Urogenital function 3 years after abdominoperineal excision for rectal cancer

A. Ledebo*, D. Bock†‡, M. Prytz†‡, E. Haglind†‡ and E. Angenete†‡

*Department of Surgery, NU Hospital Group, Trollhättan, Sweden, †Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, and ‡SSORG – Scandinavian Surgical Outcomes Research Group, Sahlgrenska University Hospital/Ostra, Gothenburg, Sweden

Received 4 December 2017; accepted 6 April 2018; Accepted Article online 21 April 2018

Abstract

Aim The aim of this study was to explore urogenital dysfunction and associated risk factors after treatment of rectal cancer, in a large national cohort of patients 3 years after abdominoperineal excision, and to compare outcomes with a reference population and a cohort of patients operated for prostate cancer.

Method Patients treated with abdominoperineal excision in 2007–2009 were identified using the Swedish Colorectal Cancer Registry. All consenting patients received a questionnaire. A sample of the Swedish population was contacted and completed a questionnaire. Patients undergoing radical prostatectomy in a prospective multicentre trial received questionnaires 24 months after surgery.

Results In the abdominoperineal excision, reference and radical prostatectomy populations 72%, 51% and 91% of the questionnaires were returned. Within the abdominoperineal excision group 36% of the men and 57% of the women were incontinent postoperatively. A sample of the Swedish population was contacted and completed a questionnaire. Patients undergoing radical prostatectomy in a prospective multicentre trial received questionnaires 24 months after surgery.

Results In the abdominoperineal excision, reference and radical prostatectomy populations 72%, 51% and 91% of the questionnaires were returned. Within the abdominoperineal excision group 36% of the men and 57% of the women were incontinent postoperatively. Fifteen per cent and 37% of men and women in the reference group were incontinent. Two years after radical prostatectomy 49% were incontinent. Seventy-four per cent of the men had erectile dysfunction after abdominoperineal excision. Nineteen per cent of the women experienced reduced ability to reach orgasm. Fewer men and women experienced their present sex life as satisfying after abdominoperineal excision for rectal cancer compared with the reference population.

Conclusion A large proportion of patients endure persistent urogenital dysfunction after abdominoperineal excision for rectal cancer as do men after radical prostatectomy. Effects on sexual and urinary function should be part of preoperative information and after surgery patients should be asked about function in order to identify those in need of further assistance.

Keywords Rectal cancer, prostate cancer, urinary dysfunction, sexual dysfunction, urogenital dysfunction

What does this paper add to the literature? Rectal cancer treatment is associated with impairments such as urogenital dysfunction. Surgery is found to be associated with sexual dysfunction and associated distress. Prevalence estimates of dysfunction are based on a large cohort using a validated questionnaire with a large response rate. Patients should be advised about possible effects on urogenital function at the time of decision on treatment and asked about function after surgery in order to identify those in need of further assistance.

Introduction

Abdominoperineal excision (APE) is a surgical treatment for low rectal cancer. In addition to surgery, patients with advanced tumours receive (chemo)radiotherapy preoperatively. The neoadjuvant (chemo)radiotherapy may cause nerve and tissue damage and decrease the production of sexual hormones [1,2]. The operation causes substantial anatomical changes and may also damage nerves to the urinary bladder and sexual organs. Consequently the treatment of rectal cancer may result in incontinence and sexual dysfunction in both men and women. Previous studies have reported that 0–35% of patients suffer from bladder dysfunction after treatment for rectal cancer [3–5], and
approximately 40% of sexually active patients become sexually inactive after treatment for rectal cancer \[6,7\].

Risk factors for urogenital dysfunction after rectal cancer surgery have been suggested to be neoadjuvant (chemo)radiotherapy, type of surgical procedure and older age at surgery \[4,7–10\].

The aim of this study was to explore self-reported urogenital dysfunction in a large national cohort of patients who had undergone APE as treatment of rectal cancer 3 years previously and to compare outcome with a randomly selected reference population as well as a cohort of patients 2 years after radical prostatectomy for prostate cancer.

**Method**

**APER study**

This is a sub-study within the framework of a study on oncological outcome after APE, the Abdomino Perineal Extralevator Resection (APER) study \[11,12\]. Patients who had been treated by APE due to rectal cancer between 2007 and 2009 were identified using the Swedish Colorectal Cancer Registry. A detailed description of the study has been published previously \[12,13\]. All patients alive 3 years postoperatively were contacted and those who consented were sent a questionnaire.

The validation process of the questionnaire is described in Fig. 1 and has been described in detail previously \[11–15\]. The questionnaire was developed according to an established method that involved semi-structured interviews with patients operated by APE, followed by a qualitative content analysis and development and selection of questions by an expert panel. Many of the questions in the questionnaire have been used earlier in other cohorts of cancer patients \[14–17\]. A research nurse performed repeated face-to-face validation with patients, revising the questionnaire as needed \[16\].

