the need for the use of a urinary catheter.

With the exception of frequency of sexual intercourse, which was represented by the number of episodes per month, each domain of urinary and sexual function was set as a binary outcome (yes/no) and was prospectively recorded at eight time intervals: preoperatively, four months, eight months, one year, two years, three years, four years, and five years after surgery.

Patient comorbidity was assessed by the American Society of Anesthesiologists grade[14] and the tumor stage according to the TNM (tumor, nodes, metastases) stage and stage grouping of the American Joint Committee on Cancer (AJCC).[15] The presence of intra-abdominal sepsis was defined as the radiologic and/or intraoperative evidence of an intra-abdominal/pelvic abscess or anastomotic separation.

Statistical Analysis

Univariate multilevel logistic regression analysis for repeated measures was used to identify risk factors related to impairment of sexual and urinary function. Continuous variables, such as age and tumor height from the anal verge, were categorized into clinically relevant subgroups representing groups of increasing risk. Risk factors with a univariate $P < 0.25$ were included in the multivariate analysis, and $P < 0.05$ was considered to represent statistical significance. The chi-squared test was used to compare demographic characteristics between the two groups, and the impact of variables, such as preoperative radiotherapy and tumor height on sexual and urinary function.

A two-level logistic regression analysis was used to adjust for multiple risk factors and their interactions. The two levels accounted for by the model represented repeated measures of outcomes within the same patient in level one, and the individual patient related risk factors at the second level. The between-subject variability was assessed by the level two variance and the variability of outcomes over different measurement times within subjects was represented by the level one variance, which was set to assume an extrabinomial distribution.

Each risk factor was manually entered into the model starting from the most relevant, smallest P value, and adding each factor in turn. By observing the odds ratios, the 95 percent confidence intervals for each new factor, and the change in the log-likelihood statistic, we were

able to ascertain whether each variable should remain in the model.

Statistical Software

Software packages used for statistical analysis were SPSS®, version 14 (SPSS, Inc., Chicago, IL) and STATA SE version 9.1 (STATA Corp., College Station, TX).

RESULTS

Study Population

The Cleveland Clinic Colorectal Cancer database included 885 patients with prospective data on urinary and sexual function undergoing rectal cancer excision, of whom 313 (35.4 percent) were women (Table 1). A total of 295 women (94.2 percent) who fulfilled the inclusion criteria were identified for the study period of 1998 to 2006. Anterior resection was performed in 222 patients (75.2 percent) and APR in 73 patients (24.7 percent). Overall the mean (standard deviation) follow-up was 3.2 years (±2.9) and the duration of follow-up did not differ significantly between the AR and APR groups.

Patients undergoing APR were significantly older (APR mean (standard deviation) 65.5 (14.1) years *vs.* AR 59.3 (13.2); $P = 0.001$) and were more likely to receive chemotherapy (APR 64.4 percent *vs.* AR 47.7 percent; $P = 0.014$) or radiotherapy (APR 60.3 percent *vs.* AR 33.8 percent; $P < 0.001$). Overall, 119 (40.3 percent) patients were irradiated: 83.3 percent preoperatively and 17.6 percent postoperatively. The AR and APR groups did not differ significantly in terms of tumor stage, the incidence of postoperative intra-abdominal sepsis, or American Society of Anesthesiologists grade. The nonresponse rate for questions on urinary function was 34 to 36 percent for the seven domains and for sexual function the nonresponse rate was 51 to 61 percent. Loss to follow-up was 2.4 percent (n = 7) for Year 1, 1.7 percent (n = 5) for Year 2, 10.2 percent (n = 30) for Year 3, 10.8 percent (n = 32) for Year 4, and 15.3 percent (n = 45) for Year 5.

Sexual Function

Patients who underwent APR were significantly less likely to be sexually active (25 *vs.* 50 percent; $P = 0.02$), and those who were sexually active had a lower frequency of intercourse than AR patients at one year after surgery (AR 3 (0–5) (median interquartile range), APR 0 (0–4); $P = 0.029$; Fig. 1). The frequency of intercourse improved significantly over time for APR patients (4 months, 0 (0–0); 5 years, 3 (0.25–4); $P = 0.028$). At 8 months, APR patients were less likely to be able to achieve arousal (APR 56 percent, AR 77.1 percent; $P = 0.039$) or orgasm (APR 42.9 percent, AR 73.3 percent; $P = 0.009$) than those who underwent AR. The ability to achieve orgasm in patients who underwent APR did improve significantly

