Pelvic organ function and quality of life after anastomotic leakage following rectal cancer surgery

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Evaluierung der Beckenbodenfunktion und der Lebensqualität bei Patienten mit Anastomosendehiszenz nach Rektumresektion

Zusammenfassung. *Einleitung:* Derzeit besteht ein Mangel an Studien, die den Einfluss einer Anastomosendehiszenz nach Rektumkarzinomresektion auf die Beckenbodenfunktion und Lebensqualität untersucht haben.

Methodik: Zwischen 1995 und 2006 wurde an einem Institut bei 500 Patienten mit einem Rektumkarzinom eine Rektumresektion durchgeführt. Sechsunddreißig Patienten (7,2%) entwickelten eine Anastomosendehiszenz nach der Operation. Davon verstarben 15 Patienten (41,6%) in der Nachbeobachtungszeit. Ein standardisierter Fragebogen, welcher den International Index of Erectile Function, Female Sexual Function Index, Short Form-12 Health Survey, International Prostatic Symptom Score, International Consultation on Incontinence Questionnaire-Short Form, Vaizey Incontinence Score und Wexner Constipation Score inkludierte, wurde an alle 21 lebenden Patienten geschickt. Patienten mit einer Rektumkarzinomresektion ohne postoperativer Dehiszenz dienten als Kontrollen für jeden Fall und wurden gematcht nach Geschlecht, Alter (±5), Art der Resektion und neoadjuvanten Therapie (Ja/Nein).

Ergebnis: Sechzehn Patienten (76,2%) waren verfügbar und wurden in die Analyse einbezogen. Stuhlinkontinenz, Verstopfung und sexuelle Funktion zeigten keinen Unterschied zwischen Patienten und Kontrollgruppe ($p = 0,1973$, $0,1189$, $0,8519$). Allerdings war die Harnkontinenz signifikant beeinträchtigt bei jenen Patienten mit Anastomosendehiszenz ($p = 0,0430$). Die Lebensqualität zeigte keinen signifikanten Unterschied zwischen den beiden Gruppen ($p = 1,0000$ und $0,1973$).

Zusammenfassung: Eine Anastomosendehiszenz nach Rektumkarzinomresektion führt zu einer deutlichen Beeinträchtigung der Harnkontinenz. Stuhlinkontinenz, sexuelle Funktion, Verstopfung und Lebensqualität sind vergleichbar zwischen Patienten mit und ohne Anastomosendehiszenz.

Summary. *Introduction:* There is a paucity of studies assessing the influence of anastomotic leakage after rectal cancer surgery on pelvic organ function and quality of life.

Methods: Between 1995 and 2006, 500 patients underwent rectal resection for malignancies at a single institution. Thirty-six patients (7.2%) developed an anastomotic leakage postoperatively. Fifteen of these patients (41.6%) died during the follow-up period. A self-administering questionnaire including the International Index of Erectile Function, Female Sexual Function Index, Short Form-12 Health Survey, International Prostatic Symptom Score, International Consultation on Incontinence Questionnaire-Short Form, Vaizey Incontinence Score and Wexner Constipation Score was sent to all 21 alive patients. Patients with rectal cancer resection without leakage served as controls for each case and were matched by sex, age (±5 years), type of resection, and neoadjuvant therapy (yes/no).

Results: Sixteen patients (76.2%) were available and were included in the analysis. The median follow-up time was 106.8 months (32.4–170.4). Fecal incontinence, constipation, and sexual function did not differ significantly between patients and controls ($p = 0.1973$, 0.1189, 0.8519, respectively). By contrast, urinary continence was impaired significantly in the leakage group ($p = 0.0430$) but not in control patients. The Quality of Life assessing Short Form-12 Health Survey reached no significant difference between both groups ($p = 1.0000$ and 0.1973).

Conclusion: Anastomotic leakage following anterior resection negatively aggravates urinary function but not fecal incontinence, constipation or sexual functions. The data indicate that patients experiencing anastomotic leakages can be relieved from the fear of gross pelvic floor function disturbances.

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Introduction

Anastomotic leakage following rectal cancer surgery represents a serious complication. The pronounced incidence varies from 2 to 19% [1–3]. Despite that leakages are associated with an increased mortality rate, major questions of the patients also relate to potential morbidities, since the latter might be more frequent. Thus, doctors might need to inform the patient about anastomotic leakage related risk not only of local tumor recurrence but also of impairment of pelvic organ functions, such as urinary and fecal incontinence or sexual function.

