Study on anorectal and colorectal diseases

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Study on anorectal and colorectal diseases

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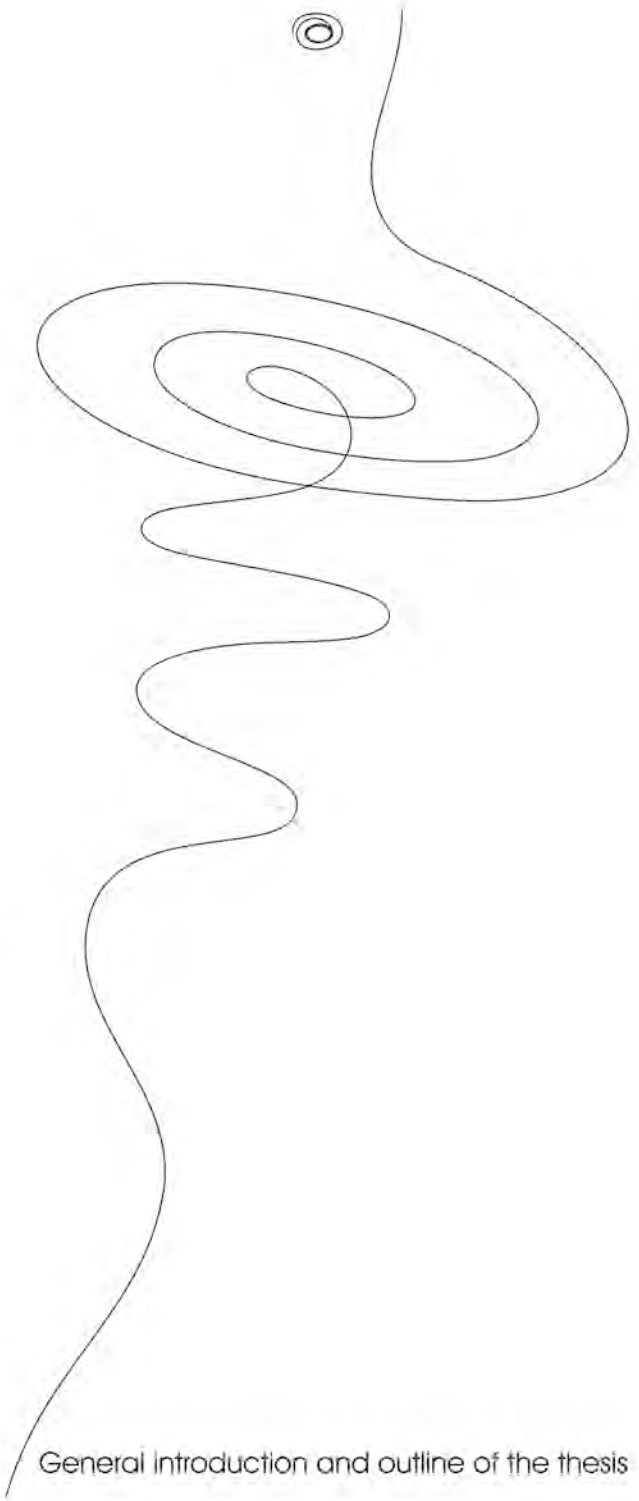
Twenty years from now
you will be more disappointed
by the things you didn't do
than by the ones you did do.
So throw of the bowlines.
Sail away from safe harbour.
Catch the trade wind in your sails.
Explore.
Dream.
Discover.

Mark Twain

Contents

1



General introduction and outline of the thesis

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Anorectal diseases

Epidemiology

Faecal incontinence is defined as the involuntary passage of feces through the anal canal [1]. It affects individuals of all ages and is associated with a great impairment of quality of life, causing social isolation because of embarrassment, humiliation and anxiety of unexpected episodes of faecal incontinence.

The exact incidence of faecal incontinence is hard to determine. Many studies mention prevalence of faecal incontinence from 11 to 15% of the population, with female predominance [2]. The exact numbers in the Netherlands are unknown. The prevalence increases steadily with age, from 4% for incontinence in those between 40 and 49 years old, to 17-66% in patients above 80 years [3]. The prevalence of faecal incontinence in nursing home residents is even higher, up to 50% [3].

Physiology

Maintenance of continence depends upon multiple anatomic, physiologic factors and on a sophisticated interaction between the central and peripheral nervous system and the muscular system. Anal sphincter complex consists of several pelvic floor muscles. The internal anal sphincter is a continuation of the circular smooth muscle of the rectum and is innervated by sympathetic and parasympathetic nerve fibers. The internal anal sphincter is the main contributer to the anal basal pressure [4]. Increasing rectal volume causes relaxation of the internal sphincter. The external anal sphincter consists of striated muscle fibers and is innervated by the pudendal nerve. This sphincter can be contracted voluntarily or by reflex when intra-abdominal pressure increases.[4] Defecation is initiated by m. puborectalis relaxation and propulsive contraction in the rectum. This elicits a simultaneous relaxation of the anal canal sphincters and pelvic floor.

Increasing intra-abdominal pressure induces relaxation of the external sphincter [4].

Etiology

Although, it seems often a problem of elderly people, faecal incontinence is still underestimated in the younger population. Childbirth, especially with difficult vaginal delivery is the most prominent factor. However, several factors contribute to incontinence. In women after delivery both a post-rupture sphincter defect and pudendal neuropathy following excessive straining can occur. The studies using 3-dimentional imaging modalities report an incidence of injury in 11% [5]. Other risk factors are anorectal surgery, trauma from impairment or pelvic fracture, immobility, dementia, diabetes, multiple sclerosis, Parkinson's disease, stroke, spinal cord injury and some congenital abnormalities, such as imperforate anus [6].
In many patients with diarrhea the cause is multifactorial and for this reason it is difficult to identify.

Diagnostic procedures

A comprehensive medical history and a thorough physical examination are essential for right diagnosis. It is important to determine the impact of the faecal incontinence on the patient and their every day live. The Vaizey score containing specific incontinence items that can be helpful to establish severity of incontinence for study purpose, where besides the frequency and consistency of the bowel movement, also the social impact and use of napkins are included [7]. Especially rectal examination gives accurate information about structural disorders.
Anorectal function test consists of anal endosonography, anal manometry and rectal compliance measurement.
Anal endosonography is widely available and the least expensive technique to visualize possible defects or atrophy of the anal sphincter complex. It has a reasonable learning curve, and is easily reproducible, especially with the 3D modus. The internal anal sphincter is visible as an

hypo-echoic layer, and the external anal sphincter exhibits a mixed echogenic pattern. In women, in whom it is not possible to obtain good rectal image, vaginal endosonography can give additional information.[8] Three dimensional imaging is a new modality which offers view from all aspects. This method can be used to detect external anal sphincter atrophy and defects [9].

Anal manometry establishes anal pressures at rest, during squeezing and during straining. The rage of normal values is large, due to the gender and age. Patients with faecal incontinence have lower pressures than healthy controls, but there is considerable overlap of values between the two groups. Therefore, anal manometry has limited diagnostic value. It could be valuable in the follow up of patients who receive biofeedback or in evaluation of surgical treatment but not in making treatment decisions [10].

Rectal compliance measures sensitivity and the volume of the rectum. There is also large range of normal values, with overlap with patients with faecal incontinence. Again, this test has limited clinical value.

Merely the extreme volumes have direct clinical impact. A rectal capacity between 60 and 100ml will lead to faecal incontinence in 50% and < 60ml will predict incontinence in 100% of patients [11].

In **chapter 2** we determine the indicated referrals for patients with anorectal symptoms for anorectal function evaluation, which lead to relevant findings or change of the therapy. In addition we have studied an effect of advice and perceived discomfort for the patients during anorectal function evaluation. Besides the tests mentioned above, other tests were evaluated.

Defecography involves imaging of the rectum with contrast material and observation of the process, rate and completeness of rectal evaluation. It is performed only on strict indications.

Endoanal Magnetic Resonance Imaging (MRI) like anal endosonography can give a good impression of the anatomy of the anus and pelvic floor. Sphincter defect can also be demonstrated. MRI is preferred in patients with high anorectal malformation, since anorectal endosonography does not

provide adequate imaging of the pelvic floor above the level of the puborectal muscle [12].

Neurophysiological testing includes conventional electromyography, single fiber electromyography (EMG) and the assessment of pudendal nerve terminal motor latency (PNTML). EMG can demonstrate functional muscle tissue in a scarred anus, and can give a good impression of the myogenic component of the sphincter. The fiber density of the external anal sphincter can be measured [13]. PNTML gives an impression of the innervation of the external anal sphincter and pelvic floor. Although, this tests have increased insight in the pathogenesis of faecal incontinence, their clinical relevance is small.

Therapy work-up

The first step in treatment of faecal incontinence is regulating defecation with fiber enriched diet and fiber supplementation.

The next available step is careful physiotherapy or biofeedback of the pelvic floor. It is safe and non-invasive procedure, which should be always be tried before referral for further diagnostic and therapy [14]. Patients are trained to increase the anal sphincter contractile capacity in response to rectal distension. This therapy may be more effective in patients with urge incontinence than in patients with passive incontinence [4]. However, the additional tests are not helpful in prediction of the long-term outcome of biofeedback [15].

When conservative treatment is unsuccessful, surgical options are possible in certain patients. Patients with sphincter defect can be offered a sphincter repair. However, only few patients have a sphincter defect suitable for repair. Other forms of surgical therapy, as dynamic gracilis plasty, neuromodulation or artificial bowel sphincter are available in few centers. Those methods of treatment carry certain side effects, and give only moderate improvement [16].

In patients without chronic diarrhea, in whom physiotherapy and surgery is not possible or have failed, treatment with cholestyramine or (intermittent)

loperamide may be a reasonable option. Sometimes enemas and rectal cleansing in the morning can diminished the chance of faecal incontinence. Anal plugs are also a therapeutic option for faecal incontinence, especially in children [17]. Both the diagnostic and therapeutic advices were evaluated.

In **chapter 3**, the new therapeutic option, temperature-controlled radiofrequency energy (SECCA) is evaluated. This procedure has shown a persisting good results. It is safe outpatient procedure for patients in whom diet regulation and physiotherapy have failed and sphincteroplasty is not indicated. This treatment give few generally acceptable side effects. This promising procedure has to be further evaluated in randomized trials [18].