TABLE 1. Characteristics of study population: AR *vs.* APR

	Total patients	*AR*	*APR*	*P value* APR vs. AR*
Patients	295	222 (75.2)	73 (24.7)	
Age (yr)	60.9 ± 13.6	59.3 ±13.2	65.5 ± 14.1	**0.001**†
ASA grade				
1	2 (0.7)	1 (0.5)	1 (1.4)	0.092
2	128 (43.4)	104 (46.8)	24 (32.9)	
3	146 (49.5)	103 (46.4)	43 (58.9)	
4	3 (1)	2 (0.9)	1 (1.4)	
Radiotherapy	119 (40.3)	75 (33.8)	44 (60.3)	**<0.001**
Chemotherapy	153 (51.9)	106 (47.7)	47 (64.4)	**0.014**
Height tumor>5 cm	178 (60.3)	168 (75.4)	10 (13.7)	**<0.001**
Tumor (T) stage				0.408
T_1	277 (93.9)	206 (92.8)	71 (97.3)	
T_2	2 (0.6)	2 (0.9)	1 (1.4)	
T_3	14 (4.7)	13 (5.9)	1 (1.4)	
T_4	1 (0.3)	1 (0.5)	0 (0)	
Nodal (N) stage				0.572
N_1	4 (1.4)	4 (1.8)	.	
N_2	4 (1.4)	4 (1.8)	.	
N_0	70 (23.7)	51 (23)	19 (26)	
Nx	5 (1.4)	4 (1.8)	1 (1.4)	
Intra-abdominal sepsis	11 (3.72)	9 (4.05)	2 (2.73)	0.064
Follow-up (yr)	3.2 ± 2.9	3.28 ± 3.2	2.95 ± 1.6	0.727†
Any recurrence	7 (2.4)	4 (1.8)	3 (4.1)	0.261

AR = anterior resection; APR = abdominoperineal excision; ASA = American Society of Anesthesiologists.
Data are numbers with percentages in parentheses or means ± standard deviations unless otherwise indicated.
*Pearson's chi-squared statistic; †ANOVA, significant *P* value (<0.05) in **bold.**

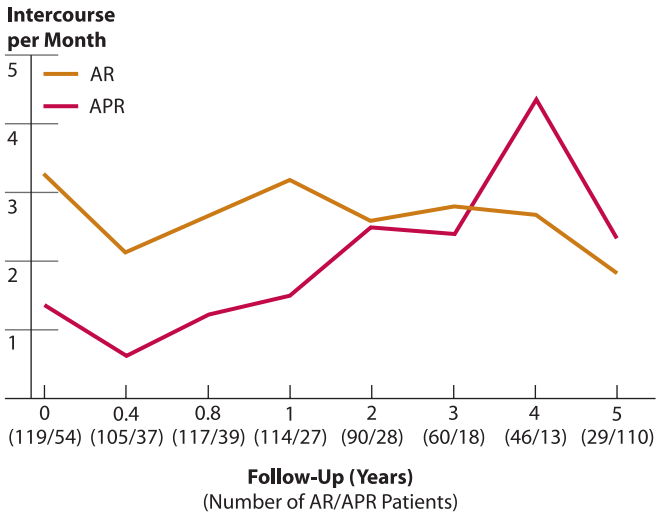

FIGURE 1. Trend in frequency of intercourse per month over time: anterior resection (AR) *vs.* abdominoperineal resection (APR).

over time (4 months 26.3 percent; 5 years 66.7 percent; $P = 0.028$). Dyspareunia became significantly worse five years after anterior resection (4 months 18.2 percent; 5 years 27.3 percent; $P = 0.03$); however, APR was associated with increased dyspareunia for up to four years follow-up (APR 80 percent *vs.* AR 25 percent; $P = 0.016$; Table 2).

$P < 0.05$ in the trend over time column of Table 2 indicates that patients within the group of a particular operation type have experienced a significant change in their symptom during the five-year follow-up (between-occasion-within-subject variance). The trend over time does not include preoperative results. $P < 0.05$ in Table 2 at fixed points of follow-up (*e.g.*, 4 months) demonstrates that there is a significant difference in the number of patients who experience symptoms between AR and APR.

On univariate regression analysis of potential explanatory variables against the five domains of sexual function (the presence of sexual activity, the ability to achieve arousal and orgasm, the frequency of sexual intercourse per month, and the presence of dyspareunia), the operation performed (AR *vs.* APR), the use of radiotherapy (no radiotherapy *vs.* radiotherapy), age at surgery (<65years *vs.* ≥65 years), and the development of intra-abdominal sepsis postoperatively (no sepsis *vs.* sepsis) were found to be significantly associated with adverse sexual outcomes ($P < 0.05$). Chemotherapy, partial resection of bladder/vagina, and diabetes were not found to be significant. Significant factors were entered into a multifactorial regression model, the results which are shown in Table 3. Dyspareunia was increased 5.75-fold after APR (95 percent confidence interval (CI), 1.87–17.6; $P = 0.002$) and was 4.68 times more likely after radiotherapy (95 percent CI, 1.83–11.9; $P = 0.001$). Dyspareunia remained a significant symptom for five years after APR ($P = 0.001$; Fig. 2).