Fortunately, with respect to tumor recurrence, a recent multicenter analysis did not find a correlation of anastomotic leakage and cancer-specific survival, despite initial studies have suggested this correlation [4]. However, there still exists a paucity of studies that addressed the question whether anastomotic leakage is related to decreased pelvic function. Nesbakken et al. found a worse ano-rectal function compared to controls, measured by the Cleveland Clinic Continence Sore [5]. In contrast, Bittdorf et al. could not demonstrate any functional impairment after symptomatic anastomotic leakage [6]. Aside from this conflicting information, long-term evaluation of urinary disorders, sexual function, and quality of life in this group of patients is still missing. This leaves the doctors and patients in uncertainties giving raise to possible unnecessary fear and depression.

To counteract this vacuum, the current case-matched study was designed to investigate the impact of anastomotic leakage after rectal resection for malignancies on overall pelvic organ function and quality of life using standardized well-established score system.

Methods

Between 1995 and 2006, 500 patients were operated for rectal cancer at the Department of Surgery at Medical University of Vienna. All patients underwent total mesorectal excision (TME) as previously described [7]. The type of resection was divided into intersphincteric or complete rectal resection with coloanal anastomosis and low anterior resection with colorectal anastomosis. The investigation was approved by the local ethics committee.

Thirty-six patients (7.2%) developed an anastomotic leakage postoperatively. Fifteen of these patients died during the follow-up period. A self-administering questionnaire was sent to all other available patients. Two patients refused to participate in the study without a reasonable cause, 1 patient could not be contacted either by telephone or mail, and 2 patients suffered from progressive disease, thus being not in a condition to answer the questions. Finally, 16 patients (76.2% of all patients alive with anastomotic leakage) were included in the analysis. The median follow-up time was 106.8 months (32.4–170.4). Additional patient data from the surgical procedure, postoperative course, and follow-up examinations were obtained from the institutional colorectal database and individual chart reviews.

According to the proposal by the international study group of rectal cancer, we defined anastomotic leakage as grade A (no change in patient's management) in 7 patients (43.7%), grade B (requires active therapeutic intervention but is managed without re-laparotomy) in 3 patients (18.8%) and grade C (requires re-laparotomy) in 6 patients (37.5%) [8].

Patients, who underwent rectal cancer resection at the same time period and had an uneventful postoperative course served as controls for each case and were matched by sex, age (±5 years), type of resection, and neoadjuvant therapy (yes/no).

We measured quality of life using the Short Form-12 Health Survey (SF-12) at the time of follow-up. Information of all 12 items is used to construct physical and mental component summary measures (PCS and MCS) [9]. Urinary function was assessed by the "International Consultation on Incontinence Questionnaire-Short Form" (ICIQ-SF) (no incontinence: 0 points, severe incontinence 21 points) and by the validated "International Prostatic Symptom Score" (I-PSS) [10, 11]. The I-PSS contains 7 questions, whereas patients with no symptoms score 0 points, and the maximum symptom score is 35 points. The Vaizey Incontinence Score was used to evaluate postoperative fecal incontinence [10]. This questionnaire ranges from 0 to 24 points and a lower score indicates a lower level of incontinence. The Wexner Constipation Score, in which a lower score indicates a lower severity of symptoms, ranges from 0 to 30 points [11]. Sexual function was evaluated by the validated and translated "Female Sexual Function Index" (FSFI), a comprehensive nineteen item tool that assesses six domains of sexual function including desire, arousal, lubrication, orgasm, satisfaction, and pain [12]. Male sexual function was investigated by the German version of the "International Index of Erectile Function" (IIEF) [13]. The IIEF consists of 15 items that measure 5 domains: erectile function, intercourse satisfaction, orgasmic function, sexual desire, and overall satisfaction. A higher score is related to a better sexual function.

Statistical analysis

Continuous data are shown as mean and standard deviation in the case of normally distributed data, and as median, minimum, and maximum otherwise. Differences between cases and controls were tested with the paired t-test for normally distributed differences and with the non-parametric Wilcoxon's signed rank test otherwise. Categorical data are described with absolute and relative frequencies. Differences between cases and controls are tested with McNemar's test for binary data, with a test for symmetry for qualitative data and with Cochran-Mantel-Haenszel tests for ordinal data. Physical and mental scores of the SF-12 questionnaire were calculated according to Bullinger and Kirchberger and described with median, minimum, and maximum. All tests are two-sided and $p \le 0.05$ was considered significant.