Data derived from the Swedish Colorectal Cancer Registry included age, sex, American Society of Anesthesiology (ASA) classification, adjuvant (chemo-)radiotherapy treatment and local recurrence. Surgical charts were retrieved and reviewed to determine the surgical method (APER, extralevator APE or ‘not stated’) by one of the authors (MP), as described in previous publications \[11,12\], and the extent of the operation regarding removal of or damage to adjacent organs (by one of the authors, AL). The operation was considered to be an extralevator APE if it was described in the operating notes as a ‘Holm’s procedure’, if the specimen was described as cylindrical, or if it was stated that the levator muscle was dissected laterally or with a distance from the rectum. The procedure was categorized as ‘extensive’ (simultaneous removal of multiple organs or the bladder), ‘moderately extensive’ (removal of one whole and/or part of an organ and/or damage to one or several organs) or ‘standard’ (no removal or damage to adjacent organs during the extralevator or standard APE procedure).

**Reference population**

A representative sample of the Swedish population in age groups from 30 to 89 years, a total of 3000 individuals, was retrieved from the Swedish Tax Agency. The individuals were contacted by mail with information regarding the study followed by contact by telephone. After receiving informed consent the questionnaire was sent with a prepaid return envelope. The questionnaire sent to the reference population was validated in a manner similar to those used for the APER and LAPPRO cohorts (Fig. 1).

**The LAPPRO population**

LAPPRO is a multicentre, prospective, non-randomized, controlled trial including patients who underwent radical prostatectomy in 2008–2012 either by a conventional open technique or by a robot assisted laparoscopic technique. Detailed descriptions of the trial have been published \[17,18\]. Consenting patients were sent questionnaires preoperatively and at 3, 12 and 24 months after surgery. Data regarding age and ASA classification were retrieved from the preoperative clinical record forms. Comorbidity was derived from the preoperative questionnaire. Data regarding urinary and erectile function were retrieved from the questionnaire at 24 months postoperatively. The questionnaire validation process is described in Fig. 1.

**Assessing urogenital dysfunction**

Answers to specific questions regarding urogenital dysfunction were retrieved from the questionnaire in the APER population (Data S1). To compare urinary dysfunction between the populations, identical questions were used in the LAPPRO and reference populations’ questionnaires. When comparing sexual dysfunction between the three cohorts, not all questions were identical and therefore similar questions addressing erectile function, pain, lubrication, orgasm and distress associated with sexual function were used for comparisons across cohorts.

**Risk factors for urogenital dysfunction**

When analysing risk factors for urogenital dysfunction in the APER population, outcome variables were chosen
that would best reflect overall urinary and sexual function. The end-point addressing urinary dysfunction was a synthesis of three questions regarding leakage during daytime, leakage during the night and the use of urinary incontinence aids. Patients with preoperative urinary leakage as well as patients with a urostomy or chronic catheter were excluded from the analysis. The end-point for sexual function/dysfunction was assessed by the question ‘Are you content with your sexuality and your current sex-life as it has been during the past month?’, where the answers were dichotomized as ‘not at all’ vs ‘a little’, ‘moderately’ and ‘much’. Patients unable to achieve orgasm or erection preoperatively were excluded from the analysis.

By clinical experience and review of previous literature [3,4,6,8–10,19,20] the following variables were identified as potential risk factors for urogenital dysfunction 3 years after APE and were included in the statistical analysis: age, sex, marital status, comorbidity, ASA, (neo)adjuvant (chemo)radiotherapy, preoperative urogenital dysfunction, surgical method, extent of surgery, postoperative infection, local recurrence and stomarelated worries (only used in analysis for sexual dysfunction).

The following variables were collected from the questionnaires: marital status (in a relationship vs not in a relationship), comorbidity (one or more of the illnesses diabetes, cardiovascular disease, high blood pressure or chronic obstructive pulmonary disease) and postoperative infection in the perineal wound (yes/no). Postoperative infection was defined as delayed perineal wound healing, longer than 4 weeks. Preoperative

Figure 1 The validation process of the questionnaires.
Urogenital dysfunction was compared across three different cohorts: patients 3 years after APE, a reference population and patients 2 years after radical prostatectomy (LAPPRO). All patients with questionnaire data were included in the evaluation. The comparisons were done for men and women separately using a Cochran–Mantel–Haenszel hypothesis test of general association [21], stratified by age group (30–49, 50–59, 60–69, 70–79, 80– years). Response options were categorized as explained in the tables. Details on categorization are given in Data S1.

In the risk factor assessment, patients with preoperative urinary leakage as well as patients with a urostomy or chronic catheter were excluded from the analysis. All the variables identified as potential risk factors were included simultaneously as predictors in a generalized linear model. Since convergence problems may arise when estimating risk ratios in binomial regression, the modified Poisson regression approach proposed by Zou [22,23] was used instead. Interaction effects and the presence of multicollinearity were explored. The results are presented as risk ratios for urinary and sexual dysfunction, two-sided 95% confidence intervals and *P* values. Assessed risk factors are presented in Data S2. No imputation of missing values was made.