Colorectal diseases

Irritable bowel syndrome (IBS) is a common functional bowel disorder in which abdominal pain or discomfort is associated with defecation or change in bowel habit and with features of disordered defecation. Throughout the world, about 10 % of adults have symptoms consistent with IBS, and most studies find a female predominance [19]. In Dutch general practitioners practice the prevalence of IBS is round 2%, but a mere 22-28% of the patients with IBS symptoms ask for help a doctor.
The pathophysiology of IBS has been thought to involve an interplay between psychosocial stressors and abnormalities in gut motility and visceral sensation. Different motility abnormalities have been described. IBS occurs usually in three subtypes; with diarrhea, constipation or mixed type. Additionally, disorders of evacuation, as seen with puborectalis dysfunction or a rectocele may play a role. Visceral hypersensitivity has long been accepted as an important feature in a subset of IBS patients. The enteric nervous system, which regulates motor, secretory and sensory functions through an extensive neural network in the gastrointestinal tract plays also a role in pathophysiology of IBS. There is currently much interest in the role of inflammatory cells or mediators in at least some types of IBS. Postinfectious

gastrointestinal immune activation, small intestinal bacterial overgrowth and celiac disease-mediated inflammation have also been postulated to play a role in development of IBS symptoms [20]. Diagnosis is based on criteria agreed at a conference in Rome [19].

IBS is a heterogeneous condition, with wide spectrum of symptoms. Sometime diagnosis is not easy, especially when more different conditions coexist. It is reported, that the worsening of IBS symptoms during menstruation in women with endometriosis may obscure the diagnosis of IBS [21]. Endometriosis is a chronic debilitating gynaecological condition which often presents with symptoms that may be similar to those of gastrointestinal disorders. It is characterized by the presence and proliferation of endometrial tissue outside the uterine cavity, which occurs in approximately 10% of women of reproductive age. The prevalence of IBS is approximately 32% in women with endometriosis without bowel lesions [22]. Therefore, wider gastroenterological evaluation is needed in overlapping symptoms so that neither accurate diagnosis is missed nor right treatment is delayed in patients with endometriosis and IBS. Successful management of IBS combines individualizing treatment of predominant symptoms and conferring insight on how symptoms may related to emotional stress. Evidence for efficacy of therapies is complicated by high placebo effect and is up to 40-50% in IBS trails. Treatment of bowel dysfunction is focused on accelerating or slowing transit as required, where fiber supplementation, antidiarrheal and non-stimulant osmotic laxatives are used. Antidepressants used is low doses have a visceral analgesic effect, and antispasmodics can be useful for abdominal pain. The complementary therapies can also give some support in the treatment of IBS, as biofeedback may help patients gain control over their symptoms, or hypnotherapy and meditation cause focused relaxation [20].

The study presented in **chapter 4** shows importance of multidisciplinary diagnostic of such complicated conditions as irritable bowel syndrome.

Diverticulair disease is one of the most common pathologies affecting the colon. During the last century diverticulosis has become more frequent, mainly in industrialized Western countries. Disease is present in up to 10% of individuals under the age of 40, and increases up to 40-70% of those above 70 years of age. Westernized lifestyle predominate for diverticula located in the left colon, for 95% in the sigmoid. In Eastern populations prevalence rates are 1-4%, and a right colon predominance is observed [23]. There is no difference in prevalence of the disease in men and women.
The development of colonic diverticula is probably determined by two factors: a weak colonic wall and increased intraluminal pressure. Increasing incidence in the developed countries suggests that environmental and lifestyle factors play an important role in the pathogenesis of diverticulair disease.
A majority of patients with diverticulosis never develop any symptoms. Approximately 15% to 25% of patients with diverticulosis will develop diverticulitis, 5% to 15% will develop divertlcular bleeding. Among patients with diverticulitis 25% will be complicated by abcess formation, a fistula, intestinal obstruction, or a perforation [23]. **Chapter 5** is an extensive review of this interesting disease.

The relation between diverticulosis and colorectal cancer is also suggested. Both diseases are more frequent in developed countries and are age-dependent, as both are uncommon in those under the age of 40. Colorectal cancer is a leading cause of cancer mortality in the Western world, with more than 1,000,000 new cases per year and with 500,000 deaths per year worldwide [24]. In the Netherlands, colorectal cancer is diagnosed in about 10,000 patients each year and causes 4,400 deaths per year [25]. A possible explanation for the association between the two diseases is that they share similar risk factors. They have the same pathogenic factors, like the western low fiber diet and rich in saturated fat [26]. A causal relationship between the two diseases has also been suggested.

In **chapter 6** we studied transversally the possible risk for colorectal neoplasia or polyps in patients with diverticulosis and diverticulitis. The study presented in **chapter 7** is related to chapter 6. The aim of this study was to assess the relationship between diverticulitis and the development of CRC and colorectal adenomas in a longitudinal study.

Patients compliance

Elective colonoscopy is very important in screening and surveillance programs for patients with colorectal disease. Especially in elderly patients, colonoscopy is recommended to exclude malignancy. Inadequate preparation can result in missed pathology, can prolong time of insertion and increase the risk of complications [27]. Therefore, effective, good cleansing, well tolerated by patients is mandatory for good quality and safety of the colonoscopy.

In **chapter 8** the importance of a good bowel preparation for appropriate and safe diagnostic is evaluated.

In **chapter 9** the taste of two polyethylene glycol preparations for chronic constipation was compared.

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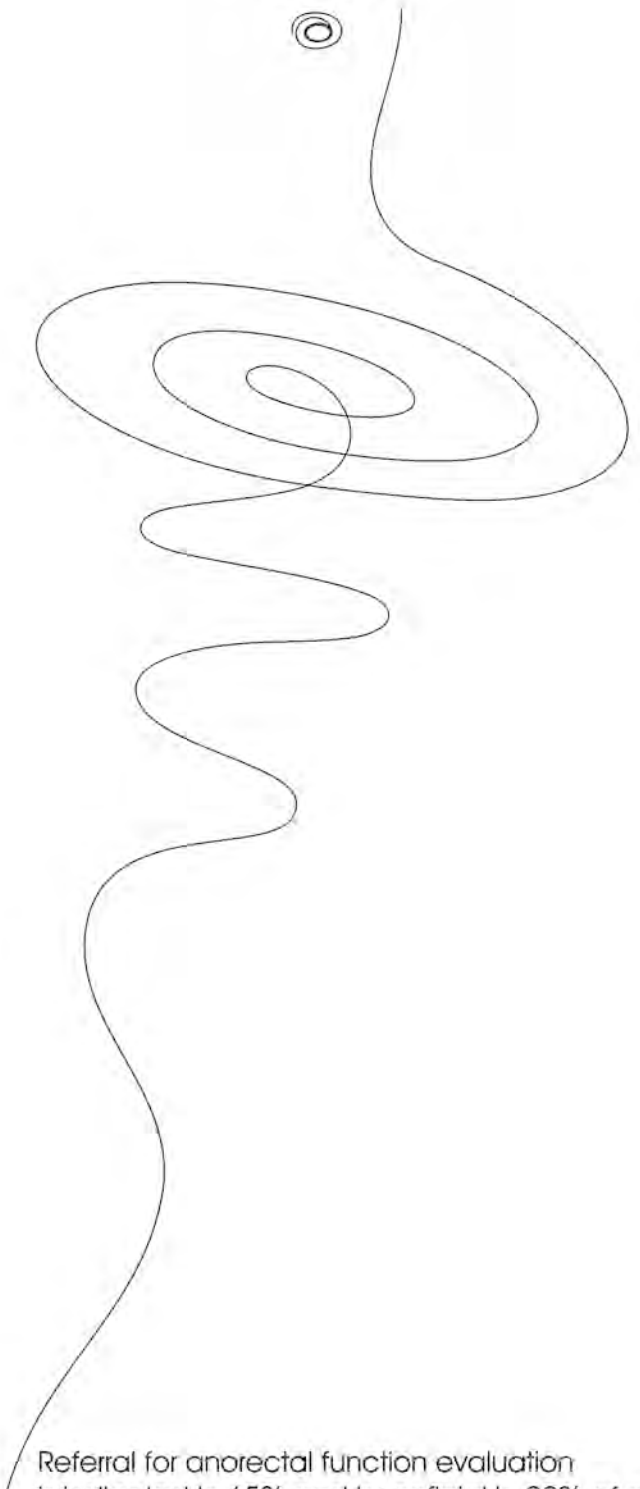
2



Referral for anorectal function evaluation
is indicated in 65% and beneficial in 92% of patients.
M.M. Szojda, E. Tanis, C.J. Mulder, R.J. Felt-Bersma
World J Gastroenterology 2008;14:272-7

Abstract

Aim

To determine the indicated referrals to a tertiary centre for patients with anorectal symptoms, the effect of the advised treatment and the discomfort of the tests.

Methods

In a retrospective study patients referred for anorectal function evaluation (AFE) between May 2004 and October 2006 were sent a questionnaire, as well as the doctors who referred them.

AFE consisted of anal manometry, rectal compliance measurement and anal endosonography. An indicated referral was defined as needing AFE to establish a diagnosis with clinical consequence (faecal incontinence without diarrhea, 3rd degree anal sphincter rupture, congenital anorectal disorder, inflammatory bowel disease with anorectal complaints and preoperative in patients for re-anastomosis or enterostoma, anal fissure, fistula or constipation). Anal ultrasound is always indicated in patients with fistula, anal manometry and rectal compliance when impaired continence reserve is suspected. The therapeutic effect was noted as improvement, no improvement but reassurance, and deterioration.

Results

From the 216 patients referred, 167 (78%) returned the questionnaire. The referrals were indicated in 65%. Of these, 80% followed the proposed advice. Improvement was achieved in 35% and a reassurance in 57% of the patients, no difference existed between patient groups. On a VAS scale (1 to 10) symptoms improved from 4.0 to 7.2. Most patients reported no or little discomfort with AFE.

Conclusion

Referral for AFE was indicated in 65%. Beneficial effect was seen in 92%: 35% improved and 57% was reassured. Advice was followed in 80%. Better instruction about indication for AFE referral is warranted.