Patients who were aged 65 years or older were significantly less likely to experience dyspareunia postoperatively

TABLE 2. Five domains of sexual function in women who underwent AR *vs.* APR for rectal cancer excision

Sexual function	*Preoperative*	*0.4 years*	*0.8 years*	*1 year*	*2 years*	*3 years*	*4 years*	*5 years*	*P value trend (time)*
Sexually active									
AR	44.8 (105)	40.2 (117)	38.6 (114)	50 (90)	37.4 (91)	43.3 (60)	43.5 (46)	34.5 (29)	0.914‡
APR	27 (37)	12.8 (39)	25.9 (27)	25 (28)	30.8 (26)	27.8 (18)	30.8 (13)	20 (10)	0.126‡
p value*	0.058	**0.002**	0.218	**0.02**	0.537	0.237	0.41	0.392	
Ability to achieve arousal									
AR	69.8 (116)	65.6(96)	77.1 (83)	77.9 (68)	74.6 (71)	77.8 (45)	87.5 (32)	66.7 (24)	0.106‡
APR	66.7 (27)	55.2(29)	56 (25)	46.2 (26)	72.2 (18)	53.3 (15)	100 (7)	65.6 (8)	0.202‡
P value*	0.749	0.306	**0.039**	**0.003**	0.834	0.069	0.323	0.83	
Frequency of intercourse per month									
AR	1 (0–5)	0 (0–4)	1 (0–4)	3 (0–5)	2 (0–4)	2.5 (0.25–4)	2 (0–4)	1.5 (0–3.25)	0.097§
APR	0 (0–1)	0 (0–0)	0 (0–2.75)	0 (0–4)	2.5 (0–4.8)	1 (0–4)	4 (0–7.5)	3 (0.25–4)	**0.028**§
P value†	**0.02**	**0.014**	0.096	**0.029**	0.926	0.314	0.461	0.485	
Ability to attain orgasm									
AR	66.7 (108)	64 (86)	73.3 (75)	76.9 (65)	73.4 (64)	77.5 (40)	86.2 (29)	56.5 (23)	0.192‡
APR	65.2 (23)	26.3 (19)	42.9 (21)	55 (20)	71.4 (14)	61.5 (13)	100 (6)	66.7 (9)	<**0.001**‡
P value*	0.894	**0.003**	**0.009**	0.057	0.878	0.257	0.334	0.599	
Dyspareunia									
AR	14.5 (110)	18.2 (88)	27.8 (72)	33.3 (63)	35.5 (62)	38.5 (39)	25 (28)	27.3 (22)	**0.033**‡
APR	25 (24)	40 (20)	55 (20)	50 (18)	76.9 (13)	50 (12)	80 (5)	62.5 (8)	0.099‡
P value*	0.21	**0.034**	**0.023**	0.197	**0.006**	0.478	**0.016**	0.077	

AR = anterior resection; APR = abdominoperineal excision.
Data are percentages of total number of patients with the event with the total number of patients within each time interval shown in parentheses or medians with ranges in parentheses unless otherwise indicated.
*Pearson's chi-squared statistic, †Mann-Whitney *U* test, ‡Gamma statistic, §Kruskal-Wallis statistic, significant *P* value (<0.05) in **bold.**

TABLE 3. Multivariate analysis of factors associated with sexual dysfunction in women who underwent rectal cancer excision

	Sexually active†		*Aroused*†		*Dyspareunia*†		*Orgasm*†		*Intercourse per month*‡	
Risk factor	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*β*	*95 percent CI*
Groups										
AR	1		1		1		1		1	
APR	0.39	0.144, 1.05	0.694	4.81, 10122.5	5.75*	1.87, 17.6	0.548	0.183, 1.64	0.454	0.182, 1.13
No radiotherapy					1					
Radiotherapy					4.68*	1.83, 11.9				
Age <65 yr	1		1		1		1		1	
Age ≥65 yr	0.016*	0.006, 0.039	0.04*	0.016, 0.102	0.095*	0.031, 0.291	0.043*	0.017, 0.112	0.093*	0.041, 0.208
No intra-abdominal sepsis	1		1				1			
Intra-abdominal sepsis	0.172	0.021, 1.38	0.085*	0.008, 0.958			0.141	0.016. 1.25		
Time interval										
Preoperative	1		1		1		1		1	
4 mo	0.443	0.191, 1.03	0.565	0.239, 1.33	2.85	1.08, 7.51	0.336*	0.138, 0.819	0.315*	0.164, 0.608
8 mo	0.001	0.214, 1.18	0.965	0.382, 2.44	5.56	2.09, 14.9	0.571	0.224, 1.46	0.337*	0.17, 0.667
1 yr	1.97	0.438, 2.61	0.564	0.211, 1.51	7.22	2.63, 19.8	0.93	0.34, 2.54	0.472*	0.229, 0.973
2 yr	0.566	0.235, 1.36	0.608	0.225, 1.64	9.25	3.36, 25.5	0.588	0.214, 1.62	0.509	0.242, 1.07
3 yr	0.089	0.273, 2.26	0.624	0.198, 1.96	12	3.89, 37.3	0.991	0.3, 3.27	0.433*	0.187, 1
4 yr	0.431	0.139, 1.34	1.824	0.307, 10.8	8.64	2.31, 32.3	1.51	0.28, 8.13	0.515	0.2, 1.33
5 yr	0.274	0.069, 2.27	0.404	0.098, 1.66	12.8	3.18, 51.3	0.592	0.152, 2.31	0.302*	0.106, 0.862
Constant	1.05	0.289, 1.81	3.17	2.31, 4.03	−3.46	−4.41, −2.61	2.81	1.97, 3.65	3.96	3.32, 4.6
Level 2 variance	11.9	8.85, 17	11	7.84, 16.2	8.99	6.22, 14	10.1	7.17, 15.1	2.19	
Level 1 variance	1.92	1.81, 2.02	1.89	1.76, 2.02	1.81	1.66, 1.97	1.86	1.72, 2	0.51	

AR = anterior resection; APR = abdominoperineal excision; OR = odds ratio; CI = confidence interval; DXT = radiotherapy.
*Significant *P* value (<0.05); †logistic regression analysis; ‡linear regression analysis.