Results

Basic characteristics of patients and controls are listed in Table 1. There were no significant differences in regard to sex, age, type of resection, and type of neoadjuvant therapy. Notably, due to the multiple match-parameters, 2 patients had an age difference of more than 5 years and 2 patients received different neoadjuvant treatment modalities. There were no significant variations between patients and controls concerning neurologic disorders, diabetes, smoking behavior, and previous pelvic floor operations. A protective stoma at primary rectal resection was created in 12 patients (75%) with anastomotic leakage. It was closed in all patients after a median of 128 days (range 47–331). In the control group, 8 patients (50%) received a pro-

Table 1. Basic characteristics and surgical data of patients and controls*

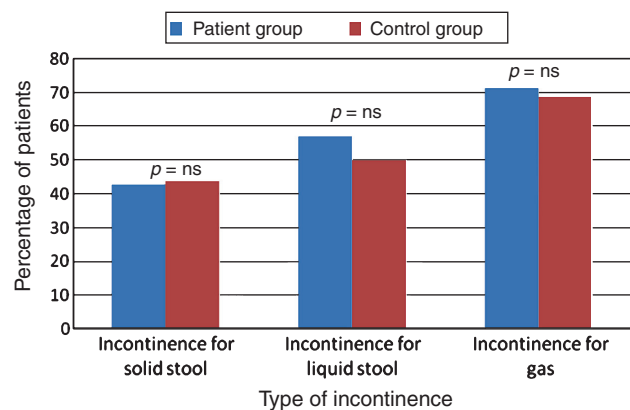|	Total	Patients	Controls	*p*-value
Sex				
Female	10 (31.3)	5 (31.3)	5 (31.3)	ns
Male	22 (68.8)	11 (68.8)	11 (68.8)	
Age	68.69 (±9.89)	67.48 (±11.24)	70.45 (±8.43)	ns
BMI	27.08 (±4.29)	28.49 (±4.09)	25.68 (±4.13)	ns
Neoadjuvant radio-(chemo) therapy	20 (62.6)	11 (68.8)	9 (56.3)	ns
Adjuvant chemotherapy	12 (37.5)	6 (37.5)	6 (37.5)	ns
Protective stoma creation				
No	12 (37.5)	4 (25)	8 (50)	0.0455
Ileostomy	16 (50)	10 (62.5)	6 (37.5)	
Colostomy	4 (12.5)	2 (12.5)	2 (12.5)	
Type of resection				
Intersphincteric	6 (18.8)	3 (18.8)	3 (18.8)	ns
Low anterior	20 (62.5)	10 (62.5)	10 (62.5)	
Complete	6 (18.8)	3 (18.8)	3 (18.8)	
Type of reconstruction				
Colonpouch	12 (37.5)	4 (25)	8 (50)	ns
End–end	20 (62.5)	12 (75)	8 (50)	
UICC stadium				
1	15 (46.9)	8 (50)	7 (43.8)	ns
2	7 (21.9)	4 (25)	3 (18.8)	
3	10 (31.3)	4 (25)	6 (37.5)	
4	0	0	0	

*Categorical variables are described as absolute numbers with percentages. Continuous variables are described as means (± standard deviation).

Fig. 1. Comparison of fecal incontinence between cases and controls

Concerning I-PSS, the patients group scored a median of 6 (range 2–33) compared with 3 (0–17) in the control group. This difference reached no statistical significance ($p = 0.1699$).

The sexual function in men was characterized by the IIEF. Comparing patients and controls, no significant difference was found [median: 39 (range 9–61) *vs.* 32.5 (range 12–57) ($p = 0.8125$)]. Moreover, no significant differences in the domain specific scores were found between patients and control subjects. Four patients in the leakage group had a score below 22 points compared with 3 patients in the control group.

The FSFI was not analyzed due to the low number of female patients. Moreover, 2/5 patients and 3/5 control subjects reported no sexual activity and did not answer those questions.

In regard to the SF-12 health survey the median physical health score of patients was 46.0 (range 29.2–56.6) compared to 52.6 (range 26.7–61.9) of the controls. This difference was not statistically significant ($p = 0.2775$). In addition, the median mental health score of patients was 50.6 (range 28.4–60.4) compared to 53.6 (range 35.2–60.8) in control subjects ($p = 1.0000$).

Discussion

In the current study, we could demonstrate that anastomotic leakage following rectal cancer surgery was associated with an impaired urinary continence compared with patients without leakage. Anorectal and sexual function as well as quality of life measured by validated instruments showed no differences between both groups.

Unlike previous studies, who only assessed anorectal functions we here for the first time assessed all aspects of pelvic organ function using validated scores [5, 6]. We believe, that this method allows a broader picture of this complication. A limiting effect of the study is certainly its small number of patients. However, in the absence of larger cohorts in the literature the data might still be of value.

Interestingly, only urinary incontinence characterized by the ICIQ-SF was significantly higher in the leakage group. The reason for this finding remains unclear. One

tective stoma during the initial operation. Median closure time was 78 days (range 38–167).

One patient in the leakage group underwent definitive Hartmann's procedure after primary closure of ileostomy due to recurrent fistula at the anastomotic side resulting in serious continence problems. Another patient developed a local tumor recurrence and received a definitive colostomy as well. In contrast, none of the controls had a stoma at the follow-up examination.