INTRODUCTION

Anorectal function evaluation (AFE) consists of several tests. Institutions differ in their selection of tests [1]. At our tertiary centre, anal manometry, rectal compliance measurement and anorectal endosonography are performed as part of our standard procedure [2]. Defecography and colon transit time are performed on strict indications. Neurophysiological tests of the pelvic floor are performed only for research purposes. Anal manometry establishes anal pressures while rectal compliance measures sensitivity and the volume of the rectum. Anal endosonography visualizes possible defects or atrophy of the anal sphincter complex. AFE is often requested in patients with anorectal symptoms, e.g. faecal incontinence, anal soiling, fistulas, anorectal tumours, anal pain, constipation e.g. AFE is available in a limited number of hospitals, mainly academic centres and some large peripheral clinics.

A clinical referral (no research purposes) is indicated when disease can be demonstrated or excluded on the basic of AFE and when it has further therapeutical consequences. Which patients benefit most from anorectal function tests (by reduction of symptoms or reassurance) is unclear. Literature concerning this issue is scarce. Most studies that mention anorectal function tests in relation to anorectal pathology limit themselves to pre- and post-treatment results. Therefore it often remains unclear whether AFE leads to relevant findings or subsequent change of therapy [1-10]. A large multi centre Dutch study referred to the value of AFE for outcome of physiotherapy in patients with faecal incontinence [1]. One conclusion was that AFE had no predictive value for outcome of physiotherapy. Further, referral for AFE largely depended on availability of these tests in the referring hospital.

The aim of this study was to determine the indicated referrals to our tertiary center for patients with anorectal symptoms, the effect of the advices on their complaints and the the perceived discomfort for the patients during AFE.

MATERIALS AND METHODS

Patients

All patients who were first clinical referrals for AFE between May 2004 and October 2006 were selected from our database. The database contained the complete medical history and extensive data of anorectal symptoms and anorectal test results. Deceased patients were excluded. The patients were sent a questionnaire. Additional data about follow-up in the outpatient clinic, hospital admittance, diagnostic and therapeutic procedures performed in our hospital could be retrieved from the (electronic) patient hospital files.

The Medical Ethical Commission of the VU University Medical Centre granted permission.

The referring doctors

The doctors who referred patients in the period 2004-2006 were also sent a questionnaire.

Anorectal function evaluation (AFE)

This consisted of anal manometry, rectal compliance measurement and anorectal endosonography according to our methods previously described [11].

Indicated referral

A referral is indicated when disease can be demonstrated or excluded on the basic of AFE and when it has further therapeutical consequences. These are patients with faecal incontinence without diarrhea, 3rd degree sphincter rupture with or without faecal incontinence, congenital disorders, patients with inflammatory bowel disease with anorectal complaints and preoperative in patients for re-anastomosis or enterostoma, anal fissure or constipation. In patients with fistula an ultrasound is always indicated but anal manometry and rectal compliance measurement only on indication regarding faecal incontinence. Test results in all these patients influence management. In patients with constipation AFE was considered indicated in suspected Hirschsprungs' disease and surgery. AFE was not considered indicated in patients with fissures treated conservatively, soiling (defined as

anal discharge without overt faecal incontinence), anal pain and hemorrhoids, since results do not change management.

Questionnaires

The questionnaire for patients [2] contained questions about the actual received therapy, changes in their symptoms by the received treatment, stated in a Visual Analogue Score (VAS) (score 1-10, 1=very bad, 10=very good) and also stated as (1) improved, (2) no change but reassurance or acceptance of situation without further need for seeking other medical advice and (3) worse and/or no reassurance. Discomfort and pain during the examination was scored with VAS (score 1-10, 1=very uncomfortable/ painful, 10=no discomfort/pain).

The questionnaire for the referring doctor[2] consisted of questions about implementing the advice (yes, no), the quality of the advice (good, neutral, poor) and the willingness to refer again (yes, no).

Treatment advice strategy

The patients with symptoms of faecal incontinence were divided into 5 diagnostic subtypes: incontinence due to a sphincter defect, neurogenic incontinence, combined incontinence (sphincter defect and neurogenic), incontinence due to small rectal capacity and incontinence due to diarrhea.

Patients with incontinence due to diarrhea were advised to have the cause of their diarrhea sorted out by the referring doctor.

All patients with faecal incontinence were prescribed fibres and physiotherapy. When unsuccessful additional therapy was advised depending of the cause. Patients with a sphincter defect >25% were offered a sphincter repair. In patients with a small rectal compliance an enterostoma was proposed (<60 ml) or strongly recommended (between 60 and 100 ml) [12].

Patients with a known 3rd degree sphincter rupture and as a result faecal incontinence were advised as other patients with faecal incontinence and the strong advice for a cesarean section with a next childbirth. If they were

not incontinent, depending on the size of the rupture, the possibility of a cesarean section for next childbirth was discussed.
Advising re-anastomosis or enterostoma depended on the total impression of the anorectal function measured with anal pressures, rectal compliance and sphincter defects or atrophy.
In patients with a fistula the extension of the fistula tract(s) with anal ultrasound determined the type of surgery in our hospital (fistulotomy in simple and curettage with mucosal advancement plasty in complicated fistulas).
Patients where AFE was not indicated also received an advice. In patients with constipation a fibre enriched diet, additional fibres and laxatives were advised. When unsuccessful and not previously attempted, pelvic floor physiotherapy was advised. When constipation coexisted with complaints of prolapse, a defecography was advised. When surgery was considered (rectocele correction or colectomy) besides an AFE, also a colon transit time was performed. Patients with fissures were treated conservatively; when treatment failed they were referred to the surgeon and AFE was indicated. Hemorrhoids and mucosal prolapse were treated with rubber band ligation. A hemorrhoidectomy was advised only in refractory cases. Local causes of anal pain were treated according to their causes. When no local abnormalities were seen in patients with anal pain, fibres and referral to the anaesthesiologist was advised.

Statistic analysis

The results were described as mean with standard deviation. The χ^2 test for independence and for trend, the Kruskal-Wallis test and the Wilcoxon matched-pair test were used when appropriate (GraphPad InStat Software, San Diego, Ca, USA).

RESULTS

Response questionnaires

There were 216 first referrals for AFE, 181 (84%) females, mean age 51 years, (SD 15, range 15-82). Two patients had died, 167 patients (137 females (82%), mean age 51 years, SD 15, range 16-82) returned an adequate (almost all questions answered) questionnaire (78%).

Indicated referrals

Table 1 shows the indicated referrals. Of the 167 referrals, 109 (65%) were indicated. The most frequent referral was faecal incontinence, from which 93% was indicated (7% had diarrhea).

	All n (% of referrals)	Indicated n (% of that group)
incontinence	71 (43)	66 (93) a
constipation	31 (19)	6 (19) b
3rd sphincter rupture	21 (13)	21 (100)
pain	9 (5)	0 (0)
re-anastomosis/enterostoma	9 (5)	8 (100)
soiling	5 (3)	0 (0)
IBD	4 (2)	4 (100)
hemorrhoids	3 (2)	0 (0)
anal atresia	2 (1)	2 (100)
fistulas	2 (1)	2 (100)
fissure	1 (1)	0 (0)
other	9 (5)	0 (0)
Total	167 (100)	109 (65*)

Table 1. Indicated referrals in the main groups of patients.

a. 5 patients with diarrhea not indicated, b. only patients suspected of Hirschsprung / surgery indicated, IBD-inflammatory bowel disease* = % of all referrals

Non indicated referrals

Two of the 31 patients with constipation had signs of anismus during physical examination and anal manometry. Of the 5 patients with soiling, 4 had a mucosal prolapse and/or hemorrhoids. The fifth patient had an anal fissure on inspection, not previously found. In two patients with anal pain a fissure was found, one treated conservatively and one eventually much later with surgery. AFE revealed no abnormalities in all patients besides high rest pressure in the patients with fissures. AFE did not influence therapeutic advice.

Effect of treatment

Symptoms improved in 54 patients (35%). In 88 patients (57%) symptoms were unchanged but patients were reassured. Despite treatment, 12 patients (8%) deteriorated. The whole group improved one point on the VAS scale (5.1-6.1) ($p<0.0001$), for those improved (35%) this was even 3.2 points (4.0-7.2). Both indicated and non indicated referred patients improved equally.

The causes of faecal incontinence were: sphincter defect (14), neurogenic (37), combined incontinence (10), incontinence due to diarrhea (5) and incontinence due to small rectal capacity (<100 ml) (5). Within these groups, the largest improvement was seen in the combined incontinence group (1.8 point) ($p=0.01$). Patients with a small rectal capacity had no improvement at all.

The actual therapies received by the patients according to the reason for referral are mentioned in table 2. Some patients received several therapies. The most frequent advice was medication, mainly fibres.

Of all referred patients, only 17% were operated. No difference between effectiveness of conservative and surgical treatment could be observed on patient symptoms ($p=0.09$).

2004-2006		Treatment according to the patients						Symptoms change after treatment				
								VAS		category		
Reason for referral	**patients**	**treatment***	**diet n (%)**	**medication n (%)**	**surgery n (%)**	**physiotherapy n (%)**	**expectave n (%)**	**before**	**after**	**improved**	**reassured**	**worse**
Incontinence#	71	100	8	32	12§	26	22	5	5.7	20	39	7
Constipation	31	35	3	12	3†	7	10	5	6.2	11	17	1
3rd sphincter rupture	21	22	2	1		2	17	7.1	7.2	2	15	1
Anal pain	9	8		1	1‡		6	3.5	5.1	3	5	
Surg/ Stoma	8	8			6		2	6.3	7	2	4	
Soiling	5	7	2	3	2			3.4	4.8	3	1	1
IBD	4	4		2			2	4.8	6.5	2	2	
Hemorrhoids	3	6	1	3	2◊			4.3	6.3	2	1	
Anal atresia	2	2		1			1	6	7.5	2		
Fistula	2	2					2	4	5.5	1	1	
Fissure	1	2		1	1‡			2	8	1		
Pouchitis	1	1					1	8	7			1
Other	9	12	1	1	8	1	1	5.1	6.7	5	3	1
Average (SD)								5,1• (2.4)	6.1• (2.3)			
Total (%)	167	209	17 (8)	57 (27)	35 (17)	36 (16)	64 (31)			54 (35)	88 (57)	12 (8)

Table 2. Reason for referral and effect of treatment on patients.

*treatment as answered by patients, several treatments per patient possible, # including all subgroups, § sphincter repair, † rectocele repair, ‡ fissurectomy, ◊ hemorroidectomy •p<0.0001

AFE induced little stress, indicated by an average pain score of 7 (SD 2.7) and a discomfort score of 7.2 (SD 2.8). Two patients with fistulas experienced the examination as unpleasant and painful due to the hydrogen peroxide injection in their fistula tract during anal ultrasound. Thirty-five females (26%) preferred to be examined by a female doctor while the remaining 102 (75%) had no preference. Twenty-six males (93%) had no preference and the remaining two (7%) preferred a male and a female doctor, respectively ($p<0.0001$). Dutch ethnic minorities did not influence these data.