(odds ratio (OR)=0.095; 95 percent CI, 0.031–0.291; $P = 0.043$); however, they were less sexually active (OR = 0.016; 95 percent CI, 0.006–0.039; $P = 0.04$), had a lower frequency of intercourse (OR = 0.093; 95 percent CI, 0.041–0.208; $P < 0.001$), and had significant difficulty in achieving arousal and orgasm compared with patients younger than aged 65 years ($P < 0.001$).

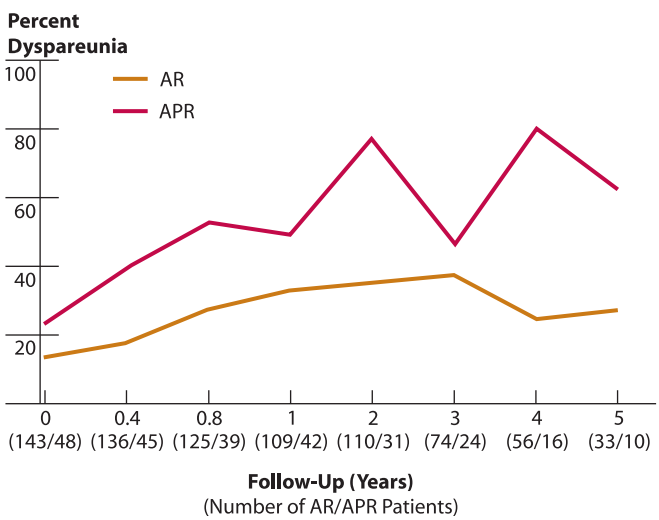

FIGURE 2. Trend in dyspareunia over time: anterior resection (AR) *vs.* abdominoperineal resection (APR).

Patients with intra-abdominal sepsis were less likely be able to achieve arousal postoperatively (OR = 0.085; 95 percent CI, 0.008–0.958; $P = 0.046$). Tumor height was not associated with a significant increase in sexual dysfunction on multivariate analysis.

Urinary Function

The results of changes in urinary function for anterior resection and APR over time can be seen in Table 4. Poor stream was more common after APR than AR at four months, eight months, one year, and two years ($P = 0.007$) and became worse over time. Urinary urgency was more frequent in APR patients for up to one year after surgery (APR 54.8 percent *vs.* AR 35.8 percent; $P = 0.034$), but symptoms of urgency increased over time for anterior resection patients (32.4 percent at 4 months *vs.* 54.5 percent at 5 years; $P = 0.008$). APR patients were significantly more likely to develop urinary retention than anterior resection patients up to two years after operation (APR 38.7 percent *vs.* 17.6 percent AR; $P = 0.013$); however, use of a catheter was only significantly higher for APR patients four months postoperatively (APR 9.1 percent *vs.* AR 1.5 percent; $P = 0.014$).

APR patients had a higher incidence of incontinence than anterior resection patients at four months (APR 42.2 percent *vs.* AR 16.2 percent; $P < 0.001$) and at one year (APR 36.6 percent *vs.* AR 17.8 percent; $P = 0.015$). Anterior resection patients had an increased risk of