Statistical analyses were performed using SPSS v. 21.0 (IBM SPSS Inc., Armonk, New York, USA) and SAS v. 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Due to the explorative nature of this study, results should be interpreted with care and regarded as interesting findings rather than conclusive evidence.

### Results

The APER cohort consisted of 1373 patients of whom 852 were alive 3 years postoperatively. Of 761 patients who were mentally and physically able to participate, 545 (72%) returned the completed questionnaire (Fig. 2a). Of the 545 responders 502 (92%) and 43 (8%) were operated by open and laparoscopic surgery, respectively. The questionnaire sent to 2094 of the individuals in the reference population was answered by 1078 (51%) individuals (Fig. 2b). The LAPPRO cohort initially enrolled 4003 patients in this study and after exclusions consisted of 3706 patients operated with radical prostatectomy for prostate cancer (Fig. 2c) of whom 91% responded to the questionnaire at 24 months.

The demographics are shown in Table 1. The median age was 69 years in the APER cohort, 63 years in the reference cohort and 66 years in the LAPPRO cohort.

The APER cohort consisted of 60% men, as expected, whereas in the reference population there was an equal distribution between sexes (48% vs 52%).

There was a difference in level of education where 20% of the APER patients had a higher level of education, i.e. university or similar, compared with 32% of the reference population and 38% in the LAPPRO trial. Marital status differed, with 73% in a relationship in the APER study, 76% in the reference population and 81% in the LAPPRO population. The reference and LAPPRO cohorts reported less comorbidity (34% and 35%) compared with the patients with rectal cancer (APER) (48%).

### Urinary function

Urinary function differed significantly between the groups. In the APER population 36% of the men were incontinent, in comparison with 15% of the men in the reference cohort and 49% in the LAPPRO cohort, respectively (Table 2). If current bladder dysfunction were to remain the same throughout their life 28%, 16% and 39% of the men in the three populations stated it would have a negative impact. Eight (2%) and 15 (7%) of the men and women, respectively, stated that they experienced urinary leakage prior to surgery. Thirty-five (6%) reported that they had a urostomy or chronic catheter.

In women, rates of urinary incontinence was significantly higher in the APER study compared with the reference population (57% vs 37%) (Table 3). Forty-two per cent of women would be distressed if their urinary incontinence after APE were to remain the same for the
Figure 2 Flowchart of patients (a) in the APER study, (b) in the reference population and (c) in the LAPPRO population.
rest of their lives, compared with 32% in the reference population.

Female sex was a risk factor for urinary incontinence (risk ratio 1.60; 95% CI 1.18–2.16). Among both men and women, individuals with ASA III classification had a significantly increased risk for urinary incontinence after APE compared with individuals classified as ASA II (risk ratio 1.49; 95% CI 1.09–2.05) (see Fig. 3a).

Sexual function

In the APER population 74% of the men experienced erectile dysfunction compared with 9% in the reference population (Tables 4 and 5).

Sexual function

In the APER population 74% of the men experienced erectile dysfunction compared with 9% in the reference population (Tables 4 and 5).

Sixty-seven per cent of the men in the APER study reported that if the erectile dysfunction were to be permanent this would distress them (Table 4a), compared with 73% in the LAPPRO cohort (Table 5).

Seventy-one per cent of the women in the APER cohort had been sexually inactive the past month compared with 44% in the reference population (data not shown). The prevalence of deep pain during intercourse was similar in the two populations (9% and 8%, respectively; Table 6).

In the APER population the ability to achieve orgasm had changed or diminished in 53% and 19% of men and women, respectively. Thirty-nine per cent and 65% of the men in the APER and reference populations, respectively, were satisfied with their current sex-life. For women the corresponding numbers was 48% and 70%, respectively.

A risk factor for dissatisfaction with sexual life and sexuality was male sex (risk ratio 1.55; 95% CI 1.16–2.05) (see Fig. 3b).

Discussion and conclusions

The results of this study confirmed that patients operated for rectal cancer with APE had significant urogenital dysfunction 3 years after surgery. A third of the men and more than half of the women were incontinent and most of those patients regarded this as having a negative impact. Even more frequent was sexual dysfunction, which was reported by a majority of all men. More than half the men and one-third of the women were dissatisfied with their current sexual lives.