Questionnaires referring doctors

Of the 214 questionnaires, 102 (48%) responses were obtained. The advice was nearly always implemented (96%). The quality of the advice was considered good in 76% and neutral in 24%. All doctors except one (98%) were willing to refer again.

Agreement between proposed and followed advises.

The proposed and followed therapies are shown in table 3. Therapies could also be a combination of medication, physiotherapy or surgery. Dietary advice was always followed (100%), while surgical advice was generally followed (89%). Less accepted advices included medication (71%) and physiotherapy (73%) ($p=0.005$, 99%CI).

	All Therapies (%)	Diet (%)	Medication (%)	Physiother. (%)	Expectative (%)	Surgery (%)
Followed	130 (80)	7 (100)	54 (71)	32 (73)	31 (100)	36 (90)
Not followed	32 (20)	0	22 (29)	12 (27)	0	4 (10)
Total	162 (100)	7 (100)	76 (100)	44 (100)	31 (100)	40 (100)

Table 3. A comparison between the proposed therapeutic advices and followed therapy. A therapy can consist of more components.

DISCUSSION

The 78% response to the questionnaires of the patients was good. In our previous study we reported a similar result [2]. Only 65% of the referrals were indicated. In 35% the diagnosis could have been established by clinical examination or added nothing. This is a signal that more communication and education is warranted, especially in times with restrictions and limited resources. However, many of the referred patients suffered from chronic symptoms, bringing both patient and doctor to despair. The possibility of referring the patients to another centre may come as a welcome alternative. The symptoms of the whole group improved an average of one point from 5.1 to 6.1 on a scale of 10. Actual improvement took place in 35% of the referred patients; they improved an average of 3.2 points. The moderate improvement might be explained by the fact that it concerned patients with chronic disorders, already treated conservatively for a long time. Success was not related to a specific symptom, diagnosis or treatment, only the five patients with faecal incontinence due to small rectal capacity did not improve. Deterioration in 8% of the patients was mainly due to the fluctuating course of the chronic complaints combined with their reluctance to follow the advice. In 80% the patients followed the advices. Medication and physiotherapy were the least applied therapies (table 3). Some disagreement between advised and followed therapy could be explained by the fact that patients considered fibres a diet instead of medication. Physiotherapy was advised in 44 patients (26%) and effectuated in 32 (73%). Ten years ago this was only respectively 18% and 67% [2]. Increasing interest in pelvic floor disorders and special training for physiotherapists has certainly contributed to the change in attitude towards physiotherapy [1,13]. Although therapeutic advices were given after AFE, actual improvement in symptoms is not necessarily caused by AFE. A placebo effect due to the referral to a specialized centre and the knowledge present in a 3rd referral centre may play a role. This is comparable with biofeedback studies for faecal incontinence, were the added value of the biofeedback was very difficult to separate from the received specialized care and treatment [13,14].

The examination was generally well tolerated, except in two patients with fistulas who experienced the examination as painful. This was caused by local injection of hydrogen peroxide into the external fistula opening in order to visualize the fistula tract. Remarkable is that ten years ago only 13% of the females [2] and now 26% of the females preferred a female doctor. The larger number of referred Dutch ethnic minorities could not explain this.
Although the questionnaire was retrospective and has not been officially validated (we used it before [2]) has proven to be very useful. Questions about for instance surgery or 3-6 months of physiotherapy could not easily be misunderstood. In patients treated in our own hospital follow up data were also obtained from the (electronic) patient files and no discrepancies were found with the answers provided by these patients.
Our treatment advice strategy is derived from clinical practice and the literature. In patients with faecal incontinence, regulating defecation and thickening of the faecal mass has proven to be effective and should always be tried first [15-17]. Biofeedback aimed at improving rectal sensation, recto-anal coordination and training external anal sphincter contraction is the next step and has a success rate varying from 40-85% and is closely related to patient motivation [18]. Diarrhea should be properly diagnosed and treated before referring the patient for AFE since this overwhelming factor makes it impossible to establish the (possible) importance of anorectal causes. A rectal capacity between 60 and 100 ml will lead to faecal incontinence in 50% and <60ml in 100% of patients [12]; they will often need an enterostoma. Patients with faecal incontinence with a significant sphincter defect (>25%) without severe neuropathy leading to atrophy can be identified as suitable candidates for a sphincter repair [1,19-21].
In our group of incontinent patients only 12 (18%) ultimately underwent sphincter repair. Two patients were later referred for sacral neuromodulation elsewhere and eleven patients [22] were treated with SECCA® (radio frequent energy application to the external sphincter [23,24]).
Women who experienced a 3rd degree sphincter rupture are indicated for AFE, even without complaints. There in always some damage to the external

anal sphincter and appropriate advices concerning defecation regulation, physiotherapy and possible future cesarean section can be discussed. Most patients with constipation were referred for assessment of anismus/hyper tonic pelvic floor or rectocele. Generally AFE is not needed in these patients. Both anismus and a rectocele can be diagnosed by proper rectal examination [6,25,26]. When prolapse complaints dominate a defecography is indicated to demonstrate a possible enterocele as this can be corrected surgically. In patients with constipation correction is not indicated in accidentally found intussusception since the obstructed defection will not improve [26-29]. AFE is indicated when (partial) colectomy is considered to be informed about the continence reserve. For patients with fistulas anal endosonography demonstrates the fistula tracts and anal manometry will establish the continence reserve [21,30-33]. In patients with soiling (anal secretion), medical history, good physical and rectal examination and an additional proctoscopy have proven be sufficient to establish a diagnosis [10], without the need for AFE, as was shown again in our patients. For patients with pain AFE does not contribute [34]. Suspected discrete abnormalities e.g. an occult abscess, could not be demonstrated in our study as well. Sometimes a fissure is found in these patients, diagnosed on the basis of the medical history and rectal examination. In patients with a fissure high pressures are usually found using manometry, but this does not alter therapy [35]. Only in those who where conservative measures have failed and will undergo surgery AFE seems indicated. In patients with haemorrhoids anal manometry can also reveal high pressures and anal endosonography can demonstrate a thickened mucosa; however, these findings have no influence on therapy [36,37]. AFE is indicated in patients with an enterostoma when re-anastomosis is considered. In some rare disorders like anal atresia AFE can also be indicated to document anorectal problems and help choose a specific therapy.

In conclusion, Referral for AFE was indicated in 65%, communication and education to colleagues seems warranted. Indications are faecal

incontinence without diarrhea, 3rd degree sphincter rupture, pre-operative for stoma or re-anastomosis, fistula, fissures or constipation. Anal ultrasound is always indicated in patients with fistula, anal manometry and rectal compliance when impaired continence reserve is suspected. Generally, in patients with constipation and soiling the medical history, physical examination and additional proctoscopy is sufficient and AFE is not necessary.

In 80% the patients followed the advices. After AFE 92% benefited (35% of the patients improved and 57% was reassured). AFE is well tolerated. Women preferred a female doctor in 26%.

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COMMENTS

Background

Anorectal disorders like faecal incontinence, peri-anal fistula, pre-operative decisions for stoma e.g. are distressing and isolating conditions, with have a large impact on quality of life. With restricted resources it is important to make a good selection of referrals for anorectal function evaluation, those patients who benefit most. In this study we established the indicated referrals our tertiary referral centre for patients with anorectal symptoms, the effect of the advised treatment and the discomfort of the tests.

Research frontiers

A clinical referral is indicated when disease can be demonstrated or excluded on the basic of anorectal function evaluation and when it has further therapeutical consequences. Which patients benefit the most from anorectal function tests (by reduction of symptoms or reassurance) is unclear.

Innovations and breakthroughs

Most studies mention anorectal function tests in relation to anorectal pathology limit themselves to pre- and post-treatment results. Therefore it often remains unclear whether anorectal function evaluation leads to relevant findings or subsequent change of therapy. Literature concerning this issue is scarce.

The aim of our study was to determine the indicated referrals to our tertiary center for patients with anorectal symptoms, the effect of the advices on their complaints and the perceived discomfort for the patients during anorectal function evaluation.

Applications

It is very important to understand the usefulness of the anorectal function evaluation to provide referrals of those patients, which could benefit the most.

Indications for anorectal function evaluation are faecal incontinence without diarrhea, 3rd degree sphincter rupture, pre-operative for stoma or re-anastomosis, fistula, fissures or constipation. Anal ultrasound is always

indicated in patients with fistula, anal manometry. Rectal compliance is indicated when impaired continence reserve is suspected. Generally, in patients with constipation and soiling the medical history, physical examination and additional proctoscopy is sufficient and anorectal function evaluation is not necessary.