TABLE 4. Seven domains of urinary function in women: AR *vs.* APR

Urinary function	*Preoperative*	*0.4 years*	*0.8 years*	*1 year*	*2 years*	*3 years*	*4 years*	*5 years*	*P value trend (time)*
Poor stream									
AR	7 (10)	14.1 (19)	8.9 (11)	5.6 (6)	11.8(13)	15.1(73)	17.9 (56)	15.6 (32)	0.343*
APR	12.5 (48)	28.6 (42)	28.9 (38)	25.6 (39)	32.3 (31)	30.4 (23)	31.3 (16)	30.8 (13)	0.861*
P value†	0.239	**0.031**	**0.002**	**0.001**	**0.007**	0.1	0.245	0.25	
Nocturia									
AR	33.3 (144)	25.7 (136)	22.2 (126)	21.1 (109)	22.5 (111)	16.4 (73)	23.2 (56)	30.3 (33)	0.597*
APR	27.1 (48)	35.6 (45)	35.9 (39)	28.6 (42)	25 (32)	24 (25)	20 (15)	15.4 (13)	0.053*
P value†	0.421	0.204	0.087	0.33	0.769	0.399	0.791	0.299	
Strain water									
AR	2.8 (144)	8.8 (136)	8.8 (125)	5.5 (109)	6.3 (111)	5.5 (73)	12.7 (55)	9.4 (32)	0.974*
APR	8.3 (48)	24.4 (45)	15.4 (39)	14.3 (42)	9.7 (31)	13 (23)	18.8 (16)	7.7 (13)	0.145*
P value†	0.095	**0.006**	0.239	0.074	0.517	0.224	0.542	0.857	
Urinary retention									
AR	16.3 (141)	22.1 (136)	22.4 (125)	22.2 (108)	17.6 (108)	31.1 (74)	20 (55)	27.3 (33)	0.473*
APR	18.8 (48)	48.9 (45)	51.3 (39)	40.5 (42)	38.7 (31)	44 (25)	43.8 (16)	30.8 (13)	0.225*
P value†	0.697	**0.001**	**0.001**	**0.024**	**0.013**	0.24	0.055	0.813	
Urgency									
AR	35 (143)	32.4 (136)	36 (125)	35.8 (109)	36.4 (110)	47.3 (74)	42.9 (56)	54.5 (33)	**0.008***
APR	47.9 (48)	60 (45)	59 (39)	54.8 (42)	48.4 (31)	45.8 (24)	62.5 (16)	39.5 (13)	0.221*
P value†	0.11	**0.001**	**0.011**	**0.034**	0.225	0.901	0.165	0.326	
Incontinence									
AR	20.7 (140)	16.2 (136)	21.8 (124)	17.8 (107)	28.4 (109)	29.7 (74)	34.5 (55)	33.3 (33)	<**0.001***
APR	25 (48)	42.2 (45)	28.9 (38)	36.6 (41)	29 (31)	29.2 (24)	37.5 (16)	23.1 (13)	0.305*
P value†	0.535	<**0.001**	0.361	**0.015**	0.949	0.958	0.828	0.496	
Catheter									
AR	0.7 (143)	1.5 (136)	0.8 (125)	1.9 (108)	1.8 (109)	0 (73)	0 (55)	0 (33)	0.304*
APR	0 (48)	9.1 (44)	2.6 (39)	4.8 (42)	3.2 (31)	1 (25)	0 (16)	7.7 (13)	0.393*
P value†	0.561	**0.014**	0.381	0.321	0.637	0.086		0.107	

AR = anterior resection; APR = abdominoperineal excision; strain water = symptoms of straining to pass water; catheter = patient required insertion of urinary catheter. Data are percentages of total number of patients with the event with the total number of patients within each time interval shown in parentheses unless otherwise indicated.

*Gamma statistic; †Pearson's chi-squared statistic, significant *P* value (<0.05) in **bold.**

developing incontinence over time (16.2 percent at 4 months *vs.* 33.3 percent at 5 years; $P \leq 0.001$). There was no significant improvement in the number of patients who experienced incontinence during the five-year follow-up for APR. There was a trend of worsening function; however, this was not significant. Straining was worse in APR patients than anterior resection at four months (APR 24.4 percent *vs.* AR 8.8 percent; $P = 0.006$); however, the APR patients improved slowly over time. There was no significant difference in nocturia between the two groups and there was a nonsignificant trend for improvement in the incidence of nocturia over time for APR patients.

On univariate regression using the seven domains of urinary function, operation (AR *vs.* APR), tumor height (≤5 cm *vs.* >5 cm), use of radiotherapy (no radiotherapy *vs.* radiotherapy), age (<65 years *vs.* ≥65 years), and development of intra-abdominal sepsis postoperatively (no sepsis *vs.* sepsis) were found to be associated with impaired urinary function. The results of the multifactorial regression analysis for five of the seven domains of urinary function are shown in Table 5. Abdominoperineal resection was associated with a higher risk of urinary urgency (OR = 8.52; 95 percent CI, 2.82–25.8; $P < 0.001$), incontinence (OR = 2.41; 95 percent CI, 1.11–5.26; $P = 0.026$), and poor stream (OR = 5.64; 95 percent CI, 2.55–12.5; $P \leq 0.001$). The risk of experiencing symptoms of poor stream remained poor during the five years of follow-up (5 years OR = 5.96; 95 percent CI, 1.65–21.5; $P = 0.006$). The risk of urinary incontinence was greater at two and four years of follow-up. Patients older than aged 65 years had a higher risk of nocturia (OR = 2.05; 95 percent CI, 1–4.2; $P < 0.05$) but were 60 percent less likely to strain to pass urine (95 percent CI, 0.166–0.943; $P = 0.036$). Risk of straining to pass urine was significantly worse at the follow-up of four and eight months.

Radiotherapy and the presence of intra-abdominal sepsis were not significant risk factors for any of the seven domains of urinary function. APR was the only significant independent predictor for catheter use on multivariate analysis (OR = 3.96; 95 percent CI, 1.32–11.8; $P = 0.014$). APR was associated with an increased risk of urinary retention postoperatively (OR = 11.7; 95 percent CI, 4.15–32.9; $P < 0.001$). Age older than 65 years was

TABLE 5. Multivariate analysis of factors associated with urinary dysfunction in women who underwent rectal cancer excision