Table 1 Demographics of the three populations.

|                | APER (%) | Reference (%) | LAPPRO (%) |
|----------------|----------|---------------|------------|
|                | Men      | Women         | Total      | Men      | Women         | Total      |
| Age, median (Q1; Q3) | 69 (63; 76) | 68 (62; 75) | 69 (63; 76) | 64 (53; 74) | 61 (46; 71) | 63 (49; 72) | 66 (61; 69) |
| Sex (%)        | 327 (60) | 218 (40) | 545 (100) | 512 (48) | 566 (52) | 1078 (100) | 3706 (100) |
| In a relationship (%) | 270 (83) | 129 (59) | 399 (73.2) | 413 (81) | 408 (72) | 821 (76) | 3018 (81) |
| Education (%)  | 259 (83) | 161 (77) | 420 (80) | 364 (71) | 361 (65) | 725 (68) | 2003 (62) |
| University/college | 53 (17) | 49 (23) | 102 (20) | 147 (29) | 198 (35) | 345 (32) | 1233 (38) |
| Occupation (%)  | 251 (77) | 165 (76) | 416 (76) | 267 (52) | 260 (46) | 2067 (56) | 2067 (56) |
| Retired        | 64 (20) | 46 (21) | 110 (20) | 233 (46) | 276 (49) | 509 (47) | 1348 (36) |
| Working        | 8 (2) | 4 (2) | 12 (2.2) | 2 (0.4) | 8 (1) | 10 (1) | 12 (0.3) |
| Sick leave     | 51 (16) | 22 (10) | 73 (13) | 5 (1.0) | 9 (2) | 14 (1) | 47 (1) |
| Unemployed     | 2 (1) | 3 (1) | 5 (0.9) | 5 (1.0) | 13 (2) | 18 (2) | 232 (6) |
| ASA grade (%)  | 171 (52) | 92 (42) | 263 (48) | 190 (37) | 183 (33) | 373 (35) | 1270 (34) |
| 1              | 77 (24) | 67 (31) | 144 (26) | – | – | – | 2306 (62) |
| 2              | 191 (58) | 123 (56) | 314 (58) | – | – | – | 1226 (33) |
| 3              | 51 (16) | 22 (10) | 73 (13) | – | – | – | 75 (2) |
| 4              | 1 (0.3) | 1 (0.5) | 2 (0.4) | – | – | – | 0 (0) |
| Not depressed (%)* | 40 (12) | 26 (12) | 66 (12.1) | 63 (12) | 86 (15) | 149 (14) | 175 (5) |
| Registered comorbidity (%)† | 171 (52) | 92 (42) | 263 (48) | 190 (37) | 183 (33) | 373 (35) | 1270 (34) |

Missing data not presented. Age when answering the questionnaire is used.

* Answering ‘no’ to the question: do you feel depressed?

† Patient-reported prevalence of diabetes, heart disease, chronic obstructive pulmonary disease or high blood pressure.
Postoperative incontinence after rectal cancer surgery is well known and has been described in previous studies [3–5,24–26]. Results in the CLASSIC and COLOR II trials indicated a return to preoperative levels after 6–12 months [24,27,28] using the EORTC C38 instrument, whereas the Dutch TME trial [29] found that 38% of the patients were incontinent several years after surgery, most commonly the elderly and women with preoperative incontinence. The Dutch TME trial used multiple, not previously validated, prospective questionnaires [9,29]. Possibly some of the differences in the various reports can be attributed to using different instruments, where both questions and answering alternatives influence the results.

High rates of incontinence have been found in populations of women treated for rectal cancer [4,26]. Mild to moderate levels of long-term micturition problems have been reported by Kasparek et al. after APE, not significantly affecting quality of life [3]. In our study we found that a majority (68%) of patients, both men and women, with incontinence were troubled by this.

| Table 2 Urinary function of men in the three populations. | Table 3 Urinary function of women in the APER and reference populations. |
|-----------------------------------------------------------|-----------------------------------------------------------|
| Did you leak urine before the rectal surgery?             | Did you leak urine before the rectal surgery?             |
| No                                                        | No                                                        |
| Yes                                                       | Yes                                                       |
| Missing data                                              | Missing data                                              |
| Urinary continence*                                       | Urinary continence*                                       |
| Continent                                                 | Continent                                                 |
| Incontinent                                               | Incontinent                                               |
| Missing data                                              | Missing data                                              |
| How many times do you change incontinence pads during a   | How many times do you change incontinence pads during a   |
| typical 24 h?                                             | typical 24 h?                                             |
| Not applicable                                            | Not applicable                                            |
| Less than once per day                                    | Less than once per day                                     |
| More than once per day                                    | More than once per day                                     |
| Missing data                                              | Missing data                                              |
| If you were to live with your current urinary dysfunction | If you were to live with your current urinary dysfunction |
| the rest of your life, how would this affect you?         | the rest of your life, how would this affect you?         |
| Not applicable                                            | Not applicable                                            |
| Not at all                                                 | Not at all                                                 |
| It would affect me                                         | It would affect me                                         |
| Missing data                                              | Missing data                                              |

Details regarding categorization are presented in Data S1.

*A synthesis of three questions regarding leakage during daytime or night time and use of urinary aids was regarded as continent when the patients denied all three aspects of leakage.