Terminology

Anorectal function evaluation consists of several tests:

- anal manometry - establishes anal pressures
- rectal compliance - measures sensitivity and the volume of the rectum
- anal endosonography - visualizes possible defects or atrophy of the anal sphincter complex

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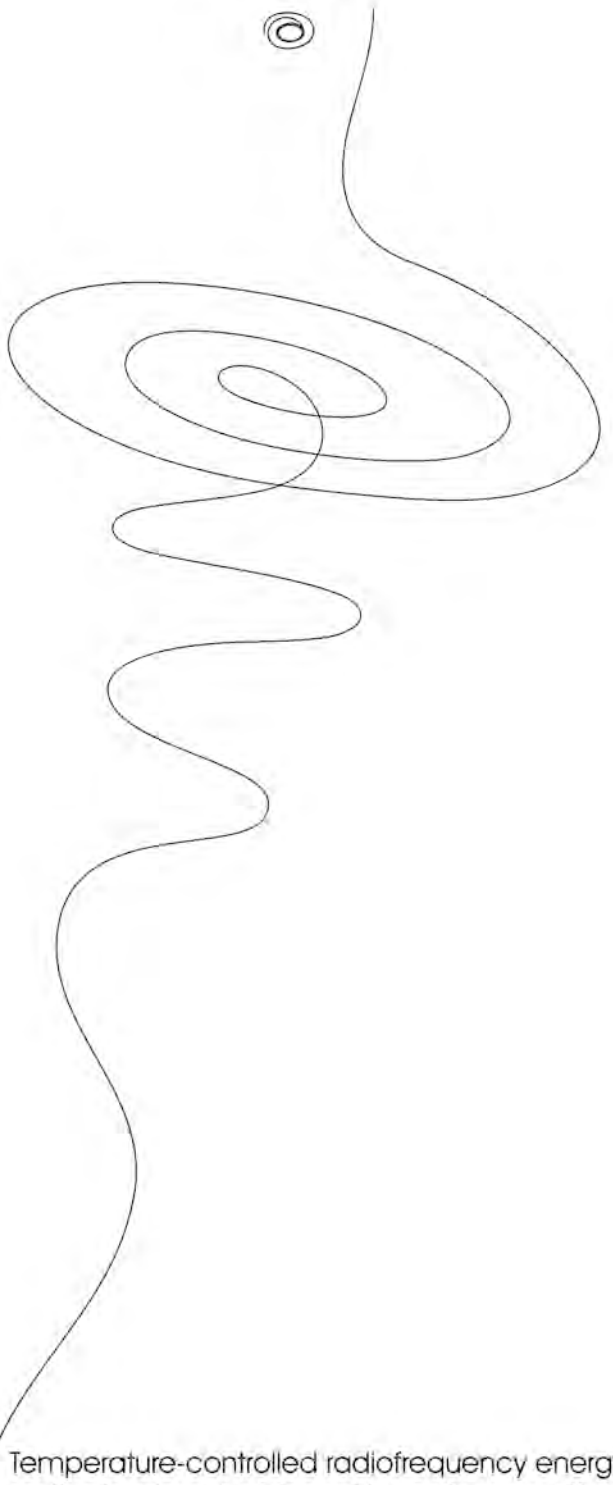


Temperature-controlled radiofrequency energy (SECCA) to the anal canal for the treatment of faecal incontinence offers moderate improvement.
R.J. Felt-Bersma, M.M. Szojda, C.J. Mulder
Eur J Gastroenterol Hepatol. 2007;19:575-80

Abstract

Background and aim

Faecal incontinence is a devastating complaint. Even after conservative treatment many patients still remain incontinent. Few patients have a sphincter defect suitable for repair. Other emerging surgical therapies like dynamic gracilis plasty, neuromodulation or artificial bowel sphincter, carry side effects and show only moderate improvement. Temperature controlled radio frequency (RF) energy (SECCA®) has shown promising results in the USA. Local tightening seems the mode of action with possible increased rectal sensitivity. We investigated the effectiveness of RF and possible changes in the anal sphincter with 3D-ultrasound in patients with faecal incontinence.

Patients and methods

Eleven females, mean age 61 years (49-73) with long standing faecal incontinence were included. Patients with large sphincter defects and anal stenosis were excluded.

The SECCA® procedure was performed under conscious sedation and local anaesthesia. Oral antibiotics were given. In 4 quadrants on 4 or 5 levels (depending upon length of the anus) RF was delivered with multiple needle electrodes. Patients were evaluated at 0, 6 weeks, 3 and 6 months and one year. Three dimensional anal ultrasound was performed at 0 (before and after the procedure), 6 weeks and 3 months. Anal manometry and rectal compliance measurement were performed at 0 and 3 months.

Results

At 3 months, 6 of 11 patients improved, which persisted during follow up of one year. The Vaizey score changed from 18.8 to 15.0 (p=0.03) and in those improved from 18.3 to 11.5 (p=0.03). Anal manometry and rectal compliance showed no significant changes, there was a tendency to increased rectal sensitivity concerning urge and maximal tolerated volume (both p=0.3). Responders compared to non-responders showed no difference in test results. Side effects were local haematoma (2), bleeding 3

days (1), pain persisting 1-3 weeks (4) and laxatives related diarrhea during 1-3 weeks (4).

Conclusion

The SECCA® procedure seems promising for patients with faecal incontinence with a persisting effect after one year. No significant changes in tests were found.

Presented at the UEGW October 2006 (Berlin, Germany), DDW May 2006 (Los Angeles, CA, USA) and the Dutch Society of Gastroenterology October 2005 (NVGE, Veldhoven, The Netherlands)

INTRODUCTION

Faecal incontinence is a complex problem that has a high impact on the quality of life [1]. Damage to the anal sphincters (external and/or internal anal sphincter defect) or to the pudendal nerve (denervation) during vaginal delivery are the most frequently encountered cause in women with faecal incontinence. Anal sphincter trauma and damage of the pudendal nerve often occur simultaneously [2].

The exact incidence of faecal incontinence is hard to determine and relates to the reluctance to report this complaint due to embarrassment. Several studies with questionnaires in the general population report prevalence up to 7%, increasing with age [3].

Treatment of faecal incontinence starts conservatively consisting of regulation of defecation with a fibre enriched diet, physiotherapy of the pelvic floor and medication inducing constipation like loperamide or cholesteramine. When unsuccessful, patients with an anal sphincter defect can be offered a sphincter repair. New surgical options for patients with or without a sphincter defect are dynamic gracilis plasty [4] or sacral neuromodulation [5] or artificial bowel sphincter [6]. Yet all these treatments have success percentages defined as substantial improvement varying around 70%, carry some side effects, demand specific expertise and are not generally available.

A new emerging technique is radiofrequent energy (RF) delivery to the anorectal junction. Tissue heating with the delivery of RF energy results in immediate collagen contraction, followed by local wound healing, remodelling and tightening [7]. It has been applied for non gastrointestinal diseases (obstructive sleep apnoea, snoring, benign prostatic hyperplasia, joint capsule laxity) and has also been successfully used in the gastroesophageal junction for gastroesophageal reflux disease [8].

Two recent open-label trials suggested improvement in the faecal incontinence score and the quality of life [9,10], one with a follow up of two [11] and five [12] years. The clinical results varied in these two studies. The technique is feasible as an outpatient procedure and has little side effects

concerning local discomfort. Anorectal function tests suggested some changes in rectal sensitivity, but no other changes in anorectal function or ultrasound were found.
The aim of this pilot study was to treat patients with SECCA® to establish the decrease of their complaints of faecal incontinence and to study possible changes in anorectal function and three dimensional ultrasound.

PATIENTS AND METHODS

Patients

Patients with faecal incontinence for at least six months, a Vaizey incontinence score [12] of at least 12 and failure of conservative treatment, based on diet recommendations, antidiarrheals and physiotherapy without a significant sphincter defect suited for sphincter repair were included. Patients were excluded if they had proctitis or inflammatory bowel disease, chronic diarrhea, chronic constipation, overflow incontinence, previous ileoanal or coloanal anastomosis, rectal prolapse, anal stenosis, anal fissures or fistulas, pelvic radiation, coagulation disorders or the use of anticoagulants. Patients with haemorrhoids or mucosal prolaps were treated first with rubber band ligation and could be included 6 weeks later. Medical history was obtained at baseline and after 3, 6 and 12 months including Vaizey score (0 = no complains, 24 = fully incontinent) [13], improvement (none, slightly improved and improved) and side effects.
On digital palpation sphincter pressure was scored as low, normal or high. Defects were also described and measured in hours (1-12 hours, with 12 hours being anterior).
All patients underwent colonoscopy in their previous work up.

Methods

Anal manometry

Anal manometry was performed with an open tip perfusion system using a disposable catheter with four 90° radial orientated side ports connected to a Polygraf ID (Medtronic, Skovlunde, Denmark). After calibration, the

catheter is automatically withdrawn by a puller at a speed of 3 cm per second.

The average increase in pressure to the atmosphere pressure is the maximum basal pressure (MBP). The length over which the increase is present is the sphincter length (SL). The catheter is introduced again and manually withdrawn with steps of 0.5 cm, while the patient is asked to squeeze maximally. The average maximum increase in pressure above the existing basal pressure is the maximum squeeze pressure (MSP). The distension reflex was elicited by inflating the rectal balloon and the volume was registered.

Rectal compliance measurement

A compliant balloon catheter is introduced into the rectum. Air is inflated manually with a syringe with a speed of 60 ml in 15 seconds to a maximum to 300ml. The volume of first sensation (FS), urge to defecate (Urge) and maximum toleration (MTV) is notated.

Three dimensional (3D) anal ultrasound

Anal ultrasound was performed using a three dimensional diagnostic ultrasound system (Falcon type 2101 EXL, B-K Medical, Naerum, Denmark) with a 5-16 MHz rotating endoprobe (type 2050, focal range 2 to 4.5 cm) with an internal puller (diameter 1.7 cm) producing a 360° view. 3D anal ultrasound was performed according to a standard procedure with an automatic puller. The endoprobe was covered with a lubricated condom which was filled with ultrasound gel. The probe was then introduced into the rectum and a recording was made of the distal part of the rectum, the puborectalis muscle and the anal canal. After the ultrasound, images were reconstructed to three dimensional images by computer software.

Defects

External anal sphincter (EAS) defects were described as hypoechogenic lesions and the extent of the defect was axially measured in hours (1-12 hours, with 12 hours anterior, three hours left lateral, etc). The length of the defect was indicated as proximal, distal or total. A defect comprised at

least one hour of the circumference of the sphincteric ring. Internal anal sphincter (IAS) defects were described as a disruption of the internal ring.

Atrophy

Atrophy of the EAS was judged upon its reflection of the outer interface (border external anal sphincter and subadventitial fat), reflection pattern and length. Atrophy was scored as none (clearly visible outer interface, mixed reflection pattern), moderate (partly visible outer interface, intermediate reflection, moderate shortening) and severe (hardly visible outer interface, hyperechogenic reflection pattern, severe shortening) [14].

SECCA® procedure

Patients were treated in the outpatient department in the endoscopy unit. Prophylactic antibiotics (metronidazol 500mg and amoxycilline 500mg/clavulanacid 125mg) were taken before the procedure and repeated afterwards and 8 hours later. One hour before the procedure patients received a rectal enema. An intravenous catheter was placed and sedation with 0.05 mg fentanyl and 7.5 mg midazolam was administered. During the procedure more sedation could be added when necessary. Local perianal anaesthesia with 10 ml lidocaine 0,5% with epinephrine 1:200.000 was administered in 4 quadrants. A standard electrosurgical ground pad was placed on the patient's back or flank according to hospital safety standards. The radio frequency generator was turned on, the ground pad connected to the generator, the SECCA® hand piece connected to the generator, and the IV tubing and sterile water bag attached to the hand piece and the pump on the generator.