	Strain water†		*Urgency*†		*Incontinence*†		*Nocturia*†		*Poor stream*†	
Risk factor	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*OR*	*95 percent CI*	*OR*	*95 percent CI*
Groups										
AR	1		1		1		1		1	
APR	4.72*	1.91, 11.7	8.52*	2.81, 25.8	2.41*	1.11, 5.26	1.45	0.647, 3.27	5.64*	2.55, 12.5
Tumor>5 cm			1							
Tumor ≤5 cm			0.194*	0.072, 0.527						
Age<65 yr	1						1			
Age ≥65 yr	0.396*	0.166, 0.943					2.05*	1, 4.2		
No intra-abdominal sepsis							1			
Intra-abdominal sepsis							6.82	1.25, 37.2		
Time interval										
Preoperative	1		1		1		1		1	
4 mo	5.84*	2.07, 16.5	0.846	0.430, 1.67	1.128	0.564, 2.26	0.771	0.407, 1.46	4.36*	1.86, 10.2
8 mo	4.47*	1.51, 13.2	1.22	0.607, 2.46	1.13	0.66, 2.73	0.653	0.332, 1.29	2.52*	1.04, 6.13
1 yr	3.13	0.996, 9.81	1.18	0.579, 2.41	1.34	0.586, 2.55	0.448	0.219, 0.918	1.94	0.754, 5.01
2 yr	3.34*	1.02, 10.9	1.08	0.517, 2.24	1.22	1.06, 4.56	0.503	0.243, 1.04	4.37*	1.76, 10.9
3 yr	2.61*	0.711, 9.61	2.06	0.91, 4.66	2.16	0.918, 4.64	0.26	0.107, 0.637	4.75*	1.77, 12.7
4 yr	7.22*	2.04, 25.6	1.83	0.731, 4.56	2.07	1.65, 9,88	0.395	0.147, 1.06	5.33*	1.83, 15.5
5 yr	3.45	0.705, 16.9	1.63	0.539, 4.95	4.03	0.761, 6.24	0.518	0.163, 1.65	5.96*	1.65, 21.5
Constant	−5.02	−6.1, −3.94	0.766	−0.523, 2.05	2.18	0.045, 0.154	−1.81	−2.46, −1.16	0.012	0.005, 0.027
Level 2 variance	7.38	5.17, 11.4	10.2	7.56, 14.5	9.64	7.21, 13.5	9.78	7.31, 13.7	7.74	5.66, 11.2
Level 1 variance	1.73	1.57, 1.9	1.86	1.74, 1.98	1.84	1.72, 1.96	1.85	1.73, 1.96	1.75	1.61, 1.9

CI = confidence interval; OR = odds ratio;
*Significant *P* value (<0.05); †logistic regression analysis.

associated with a 69 percent decrease in urinary retention (95 percent CI, 0.152–0.647; $P = 0.002$).

DISCUSSION

This study has highlighted how urinary and sexual function is significantly impaired in women after radical excision of rectal cancer. Fewer than half of the patients studied were found to be sexually active one year after surgery, and of those who were, a significantly higher proportion had undergone AR compared with APR. On multivariate analysis, accounting for factors, including the age of the patients and the height of their tumors above the anal verge, APR was associated with reduced sexual activity, an increased incidence of dyspareunia, and poor urinary function in terms of symptoms of urgency, incontinence, impaired stream, and episodes of retention. Long-term sequelae of postoperative intra-abdominal sepsis were found to include significant reductions in the ability to achieve arousal and orgasm compared with those patients with an uncomplicated postoperative course.

There are limitations to this study, which should be recognized when interpreting the data. There was a progressive decrease in the number of patients included at each follow-up time interval. Patients were mainly lost to follow-up through death and changes in geographic location. The information was collected using nonvalidated questionnaires, which would have allowed greater reliability and also provided information on domains such as desire, lubrication, and overall sexual satisfaction. Although sexual activity and frequency of intercourse are not used as indicators of sexual function in the most commonly used female sexual function questionnaires (Female Sexual Function Index,[16] and the Golombok Rust Inventory of Sexual Satisfaction[17]), they are important and may act as indicators of sexual function.

Urinary function was assessed through patients' symptoms rather than invasive urodynamic and flow studies. This should be taken into account when interpreting the results; however, the questions act as a screening tool for dysfunction and provide an indication of bladder function. The purpose of the data collected was to allow an overview of the functional outcomes of patients postoperatively. The relationship status and sexual orientation is not known for the patients and this may have an impact on sexual activity and frequency of sexual intercourse. We have not addressed the menopausal status of the patients, which can affect levels of desire, lubrication, and dyspareunia[18,19] and is associated with vaginal atrophy. The mean age for both APR and AR patients was older than 55 years, therefore, it is likely that the majority of patients were menopausal or perimenopausal. Information on the menopausal state, the use of hormone replacement therapy, and previous pelvic surgery is important, and the information collected in

the future for the database will be amended to include these aspects. The response rate of 40 percent for questions on sexual function is similar to previously published studies[20,21] and is related to topic and the nature of the questions.