Postoperative incontinence after rectal cancer surgery is well known and has been described in previous studies [3–5,24–26]. Results in the CLASSIC and COLOR II trials indicated a return to preoperative levels after 6–12 months [24,27,28] using the EORTC C38 instrument, whereas the Dutch TME trial [29] found that 38% of the patients were continent several years after surgery, most commonly the elderly and women with preoperative incontinence. The Dutch TME trial used multiple, not previously validated, prospective questionnaires [9,29]. Possibly some of the differences in the various reports can be attributed to using different instruments, where both questions and answering alternatives influence the results.

High rates of incontinence have been found in populations of women treated for rectal cancer [4,26]. Mild to moderate levels of long-term micturition problems have been reported by Kasparek et al. after APE, not significantly affecting quality of life [3]. In our study we found that a majority (68%) of patients, both men and women, with incontinence were troubled by this.

Similar rates of bother were found in the LAPPRO and reference populations, indicating that incontinence is a problem where improved care could benefit many patients. There were various degrees of inconsistency between the prevalence of dysfunction and the corresponding distress. This inconsistency may be due to lack of construct validity, but also depends on the outcome definition used.

Our study confirmed female sex as a risk factor for postoperative incontinence [25]. Pregnancy is one reason why women are more affected [29]. Results from the TME trial indicated that radiotherapy did not affect long-term bladder dysfunction after treatment for rectal cancer [30] whereas other studies have proposed a transient effect on male urinary dysfunction after radiotherapy due to swelling of the prostate [24,27]. We could neither confirm nor discard these suggestions due to the high number of irradiated patients in the APER population. Neither were other proposed risk factors such as older age or preoperative urinary dysfunction confirmed in our study. Instead, we found that
**Figure 3** Forest plot demonstrating risk factors for (a) urinary function 3 years after abdominoperineal excision and (b) sexual dysfunction 3 years after abdominoperineal excision.
comorbidity as indicated by a higher ASA grade predisposed patients to postoperative incontinence. ASA grade has not previously been reported as a risk factor and may require further studies for corroboration.

Rates of sexual dysfunction after treatment for rectal cancer vary greatly in the literature. We found that 74% of the men in the APER population reported a decline in erectile function after surgery. Our figures are similar to those reported in previous studies.

Table 4 Sexual function of men in the APER and reference populations. (a) Men in the APER population, $n = 327$. (b) Men in the reference population, $n = 512$.

| Question                                                                 | Not applicable (%) | Don’t know (%) | No (%) | Yes (%) | Missing (%) |
|--------------------------------------------------------------------------|--------------------|----------------|--------|---------|------------|
| (a) Has your erection been diminished after your surgical treatment for rectal cancer? | 25 (8)             | 13 (4)         | 24 (7) | 243 (74) | 22 (7)      |
| Has your ability to reach orgasm been reduced after your surgical treatment for rectal cancer?* | 20 (6)             | 70 (21)        | 35 (11) | 173 (53) | 29 (9)      |
| If you have had a reduced erection or no erection at all after your rectal cancer surgery, and it would remain the same for the rest of your life, would this affect you negatively?† | 34 (10)            | 24 (7)         | 34 (10) | 220 (67) | 15 (5)      |
| Are you satisfied with your sexuality and your sexual life, as it has been the last month (regardless of whether you have a partner or not)? | –                  | –              | 172 (53) | 126 (39) | 29 (9)      |
| (b) Has your erection been diminished the last month? | 87 (17)            | 23 (5)         | 349 (68) | 46 (9)  | 7 (1)       |
| Has your ability to reach orgasm been reduced the last month?* | 13 (3)             | 135 (26)       | 314 (61) | 42 (8)  | 8 (2)       |
| If you have had a reduced or diminished erection, and it would remain the same for the rest of your life, would this affect you negatively?† | 247 (48)           | 87 (17)        | 52 (6)  | 133 (26) | 13 (3)      |
| Are you satisfied with your sexuality and your current sexual life, as it has been the last month (regardless of whether you have a partner or not)? | –                  | –              | 165 (32) | 331 (65) | 16 (3)      |

*Not applicable is equivalent to answering ‘I didn’t achieve orgasm before the operation/this month’. Yes is equivalent to answering ‘it has become more difficult’.
†Not applicable is equivalent to answering ‘I didn’t achieve erection before the operation/this month’ and no is equivalent to answering ‘there has been no change in my erection’.