The SECCA® device (figure1) comprises an anoscopic barrel with four nickel-titanium cursed needle electrodes deployed from within (22 gauge, 7 mm length; Curon medical, SunVally, CA, USA). The hand piece is positioned under direct vision at the proper position in the anal canal (figure 2), needles deployed into the muscle (figure 3). Irrigation of the mucosa begun via the coolants ports on the hand piece, and RF (465 kHz, 2-5 Watt) was delivered for 60 seconds, resulting in 4 thermal lesions. Target lesion temperature was 85°. After the 60 seconds interval, the needles were

retracted and the hand piece was repositioned. In total 5 levels, starting at the dentate line, going up with steps of 1 cm until 4 cm above the dental line, and four quadrants, are treated, thus 80 RF deliveries. When during the procedure displacement of the needles or drop out of the device occurred before 30 seconds, the procedure was repeated at the place after repositioning. If the recto-vaginal septum was thin and short, less than 5 applications were performed anteriorly. The RF procedure took about 30 minutes, including preparation about one hour.

Figure 1. SECCA® Hand piece (probe)

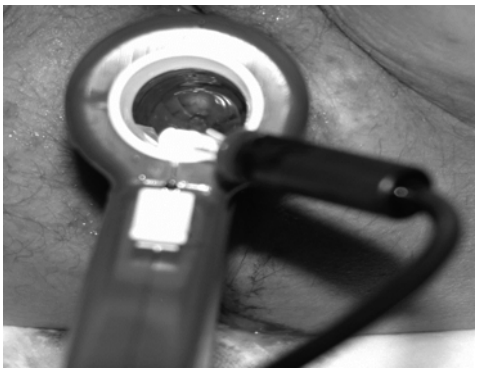
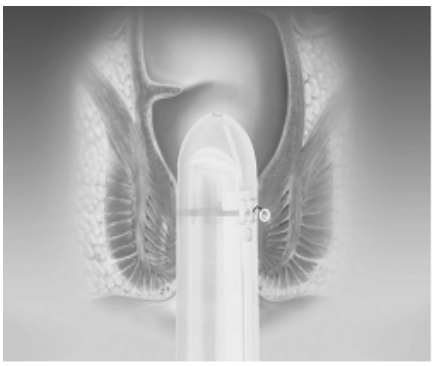


Figure 2. Introduction of probe with mucosa visible



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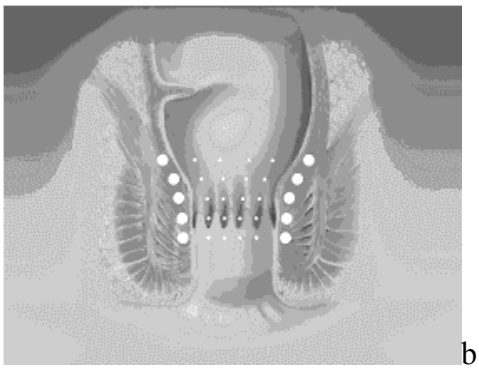

b

Figure 3. Schematic design of the probe in the anus (a) and after treatment (b)

Post-Treatment Care

Patients were recovered in a monitored unit for one hour or longer when necessary and were subsequently discharged. After the treatment and 8 hours later the antibiotic intake was repeated. Patients were refrained from NSAID use during two weeks, paracetamol was allowed when needed. Constipation was treated with a polyethylene glycol when necessary. Patient follow-up was scheduled at six weeks, 3 months, 6 months, 9 months and one year.

Statistical analysis

Results were be described and presented as mean, median and interquartile range when suitable. Differences were calculated with the paired T-test.

RESULTS

Clinical response

Eleven patients were included, all women, mean age 61 years (range 49-73). Their characteristics are shown in table 1. The mean time of complaints of faecal incontinence was 12 years (range 2-38). All but one had vaginal deliveries.

age	years with faecal incontinence	vaginal deliveries	anorectal trauma	anorectal surgery	wears pads	stool	stool frequency	urinary incontinence	other disease
Patients improved in continence									
55	30	0	-	-	yes	norm	1 day	no	Sjøgren
60	7	3	episiotomy	hysterectomy	yes	norm	1 day	no	cva
60	3	3	episiotomy	-	yes	soft	2 day	no	type 2 DM
58	3	2	-	-	yes	norm	2 day	yes	melanoma
49	5	2	episiotomy	-	yes	solid	1 per 3 day	no	no
67	2	6	-	-	yes	norm	1 day	no	hypertension
Patients not improved in continence									
64	38	2	-	hysterectomy	yes	soft	3-4 day	yes	rheumatic disease
73	4	2	straining	-	yes	soft/ norm	0-1 day	no	regulated thyroid dis
57	10	2	episiotomy	-	no	soft	2 day	no	no
60	2	2	3th degree sphincter rupture	bladder fixation	yes	hard	1 per 3 day	yes	haemo-chromatosis
60	10	2	-	-	yes	soft	2 day	no	hypertension

Table 1. Patient baseline characteristics.

Six of eleven (55%) patients stated that they had improved (one patient only slightly) (table 2). The Vaizey scores of all patients decreased from pre-treatment to 3 months from 18.8 to 15.0 (p=0.03, mean 3.7, SD 4.0) and of the improved from 18.3 to 11.5 (p=0.03, mean 6.8, SD 4.5), persisting after 6 and 12 months. There were no differences in biological characteristics between the responders and none responders.

Patient	Vaizey 0	Vaizey 3 months	Vaizey 6 months	Vaizey 12 months	
1	19	11	11	11	improved
2	19	12	12	12	improved
3	22	22	22	22	no
4	19	19	19	19	no
5	21	10	10	10	improved
6	17	14	14	14	improved
7	19	19	19	19	no
8	15	9	9	9	improved
9	19	13	13	13	slightly improved
10	18	18	18	18	no
11	19	19	19	19	no
mean	19	15	15	15	
SD	2	4	4	4	

Table 2. Vaizey incontinence score in time.

The remarks of the patients were extensively registered. Those who improved were very pleased with the treatment. The most striking remarks were that the four patients said that they felt urge and now had 5 minutes to reach the toilet instead of one. No predictive factors concerning the demography of the patients and their clinical result or Vaizey score was found.

Anal manometry, rectal compliance measurement and 3D anal ultrasound

Anal manometry and rectal compliance showed no significant changes after 3 months, neither in those who improved nor in those who did not. There was a tendency of decrease in urge and MTV after 3 months, but this was not significant in the whole group (both p=0.3) as well in the improved (p=0.8 and p=0.6) and those who did not (p=0.6 and p=0.8).

Anal ultrasound showed pre-treatment a small scar in the external anal sphincter in one patient. Slight atrophy was seen in all patients. Immediately after the procedure no changes were seen, except for some small fluid accumulations due to the local anaesthetic in some patients. After 3 months, no differences with pre-treatment anal ultrasound were seen (table 3).

anal manometry rectal compliance

MBP 0	MBP 3	MSP 0	MSP 3	SL 0	SL 3	DRvol 0	DRvol 3	FS 0	FS 3	URGE 0	URGE 3	MTV 0	MTV 3
Patients improved in continence													
45	55	75	60	3	4	20	10	15	40	210	130	240	200
20	10	30	30	3	x	10	20	145	100	270	190	320	240
70	40	30	30	4,5	4,5	20	50	55	40	80	150	125	200
20	20	10	10	3	3	40	20	20	45	100	80	165	100
40	40	20	40	4	4	20	20	75	15	250	180	315	210
20	20	25	30			10	20	70	180	90	200	145	240
Mean (SD)													
36 (20)	31 (17)	32 (23)	34 (16)	3,5 (0,7)	3,9 (0,6)	20 (11)	23 (14)	63 (47)	70 (61)	167 (86)^	155 (45)^	218 (86)'	198 (51)'
Patients not improved in continence													
30		20		3		20							
50	55	40	50	3,5		30	30	120	70	150	100	240	200
40	40	20	20	4	4	10	20	15	15	50	35	80	70
30	20	15	15	3	3,5	20	40	155	145	210	200	240	245
30	20	10	30	3,5		30	30	70	100	140	110	250	240
Mean (SD)													
36 (9)	34 (17)	21 (11)	29 (15)	3,4 (0,4)	3,8 (0,4)	22 (8)	30 (8)	90 (61)	83 (55)	138 (66)^^	111 (68)^^	203 (82)"	189 (82)"
All patients mean (SD)													
36 (15)	32 (16)	27 (18)	32 (15)	3 (0,5)	4 (0,5)	21 (9)	26 (12)	74 (52)	75 (56)	155 (76) #	138 (56) #	212 (80) *	195 (61) *

Table 3. Anorectal function tests (anal manometry and rectal compliance) at baseline and after 3 months.

MPB = maximum basal pressure (mmHg), MSP = maximum squeeze pressure (mmHg), SL = sphincter length (cm), DRvol = volume to evoke distension reflex, FS = first sensation (ml), URGE = urge to defecate (ml), MTV = maximum toleration (ml), 0 = before treatment, 3 = results after three months.

^p=0.8, 'p=0.6, ^^p=0.6, "p=0.8, #p=0.3 , *p=0.3

Side effects

The procedure was well tolerated and almost without discomfort. Two patients had slight and one moderate pain during the procedure.
There were no major side effects. No hospital admissions or outpatient clinic visits were needed. Eight patients (73%) had a slightly painful anus during the first 1-3 days, 2 patients moderate pain and one patient severe pain during one week. Five patients (45%) had haematoma and/or minor bleeding during 2-7 days. Three patients (27%) had antibiotic associated diarrhea and one had subsequently transient worsening of the faecal incontinence.

DISCUSSION

This prospective study has demonstrated that RF energy application has a significant therapeutic effect in some patients on the symptoms of faecal incontinence.
The results of our study are comparable with those described by Effron [10] in a multicentre study in 50 patients (43 women) after 6 months. We had a clinical response of 55% compared to 60% in the Effron study. The faecal incontinence scores were also quite similar. Although we used the Vaizey score and Effron the Cleveland Clinic Incontinence score, patients improved respectively in these scores 13% and 17% respectively.
The initial study of Takahashi [9] from 2002 in 10 women showed better results after 2 years [11] persisting after 5 years [12]. Here 80% of the patients improved and the Wexner score improved from 13,5 to 5 (43%).
In our patients the result was reached after 3 months and remained stable throughout the year. In the Effron study there was an additional improvement of 3 patients (6%) after 6 months.
Takahashi's patients remained stable, after 5 years their situation was comparable with 3 months [12]. No further improvement in the Takahashi study was seen between 6 and 12 months. So basically the improvement can be judged after 3 months.