During the follow-up period 1 patient developed a local disease recurrence and in 2 patients distant metastasis (lung and liver) were detected. In the control group liver metastasis was found in 2 patients.

The Vaizey incontinence score showed no significant difference between patients and controls ($p = 0.1973$). The median score was 8 (range 0–24) in the patient group and 5 (0–16) in the control group. Figure 1 describes anorectal function in more detail. Median Wexner Constipation Score of the control group was slightly lower compared to the patients group [2 (0–12) *vs.* 5 (0–16)] ($p = 0.1189$). In regard to the ICIQ-SF, the control group showed a significantly lower score compared to the patient group [median: 0.5 (0–10) *vs.* 0 (0–8)] ($p = 0.0430$). Three patients complained about symptoms of stress incontinence and 4 patients of urge incontinence. In contrast, 2 control subjects reported urge incontinence and 1 suffered from mixed incontinence.

could speculate that the inflammation process caused by an anastomotic leak with subsequent fibrosis deteriorates neural function. Lange et al. investigated urinary dysfunction after rectal cancer resection in patients with and without preoperative radiation therapy [14]. The overall incidence of urinary incontinence was 38.1%, but was not related to neoadjuvant treatment modality. As a consequence, Lange et al. suggested that direct damaging of the nerve supply of the bladder may play a key role in developing urinary disorders. Sterk et al. pointed out that partial nerve damage of the bladder can usually recover after rectal surgery [15]. In their series 90% of patients with urinary disorders improved within 6 months, whereas 10% suffered from persistent bladder dysfunction. In the present study, over 40% of patients had sustained urinary incontinence. Generally, the majority of studies did not use validated measurements to assess pelvic function, thus making comparison difficult.

What are the clinical consequences of our findings? We suggest informing our patients about this potential complication. Thus, patients will become aware of urinary disorders and will seek help from urologists at an early stage of complaints. Consequently, early treatment strategies could help patients to improve urinary dysfunction.

Interestingly, to the best of author's knowledge, only 3 studies investigated the influence of anastomotic leakage on fecal continence so far [5, 6, 18]. Nesbakken et al. included 11 patients in their analysis. After at least 12 months following stoma closure the authors found a trend toward increased fecal urgency and incontinence in patients, who developed anastomotic leakage. However, this difference failed to achieve statistical significance. Additionally, in line with Hallböök and Sjodahl, the authors described a reduced neorectal capacity after leakage compared with controls, probably as a result of granulation tissue formation and subsequent fibrosis [16]. Bittdorf et al. concluded that anastomotic leakage did not affect anorectal function measured by the Cleveland Clinic Incontinence Score [6]. This outcome was comparable with our results. Notably, is worth mentioning that the number of patients with severe fecal incontinence in our study was considerable high in both groups.

In the present investigation, sexual function in men showed no difference between patients with and without leakage. In female patients, sexual activity was too low to enable statistical analysis using the FSFI. Sexual dysfunction is a well-known complication following rectal resection for malignancy. Several studies evaluated the impact of rectal resection on sexual function [17]. In one study, 45% of men stated that "surgery made their sexual lives worse"[18]. A reduced sexual function and activity after rectal resection was found by others as well [17, 21–23]. Anyway, this might also be result of the increased prevalence of urinary and fecal incontinence in operated patients, leading to anxiety and social impairment.

Mental and physical quality of life measured by the SF-12 questionnaire also showed no significant difference between patients with and without leakage. This result is not surprising as the majority of pelvic organ functions were comparable in both groups as well. Moreover, other factors that might contribute to a lower level of quality of life, such as neoadjuvant radiation, age, and tumor stage were nearly equally distributed [19].

In the present analysis we used the definition of anastomotic leaks as recommended by the international study group of rectal cancer [8]. The severity of anastomotic leaks is staged according to the necessity and extension of therapeutic management. Few patients in our series showed only subclinical leakages and were classified as grade A. Nevertheless, all leaks were verified by radiological diagnostic. Therefore these patients were included in the final analysis as well.

Conclusion

Our data demonstrate that anastomotic leakage after rectal cancer surgery had no impact on long-term anorectal and sexual function, a finding which might relieve the fear of some patients. Notably, urinary continence was reduced significantly by anastomotic leakage compared with patients without leakage. Quality of life was similar in both groups indicating that anastomotic leakage is associated with complications patients can deal with in daily life.

Conflict of interest

All authors have read and approved the manuscript. Our results have not been previously reported and are not under consideration for publication elsewhere. There were no conflicts of interest, sources of financial support, corporate involvement, patent holdings, etc. involved in the research and preparation of this manuscript.

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