Table 5 Sexual function of men in the LAPPRO population, $n = 3706$.

| Question                                                                 | Not applicable (%) | Never (%) | Less than half the times (%) | More than half the times (%) | Missing (%) |
|--------------------------------------------------------------------------|--------------------|-----------|-----------------------------|-----------------------------|------------|
| Has your penis been stiff enough to perform sexual intercourse during the last month? | 1314 (35)          | 828 (22)  | 344 (9)                     | 854 (23)                    | 366 (10)   |
| If you have morning erection, is your penis stiff enough to perform sexual intercourse? | 2057 (56)          | 489 (13)  | 294 (8)                     | 507 (14)                    | 359 (10)   |
| During sexual activity, have you reached orgasm?                         | 1025 (28)          | 169 (5)   | 343 (9)                     | 1807 (49)                   | 362 (10)   |

| Question                                                                 | Not applicable (%) | Don’t know (%) | No (%) | Yes (%) | Missing (%) |
|--------------------------------------------------------------------------|--------------------|----------------|--------|---------|------------|
| If you have reduced or no erection after your prostate surgery, and that would be the same for the rest of your life, would this affect you negatively? | 205 (6)            | 28 (1)         | 270 (8) | 2723 (73) | 480 (13)   |

Details regarding categorization are presented in Data S1.
to those of Bruheim et al. [31] and the results from the COLOR II trial [24]. Reported rates of erectile dysfunction were similar in the APER and LAPPRO populations, indicating surgery in the pelvis as an important reason. In LAPPRO baseline erectile dysfunction, as defined by stiffness of the penis during sexual activity, was 33% [32]. Due to lack of baseline data in APER the results should be interpreted with caution. However, we cannot elaborate on the role of preoperative radiation in connection with APR. It could still play a role in damage of the pelvic nerves, as the dissection for APR differs in certain aspects from that for radical prostatectomy. APE should be more nerve sparing in the pelvis compared with radical prostatectomy. Tissue inflammation, scarring and subsequent nerve damage can be a result of radiotherapy and some studies argue that radiotherapy is a risk factor for erectile dysfunction [7,10,31]. However, a majority of the APER population received radiotherapy, and the resulting rate of erectile dysfunction is similar to that in the LAPPRO population. This could indicate that both surgical technique and radiotherapy affect postoperative sexual function.

The rate of sexual inactivity among women in the APER population was high (71%), in accordance with previous studies [8,19,26,28,30,33,34]. This could be due in part to age and relationship status, and a similar trend was seen in the reference population, but several studies have reported a significant decrease in sexual activity after rectal cancer treatment [24,33]. Among the sexually active women in the APER population dyspareunia was common and could be due to adhesions, retroflection of the uterus, scarring of the vaginal wall and vaginal dryness caused by surgery and radiotherapy.

Our results suggest that men were distressed to a greater extent than women by their sexual dysfunction and that this also affected their quality of life. A difference between men and women was also observed in the reference population, implying that gender differences in sexual satisfaction were probably not only related to surgery. Still, dissatisfaction with one’s sexual health has been shown to affect global quality of life in men and should thus be addressed in connection with rectal cancer surgery [35].

This national cohort of rectal cancer patients included patients alive 3 years after APE for rectal cancer. Strengths of the study include the large cohorts with similar follow-up time and the use of validated questionnaires [14,15]. The patients answered questionnaires at home and not in the presence of their surgeon. The questions have been used before and included questions on distress and concern, which is rather unusual in other types of questionnaire. Another strength was the relatively high response rate compared with other studies on urogenital dysfunction [5,6,30,33,34]. Asplund et al. [13] explored the potential selection bias in this cohort. Non-responders were older with more comorbidity and fewer received radiotherapy compared

| Table 6 Sexual function of women in the APER and reference populations. (a) Women in the APER population, n = 218. (b) Women in the reference population, n = 566. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | Not applicable/don’t know (%) | No (%) | Yes (%) | Missing (%) |
| (a) Has your ability to reach orgasm been reduced after your surgical treatment for rectal cancer?* | 106 (49) | 51 (23) | 42 (19) | 19 (8) |
| Did your vagina become moist during sexual arousal the last month? | 140 (64) | 7 (3) | 61 (28) | 10 (5) |
| Have you experienced pain inside the vagina or deep pain inside the pelvis during sexual intercourse or similar the last month? | 154 (71) | 31 (14) | 20 (9) | 21 (4) |
| Are you satisfied with your sexuality and your current sexual life, as it has been the last month (regardless of whether you have a partner or not)? | – | 69 (32) | 104 (48) | 43 (20) |
| (b) Has your ability to reach orgasm been reduced during the last month?* | 223 (40) | 259 (46) | 56 (10) | 25 (4) |
| Has your vagina become moist during sexual arousal the last month? | 213 (38) | 7 (1) | 324 (57) | 22 (4) |
| Have you experienced pain inside the vagina or deep pain inside the pelvis during sexual intercourse or similar the last month? | 250 (44) | 252 (45) | 43 (8) | 21 (4) |
| Are you satisfied with your sexuality and your current sexual life, as it has been the last month (regardless of whether you have a partner or not)? | – | 128 (23) | 395 (70) | 43 (8) |

Details regarding categorization are presented in Data S1.
*Not applicable is equivalent to answering ‘I didn’t achieve orgasm before the operation/this month’. Yes is equivalent to answering ‘it has become more difficult’.