We did not obtain a faecal incontinence quality of life (FIQL) score in our patients or social function questionnaire (SF-36). Since the exact mechanism of improvement is not known, we interviewed extensively our patients. A very interesting and striking remark was that four patients were very pleased that they were able to retain there faeces for a longer time. This earlier sensation of an impending bowel movement permits the patient to reach the toilet in time, thus making the difference between incontinence and continence. This improvement however did not translate into an improved Vaizey score, since an improvement up to 15 minutes is required for a change on this scale. This underlines the importance of not only questionnaires, but also the remarks of the patients. For future studies it seems wise to perform both questionnaires and remarks of the patients, since the latter are not always caught in a questionnaire.

We experienced no major side effects. Effron [10] had initially some serious side effects with two severe ulcerations in two patients, leading in one patient to worsening of the complaints. These adverse events were procedure related leading to a change in the protocol by increased mucosal cooling. The third patient had a bleeding 30 days after the procedure from a haemorrhoidal vein requiring suture ligation. Takahashi [9] also reported one serious bleeding requiring ligation.

All our patients had some local anal pain in the first days, 73% resolved within 1-3 days. Only one patient had severe pain during one week. Effron [10] reported severe pain in 10%. Self limiting bleeding was seen in 45%, Effron [10] reported 5 (10%) minor bleeding and Takahashi [9] 3 (30%). In 3 (27%) patients we observed diarrhea associated with antibiotics and Effron in 6 (12%). Effron [10] also encountered fever in two patients without signs of local infection.

Takahashi [9] reported a smaller first rectal sensation and rectal volume. Effron [10] could not confirm this in his patients, but in a subgroup analyses from his own clinic there was a decrease in first rectal sensation. We could not confirm this, there was a tendency towards a decreased urge and

maximum tolerated volume. Four patients clearly indicated that they felt urge earlier, e.g. before that it had passed the anus.
Considering the working mechanism, fibrosis and contraction in the sphincter it seems logic that if any changes are found, this has to be sensation because of a smaller distal rectal volume. In addition, our measurement tools are probably not very sophisticated to reveal small changes in anorectal function [15].
Changes in anal pressure were not found. Other treatments for faecal incontinence like sphincteroplasty [16,17] or sacral neuromodulation [18,19] have not always demonstrated increased anal pressures in those who improved. Anal ultrasound could not reveal any changes. In several patients temporary fluid collections were seen due to the local anaesthetic, but no structural changes were found after 3 months.
Although not all patients improve and some of those who improve are not totally symptom free, the treatment carries little side effects and is easy to perform on an out patient basis. Also it does not preclude patients from undergoing other procedures such as graciloplasty, sacral neuromodulation or artificial bowel sphincter. These surgical procedures however are not without complications and again success lies around 70%. Therefore, the SECCA® procedure merits more attention and warrants a randomized controlled trial, which is currently underway.

Conclusions

The SECCA® procedure seems a feasible, safe outpatient procedure with a moderate clinical effect in patients were diet regulation and physiotherapy have failed and sphincteroplasty is not indicated. The working mechanism is probably increase in local sensation thus permitting the patient more time to reach the toilet. A randomised controlled trial seems warranted.

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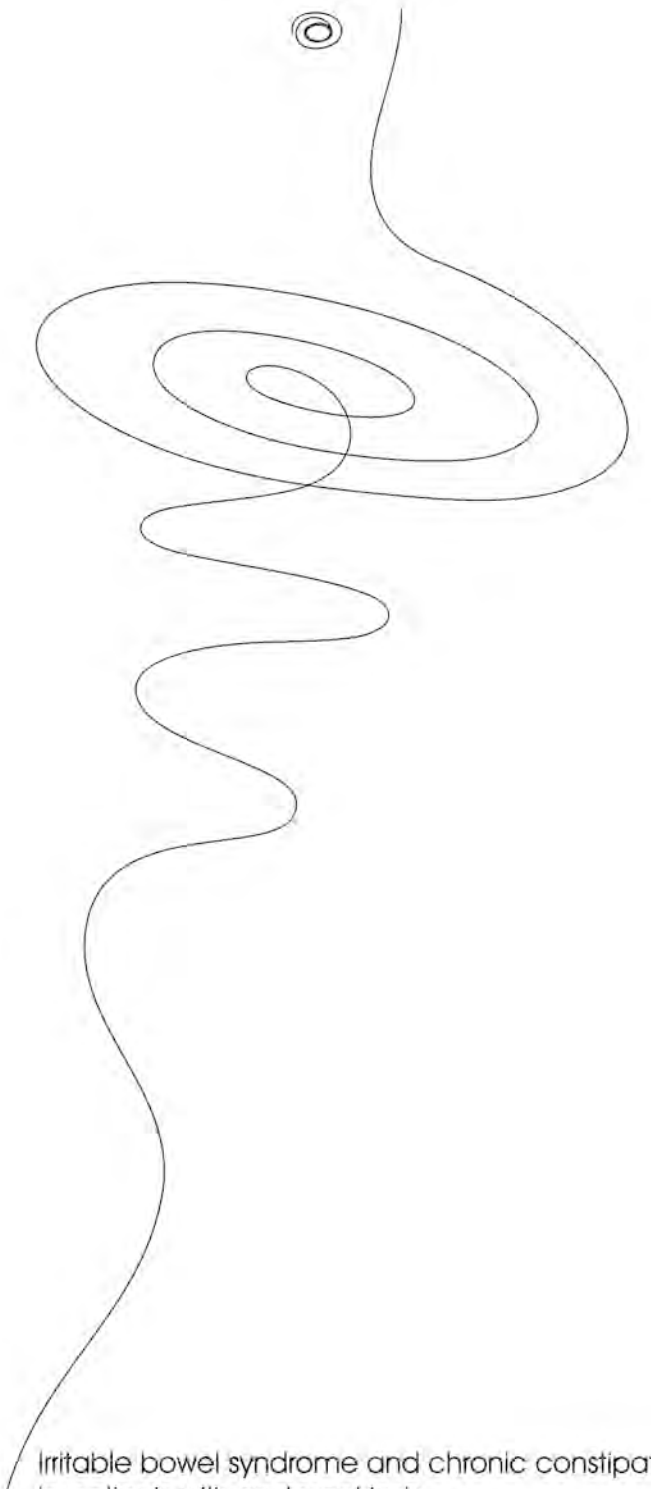

Irritable bowel syndrome and chronic constipation
in patients with endometriosis.
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Accepted for publication in Colorectal Dis.

Abstract

Aim

To evaluate how many patients with endometriosis had concomitant irritable bowel syndrome (IBS) and/or constipation according to Rome III criteria. Furthermore, the value of an additional gastroenterological consult with therapeutic advice was evaluated.

Patients and methods

Patients with proven endometriosis were included in prospective, monocentre study. A questionnaire was taken regarding IBS and chronic constipation. Patients who complied with Rome III criteria were referred to our gastroenterological outpatient clinic.

Results

In total 101 patients where included. Endometriosis was diagnosed surgically in 97%, and visually in the vagina in 3%. Fifteen percent of them had additional IBS and 14% had functional constipation without IBS. Of the 22 patients finally presented to the gastroenterologist 5 had a significant stenotic rectosigmoid and were treated surgically. The remaining 17 patients were treated conservatively. Defecation symptoms improved in 86% and pain was reduced in 64%.

Conclusion

In patients with endometriosis, 30% had also IBS or constipation. Referral to a gastorenterologist resulted in improvement of 86% of defecation and 64% of pain reduction.

Presented at the UEGW October 2009 (London, England)

INTRODUCTION

Endometriosis is a chronic debilitating gynaecological condition which often presents with symptoms that may be similar to those of gastrointestinal disorders. It is characterized by the presence and proliferation of endometrial tissue outside the uterine cavity, which occurs in approximately 10% of women of reproductive age. It causes pain and infertility affecting millions of women worldwide [1,2]. Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or change in bowel habit and with features of disordered defecation [3]. Throughout the world, about 10% of adults have symptoms consistent with IBS, and most studies find a female predominance [3,4]. IBS occurs usually in three subtypes; with diarrhea, constipation or mixed type. The worsening of IBS symptoms during menstruation in women with endometriosis may obscure the diagnosis of IBS [5].

The aim of the study was to evaluate how many patients with proven endometriosis had also IBS and/or constipation according to the Rome III criteria. Furthermore, we investigated the value of an additional consult by the gastroenterologist and the results of therapeutic advice.

PATIENTS AND METHODS

Patients

From October 2006 to October 2007, 101 patients with established endometriosis were enrolled in this prospective study. All patients were referred to the Endometriosis Centre VUmc for second opinion from affiliated hospitals or directly from General Practitioners. All patients gave informed consent for participation in this study. The study was approved by the VU University Medical Centre Ethic Commission.

Methods

Initially all patients were evaluated by one of four gynaecologists of the endometriosis team. During the first visit detailed questionnaires were completed for each patient. They included questions on endometriosis

related complains (dysmenorrhoea, deep dyspareunia, dyschezia, cyclic rectal bleeding, dysuria, hematuria), previous operations and hormonal treatments, as wel as questions regarding IBS (table 1) and chronic constipation (table 2). Endometriosis was diagnosed during laparoscopy/ laparotomy as well as by visual inspection of vagina. The follow-up of the patients was 12 months. The medical history and results of all examinations performed in our hospital were registered.

The average time between first complains of the patients and diagnosis of endometriosis was also established.

All patients, which met the diagnostic criteria of IBS and/or chronic constipation (table 1, 2) were offered referral to our gastroenterological outpatient clinic for further diagnostics and advice. Improvement was defined as a decrease of symptoms by 50%.