The main urogenital nerves that are at risk during pelvic dissection are the 1) nervi erigentes (parasympathetic sacral splanchnic nerves), 2) inferior hypogastric plexus, 3) superior hypogastric plexus, and 4) somatic pudendal nerves. Impairments in sexual and urinary function after radical rectal surgery may be the result of damage to these autonomic nerves from blunt pelvic dissection or sharp dissection without clear visualization and protection of these nerve fibers. Access to the lesser pelvis is limited by its bony limits and the autonomic nerves lie in close relation to the mesorectum and its plane of dissection. Damage to these nerves is likely to explain in part the adverse outcomes after mesorectal excision. Total mesorectal excision with dissection outside the fascia propria of the rectum has been reported to impair female sexual and urinary function.[9] The addition of autonomic nerve preservation to total mesorectal excision has been shown to maintain improved female sexual function (for arousal, ability to achieve orgasm, and vaginal lubrication) and urinary function postoperatively (for the symptoms of frequency and incontinence).[7,22] More experienced surgeons are able to perform nerve preservation techniques to a greater degree.[2] Detailed knowledge of the anatomy of the pelvic autonomic nerves is vital to minimize the potential for sexual and urinary function after rectal cancer excision.

In addition to nerve injury, postoperative scarring around the vagina may contribute to dissatisfaction during, or avoidance of, sexual intercourse. Low rectal dissection requires full mobilization through the rectovaginal septum, and studies have reported that women undergoing pelvic surgery felt that the vagina was inelastic and too short during subsequent sexual intercourse.[3,23] These problems may be exacerbated if partial excision of the vaginal wall is required for an acceptable margin of cancer excision to be achieved, or as a result of pelvic adhesions.[23] The use of advanced sphincter-sparing techniques, including intersphincteric dissection,[24] or coloanal anastomosis may cause further deterioration of sexual function by leading to fibrosis and distortion of the perineum, potentially impairing compliance of the distal vagina, leading to painful intercourse. Abdominoperineal resection has been associated with modification of the bladder's position in the pelvis and muscular pain during intercourse.[25]

The present study has demonstrated how those patients who receive radiotherapy are 4.7 times more likely to experience dyspareunia than patients who are not irradiated. Previous studies have shown radiotherapy to have a detrimental effect on female sexual function,[7,26,27] with increased dyspareunia, loss of libido, and fatigue.[28] Mechanisms for the increased incidence of dyspareunia after external beam radiotherapy have been identified as diffuse fibrosis and mucosal irritation.[7] In addition, younger, premenopausal patients undergoing pelvic irradiation may develop premature ovarian failure, which has been associated with loss of the ability to achieve orgasm and postcoital bleeding.[29]

By using multivariate regression analysis, this study has attempted to determine the significance of individual factors in urogenital dysfunction. The choice of operative procedure performed and the use or otherwise of (neo)-adjuvant radiotherapy may be regarded as the most important factors determining subsequent sexual and urinary function, not least when considering how these are the only factors over which the clinician and patient can exert choice, whereas other variables, such as age of the patient, are fixed and prediction of postoperative intra-abdominal sepsis is difficult. When the tumor characteristics dictate that there is no acceptable alternative to APR, this study provides information for potential patients concerning their likely subsequent sexual and urinary function.

It is intuitive that the age of patients with rectal cancer will impact significantly on their postoperative sexual function. The results of the present confirm how those older than aged 65 years experienced a significantly higher risk of sexual dysfunction across all domains compared with their younger counterparts. A systematic review on the impact of aging on sexual function in women concluded that women experience a decrease in sexual activity and desire with increasing age and that this decline usually begins in the fourth decade.[30] Although the majority of patients treated for rectal cancer are older than aged 60 years, it has been reported that older patients are still concerned with limitations in their postoperative sexual function,[3] therefore, it is important that the outcomes illustrated by studies such as this are communicated to patients as part of the consent process, allowing them to make better informed decisions about the management of their rectal cancers. It is important not to dismiss concern over sexual dysfunction in the older population as an insignificant problem, because it may significantly impact patients' subsequent quality of life.

CONCLUSIONS

Abdominoperineal resection, radiotherapy, age older than 65 years, and the presence of intra-abdominal septic complications are important predictors for poor sexual outcome. Abdominoperineal resection significantly reduces sexual activity, frequency of intercourse, ability to achieve arousal and orgasm, and increases the risk of dyspareunia compared with anterior resection. In

addition, APR adversely affects urinary function in the domains of urgency, incontinence, flow, and urinary retention. Further prospective studies using validated questionnaires are required to assess the full impact of rectal cancer surgery on urinary and sexual function. Although the primary goals of rectal cancer surgery are oncologic clearance of the tumor, minimizing local recurrence, and prolonging survival, the quality of life postoperatively also is important for the patient. Knowledge of potential future problems in sexual and urinary function should be incorporated into preoperative counseling and informed consent.