© 2018 The Authors. Colorectal Disease published by John Wiley & Sons Ltd on behalf of Association of Coloproctology of Great Britain and Ireland.
with responders. The high rate of non-responders in the reference group is a limitation. One reason for this was the difficulty in identifying telephone numbers for a high proportion of the individuals. An explanation for the differences in response rates may be that patients can relate to the content of the questionnaire more easily than individuals in a general population and that they are more supportive of this kind of research.

The retrospective design with no baseline data is a limitation, e.g. due to difficulties with recall bias. However, the comparison with the reference population may mitigate it to some extent. A limitation was that some of the questions addressed here were not identical across the three studies. However, we still regard these comparisons as interesting and used identical questions whenever possible, or questions as closely related as possible.

Although there are few large studies on urinary and sexual function after abdominoperineal surgery, our results clearly indicate that problems postoperatively are frequent. After prostate cancer surgery men who felt that they had been well informed about the risk for urinary and sexual dysfunction after the procedure had less anxiety 3 months postoperatively [36]. Thus there is support for modern traditions concerning patient information and participation, to inform all patients not only about the expected positive results of treatment but also about the risk of complications [36].

In conclusion, 3 years after APE urogenital dysfunction persisted. Pelvic surgery (both prostatectomy and APE) was associated with troubling sexual dysfunction particularly common in men. Even though far from all patients suffer from sexual or urinary dysfunction after pelvic surgery, we suggest that all patients should be advised about the risk for sexual and urinary dysfunction before pelvic surgery and that these aspects should be included in all follow-ups after surgery in order to identify those in need of further assistance [37,38].

Acknowledgements

The authors acknowledge the support by the research nurses at SSORG: Anette Wedin, Jane Heath, Elisabeth Gonzales and Ingrid Höglund-Karlsson. We also acknowledge the assistance of the expert panel in the questionnaire development.

Author contributions

All authors have fulfilled the Uniform Requirements for Manuscripts Submitted to Biomedical Journals statement of the International Committee of Medical Journal Editors.

Conflict of interest

None.

Ethical approval

The Regional Ethical Review Board in Gothenburg approved the studies (APER, 406-10, 407-10; LAPPRO, 277-07; reference 608-13).

Funding

The APER study was supported by grants from the Swedish Research Council (2012-1768), the Swedish Cancer Society (2010/593; 2013/497) and Sahlgrenska University Hospital (ALF grant, agreement concerning research and education of doctors). The reference population study was supported by grants from Region Västra Götaland, Sahlgrenska University Hospital ALF grant ALFGBG-4307771. The LAPPRO study was supported by grants from the Swedish Cancer Society (2008/922, 2010/593, 2013/497), the Swedish Research Council (2012-1770), Region Västra Götaland, Sahlgrenska University Hospital (ALF grants 138751 and 146201, HTA-VGR 6011; agreement concerning research and education of doctors), the Mrs Mary von Sydow Foundation and the Anna and Edvin Berger Foundation.

References

1 Buchli C, Martling A, Arver S et al. Testicular function after radiotherapy for rectal cancer – a review. J Sex Med 2011; 8: 3220–6.
2 Buchli C, Tapper J, Bottai M et al. Testosterone and body composition in men after treatment for rectal cancer. J Sex Med 2015; 12: 774–82.
3 Kasparek MS, Hassan I, Cima RR et al. Long-term quality of life and sexual and urinary function after abdominoperineal resection for distal rectal cancer. Dis Colon Rectum 2012; 55: 147–54.
4 Bregendahl S, Emmertsen KJ, Lindegaard JC et al. Urinary and sexual dysfunction in women after resection with and without preoperative radiotherapy for rectal cancer: a population-based cross-sectional study. Colorectal Dis 2015; 17: 26–37.
5 Jayne DG, Brown JM, Thorpe H et al. Bladder and sexual function following resection for rectal cancer in a randomized clinical trial of laparoscopic versus open technique. Br J Surg 2005; 92: 1124–32.
6 Ho VP, Lee Y, Stein SL et al. Sexual function after treatment for rectal cancer: a review. Dis Colon Rectum 2011; 54: 113–25.
7 Traa MJ, De Vries J, Roukema JA et al. Sexual (dys)function and the quality of sexual life in patients with colorectal cancer: a systematic review. Ann Oncol 2012; 23: 19–27.
Urogenital function after rectal cancer

A. Ledebo et al.

8 Hendren SK, O’Connor BI, Liu M et al. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. Ann Surg 2005; 242: 212–23.

9 Lange MM, Marijnen CA, Maas CP et al. Risk factors for sexual dysfunction after rectal cancer treatment. Eur J Cancer 2009; 45: 1578–88.

10 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.

11 Prytz M, Angenete E, Haglind E. Abdominoperineal extralevator resection. Dan Med J 2012; 59: A4366.

12 Prytz M, Angenete E, Bock D, Haglind E. Extralevator abdominoperineal excision for low rectal cancer – extensive surgery to be used with discretion based on 3-year local recurrence results: a registry-based, observational national cohort study. Ann Surg 2015; 263: 516–21.

13 Asplund D, Prytz M, Bock D et al. Persistent perineal morbidity is common following abdominoperineal excision for rectal cancer. Int J Colorectal Dis 2015; 30: 1563–70.

14 Steineck G, Helgesen F, Adolfsson J et al. Quality of life after radical prostatectomy or watchful waiting. N Engl J Med 2002; 347: 790–6.

15 Bergmark K, Avall-Lundqvist E, Dickman PW et al. Vaginal changes and sexuality in women with a history of cervical cancer. N Engl J Med 1999; 340: 1383–9.

16 Steineck G, Bergmark K, Henningsmoen L et al. Symptom documentation in cancer survivors as a basis for therapy modifications. Acta Oncol 2002; 41: 244–52.

17 Haglind E, Carlsson S, Stranne J et al. Urinary incontinence and erectile dysfunction after robotic versus open radical prostatectomy: a prospective, controlled, nonrandomised trial. Eur Urol 2015; 68: 216–25.

18 Thorsteinsson T, Stranne J, Carlsson S et al. LAPPRO: a prospective multicentre comparative study of robot-assisted laparoscopic and retropubic radical prostatectomy for prostate cancer. Scand J Urol Nephrol 2011; 45: 102–12.

19 Orsini RG, Vermeer TA, Traa MJ et al. Does extended surgery influence health-related quality of life in patients with rectal cancer? Dis Colon Rectum 2015; 58: 179–85.

20 Schmidt C, Daun A, Malchow B et al. Sexual impairment and its effects on quality of life in patients with rectal cancer. Disch Arztebl Int 2010; 107: 123–30.

21 Agresti A. Categorical Data Analysis. 3rd edition. Hoboken, NJ: Wiley, 2013.

22 Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004; 159: 702–6.

23 Yelland LN, Salter AB, Ryan P. Performance of the modified Poisson regression approach for estimating relative risks from clustered prospective data. Am J Epidemiol 2011; 174: 984–92.

24 Andersson J, Abis G, Gellerstedt M et al. Patient-reported genitourinary dysfunction after laparoscopic and open rectal cancer surgery in a randomized trial (COLOR II). Br J Surg 2014; 101: 1272–9.

25 Lange MM, van de Velde CJ. Urinary and sexual dysfunction after rectal cancer treatment. Nat Rev Urol 2011; 8: 51–7.

26 Tekkis PP, Cornish JA, Remzi FH et al. Measuring sexual and urinary outcomes in women after rectal cancer excision. Dis Colon Rectum 2009; 52: 46–54.

27 Quah HM, Jayne DG, Eu KW et al. Bladder and sexual dysfunction following laparoscopically assisted and conventional open mesorectal resection for cancer. Br J Surg 2002; 89: 1551–6.

28 Adam JP, Denost Q, Capdepon M et al. Prospective and longitudinal study of urogenital dysfunction after proctectomy for rectal cancer. Dis Colon Rectum 2016; 59: 822–30.

29 Milsom I. Lower urinary tract symptoms in women. Curr Opin Urol 2009; 19: 337–41.

30 Lange MM, Maas CP, Marijnen CA et al. Urinary dysfunction after rectal cancer treatment is mainly caused by surgery. Br J Surg 2008; 95: 1020–8.

31 Bruheim K, Guren MG, Dahl AA et al. Sexual function in males after radiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys 2010; 76: 1012–7.

32 Soorakumaran P, Pini G, Nyberg T et al. Erectile function and oncologic outcomes following open retropubic and robot-assisted radical prostatectomy: results from the LAParoscopic Prostatectomy Robot Open Trial. Eur Urol 2018; 73: 618–27.

33 Milbury K, Cohen I, Jenkins R et al. The association between psychosocial and medical factors with long-term sexual dysfunction after treatment for colorectal cancer. Support Care Cancer 2013; 21: 793–802.

34 Bruheim K, Tveit KM, Skovlund E et al. Sexual function in females after radiotherapy for rectal cancer. Acta Oncol 2010; 49: 826–32.

35 Schmidt CE, Bestmann B, Kuchler T et al. Gender differences in quality of life of patients with rectal cancer. A five-year prospective study. World J Surg 2005; 29: 1630–41.

36 Thorsteinsson T, Hedelin M, Stranne J et al. Intrusive thoughts and quality of life among men with prostate cancer before and three months after surgery. Health Qual Life Outcomes 2013; 11: 154.

37 Deng H, Liu D, Mao X et al. Phosphodiesterase-5 inhibitors and vacuum erection device for penile rehabilitation after laparoscopic nerve-preserving radical prostatectomy for rectal cancer: a prospective controlled trial. Am J Mens Health 2016; 11: 641–6.

38 Denton AS, Maher EJ. Interventions for the physical aspects of sexual dysfunction in women following pelvic radiotherapy. Cochrane Database Syst Rev 2003; 1: CD003750.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Demographics.

Data S2. Risk factors assessed for urogenital dysfunction in the APER population.