REFERENCES

1. Heriot AG TP, Fazio VW, Neary P, Lavery IC. Adjuvant radiotherapy is associated with increased sexual dysfunction in male patients undergoing resection for rectal cancer. Ann Surg 2005;242:502–11.
2. Havenga K, Maas CP, DeRuiter MC, Welvaart K, Trimbos JB. Avoiding long-term disturbance to bladder and sexual function in pelvic surgery, particularly with rectal cancer. Semin Surg Oncol 2000;18:235–43.
3. Platell CF, Thompson PJ, Makin GB. Sexual health in women following pelvic surgery for rectal cancer. Br J Surg 2004;91:465–8.
4. Jayne DG, Brown JM, Thorpe H, Walker J, Quirke P, Guillou PJ. Bladder and sexual function following resection for rectal cancer in a randomized clinical trial of laparoscopic *vs.* open technique. Br J Surg 2005;92:1124–32.
5. Mannaerts GH, Schijven MP, Hendrikx A, Martijn H, Rutten HJ, Wiggers T. Urologic and sexual morbidity following multimodality treatment for locally advanced primary and locally recurrent rectal cancer. Eur J Surg Oncol 2001;27:265–72.
6. Althof SE, Dean J, Derogatis LR, Rosen RC, Sisson M. Current perspectives on the clinical assessment and diagnosis of female sexual dysfunction and clinical studies of potential therapies: a statement of concern. J Sex Med 2005;2(Suppl 3):146–53.
7. Havenga K, Enker WE, McDermott K, Cohen AM, Minsky BD, Guillem J. Male and female sexual and urinary function after total mesorectal excision with autonomic nerve preservation for carcinoma of the rectum. J Am Coll Surg 1996;182:495–502.
8. Marijnen CA, van de Velde CJ, Putter H, *et al.* Impact of short-term preoperative radiotherapy on health-related quality of life and sexual functioning in primary rectal cancer: report of a multicenter randomized trial. J Clin Oncol 2005;23:1847–58.
9. 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.
10. Sterk P, Shekarriz B, Gunter S, *et al.* Voiding and sexual dysfunction after deep rectal resection and total mesorectal excision: prospective study on 52 patients. Int J Colorectal Dis 2005;20:423–7.
11. Lavery IC, Lopez-Kostner F, Fazio VW, Fernandez-Martin M, Milsom JW, Church JM. Chances of cure are not compromised with sphincter-saving procedures for cancer of the lower third of the rectum. Surgery 1997;122:779–85.
12. Lavery IC, Lopez-Kostner F, Pelley RJ, Fine RM. Treatment of colon and rectal cancer. Surg Clin North Am 2000;80:535–69, ix.
13. Lopez-Kostner F, Lavery IC, Hool GR, Rybicki LA, Fazio VW. Total mesorectal excision is not necessary for cancers of the upper rectum. Surgery 1998;124:612–8.
14. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. JAMA 1961;178:261–6.
15. AJCC. Cancer staging manual. New York: Springer, 2002.
16. Rosen R, Brown C, Heiman J, *et al.* The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000;26:191–208.
17. Rust J, Golombok S. The Golombok-Rust Inventory of Sexual Satisfaction (GRISS). Br J Clin Psychol 1985;24:63–4.
18. Avis NE, Stellato R, Crawford S, Johannes C, Longcope C. Is there an association between menopause status and sexual functioning? Menopause 2000;7:297–309.
19. Dennerstein L, Alexander JL, Kotz K. The menopause and sexual functioning: a review of the population-based studies. Annu Rev Sex Res 2003;14:64–82.
20. Bambrick M, Fazio VW, Hull TL, Pucel G. Sexual function following restorative proctocolectomy in women. Dis Colon Rectum 1996;39:610–4.
21. Timmer A, Bauer A, Dignass A, Rogler G. Sexual function in persons with inflammatory bowel disease: a survey with matched controls. Clin Gastroenterol Hepatol 2007;5:87–94.
22. Maas CP, Moriya Y, Steup WH, Kiebert GM, Klein Kranenberg WM, Van de Velde CJ. Radical and nerve-preserving surgery for rectal cancer in the Netherlands: a prospective study on morbidity and functional outcome. Br J Surg 1998;85:92–7.
23. Bergmark K, Avall-Lundqvist E, Dickman PW, Henningsohn L, Steineck G. Vaginal changes and sexuality in women with a history of cervical cancer. N Engl J Med 1999;340:1383–9.
24. Banerjee AK. Sexual dysfunction after surgery for rectal cancer. Lancet 1999;353:1900–2.
25. Pocard MZF, Haab F, Caplin S, Parc R, Tiret E. A prospective study of sexual and urinary function before and after total mesorectal excision with autonomic nerve preservation for rectal cancer. Surgery 2002;131:368–72.
26. Jensen PT, Groenvold M, Klee MC, Thranov I, Petersen MA, Machin D. Longitudinal study of sexual function and vaginal changes after radiotherapy for cervical cancer. Int J Radiat Oncol Biol Phys 2003;56:937–49.
27. Ooi BS, Tjandra JJ, Green MD. Morbidities of adjuvant chemotherapy and radiotherapy for resectable rectal cancer: an overview. Dis Colon Rectum 1999;42:403–18.
28. Quah HM, Jayne DG, Eu KW, Seow-Choen F. Bladder and sexual dysfunction following laparoscopically assisted and conventional open mesorectal resection for cancer. Br J Surg 2002;89:1551–6.
29. Monga U. Sexual functioning in cancer patients. Sexuality Disability 2002;20:277–95.
30. Hayes R, Dennerstein L. The impact of aging on sexual function and sexual dysfunction in women: a review of population-based studies. J Sex Med 2005;2:317–30.