Diagnostic criteria for Irritable Bowel Syndrome
Recurrent abdominal pain or discomfort* at least 3 days per month in the last 3 months associated with 2 or more of the following: 1. Improvement with defecation 2. Onset associated with a change in frequency of stool 3. Onset associated with a change in form (appearance) of stool *Discomfort means an uncomfortable sensation not described as pain.
Subtyping IBS
1. IBS with constipation (IBS-C) – hard or lumpy stools ≥25% and loose (mushy) or watery stools < 25% of bowel movements 2. IBS with diarrhea (IBD-D) – loose (mushy) or watery stools ≥25% and hard or lumpy stool <25% of bowel movements 3. Mixed IBS (IBS-M) – hard or lumpy stools ≥25% and loose (mushy) or watery stools ≥25% of bowel movements 4. Unsubtyped IBS – insufficient abnormality of stool consistency to meet criteria for IBS-C, D or M

Table 1. Diagnostic criteria and subtyping IBS [3]

Diagnostic criteria for Functional Constipation

1. Must include 2 or more of the following:
    a. Straining during at least 25% of defecations
    b. Lumpy or hard stools in at least 25% of defecations
    c. Sensation of incomplete evacuation for at least 25% of defecations
    d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
    e. Manual manoeuvres to facilitate at least 25% of defecations
    f. Fewer than 3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. There are insufficient criteria for IBS

Table 2. Diagnostic criteria for Functional Constipation [3]

Statistical analysis

Results are presented as mean and percentages. Data were analyzed with SPSS 15.0.

RESULTS

Gynaecological findings

A total of 101 fertile women were enrolled in this study, mean age 34 years (range 22-51 years). Eighteen patients (18%) were referred by their General Practitioner, and 83 (82%) were referred for second opinion by gynaecologists. Patients presented a wide range of gynaecological complains: dysmenorrhoea 87 (86%), deep dyspareunia 42 (42%), dyschezia 30 (30%), cyclic rectal bleeding 9(9%), dysuria 14 (14%) and hematuria 3 (3%). Subfertility was found in 48 (47.8%) women. Twelve (11.9%) patients were known to have first-degree relatives with endometriosis.
Endometriosis was diagnosed in 98 (97%) patients by laparoscopy or laparotomy in 77 (76%) and 21 (21%), respectively. In 3 (3%) patients endometriosis was detected visually in the vaginal wall. Endometriosis of the

ovaries was most frequently diagnosed (68%), followed by endometriosis in the pouch of Douglas (13%).
Rectosigmoidal localization was diagnosed in 9% of the women. Vaginal endometriosis lesions were found in 3% of the patients. Urological and multiorgan disease were encountered in 2% and in 11% of the patients, respectively.
The median time elapsed from onset of the symptoms until diagnosis of endometriosis was 2.8 years (range 0.5-11years) (figure 1).

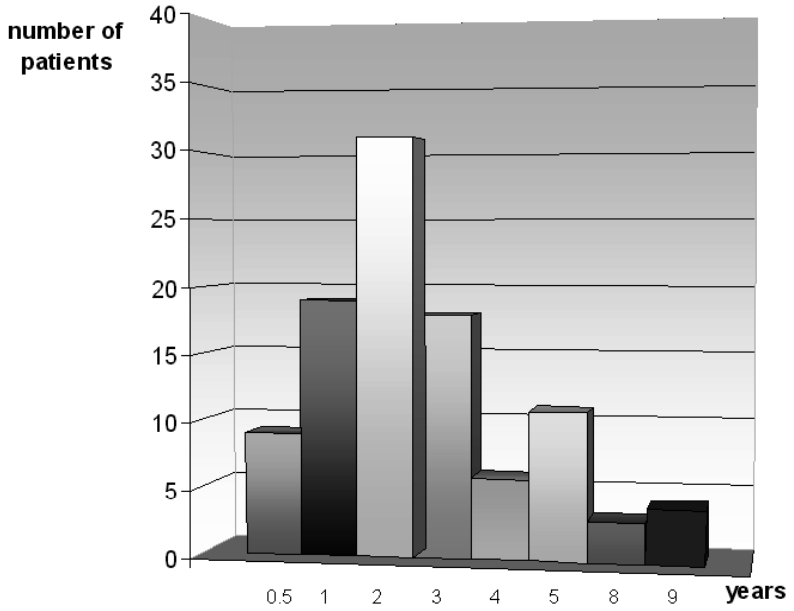

Figure 1. Time to diagnosis of endometriosis.

Gynaecological treatment

During initial evaluation the following hormonal treatments for endometriosis were used: oral contraceptive pills (OCs) in 37 patients (37%), progestins in 8 patients (8%), levonogestrel-releasing intrauterine device (IUD) in 6 patients (6%), luteinizing hormone-releasing hormone (LHRH) - analogues in 28 (28%), respectively. Twenty-two (22%) patients were without hormonal treatment at the time of inclusion.

Gastroenterological findings

Fifteen (15%) women had additional IBS symptoms: 9 (9%) with constipation, 2 (2%) with diarrhea, 2 (2%) mixed type or unsubtyped. Furthermore, 14 (14%) women had functional constipation without IBS. Both patients with IBS and with constipation reported in 80% exacerbation of their symptoms during menses.

Gastroenterological treatment

Of the 29 patients with IBS or constipation 22 (76%) agreed to a gastroenterological referral (figure 2). In five patients bowel stenosis due to endometriosis was found. Subsequently they underwent surgical resection of the involved bowel segment with primary anastomosis.
Postoperatively, four out of five patients improved clinically and had no residual symptoms. One patient was readmitted 6 weeks after the surgery with an ileus due to stenosis of the anastomosis which was successfully endoscopically dilated.

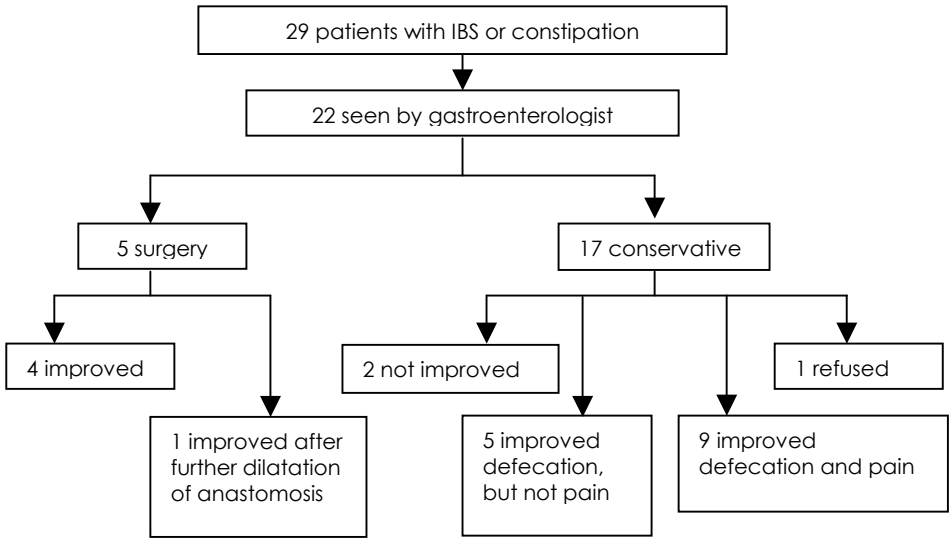

Figure 2. Patients referred to the gastroenterologist.

Seventeen of the referred patients were treated conservatively with laxatives and fibre (table 3). In 14 patients (64%) defecation improved after treatment through the time of follow-up, 2 women in spite of treatment had no improvement of the complains, 1 of them refused further any other treatment. In 9 patients there was additional relief of pain. Thus of all referred patients, in 19 out of 22 (86%) defecation improved and pain in 14 out of 22 (64%).

	initial complaints	improved	unaltered
Straining during at least 25% of defecations	7	6	1
Lumpy or hard stools in at least 25% of defecations	13	10	3
Sensation of incomplete evacuation for at least 25% of defecations	4	3	1
Manual manoeuvres to facilitate at least 25% of defecations	2	1	1
Fewer than 3 defecations per week	14	10	4
Pain	14	9	5

Table 3. Improvement of symptoms in 17 patients after treatment with fibre supplementation.

DISCUSSION

The etiology of endometriosis is not yet fully understood, but it is generally accepted that retrograde menstruation is the key component in development of endometriosis. Numerous epidemiological studies have shown that women with early menarche, short and heavy menstrual cycles are at increased risk of developing endometriosis. These epidemiological findings strongly support the menstrual reflux hypothesis [2,6].

The etiology of endometriosis is multifactorial and polygenic which explains the 5-8% risk for first-degree relatives to be affected [6-8]. In our study however, endometriosis in first-degree relatives was found in 12%. Although this is an

higher prevalence with respect to earlier reports [6-8], it is uncertain whether it reflects a stronger genetic expression for this disease in our population as no genetic data were collected.

Although the ectopic endometriotic implants are usually found on the internal genital organs, the gastrointestinal tract, in particular the rectosigmoid colon, is the most common site of extragenital endometriosis. The estimated incidence of intestinal endometriosis is between 5.3% and 12% among women with endometriosis [9,10]. In expert centers, its incidence may reach up to 35% among patients with deep pelvic endometriosis [11]. The most frequent location of bowel endometrosis is the rectosigmoid (93%), followed by appendix, ileum and caecum [10,12]. The prevalence of bowel endometriosis in our study was 9%, which is in line with previous reports [9,10]. In five patients endometriosis caused a largely restricted bowel lumen in which bowel function was greatly impaired. Resection of the obstructed bowel to achieve bowel continuity was performed with good result. Our results are consistent with several other studies demonstrating significant postoperative improvement of digestive symptoms as well as quality of live in this subset of patients [12].

Up-to-now a considerable delay between symptoms onset and a definitive diagnosis of endometriosis is reported. Women are often treated for other assumed disorders before endometriosis is established [1,6].

Some studies show a delay of up to 12 years [13-15]. In our study the average time between first symptoms and a correct diagnosis was 2.8 years (figure 1). This may be related to the fact that the majority of included patients in this prospective study had a severe form of endometriosis with distinct symptoms. In addition, an increasing awareness of endometriosis in the general population as a result of extensive information available on internet and through patients' associations may contribute in this finding. Moreover, general practitioners in the Netherlands may have undergone an increased awareness on endometriosis which may result in an accelerated referral to specialists.

Pharmacological management of endometriosis depends on the extension and severity of disease, the age of the patient and whether there is desire for pregnancy. Our patients had a very extended, severe form of endometriosis, where treatment with GnRH-agonists often is needed [12].
There are still new approaches to pharmacological therapy of endometriosis, including the levonorgestrel-releasing intrauterine device (LNG-IUD), aromatase inhibitors, immunomodulatory drugs and angiogenesis inhibitors [6].
In our study, most women were treated with OCs (36.6%) and LHRH analogues (27.7%). Only 8% were treated with progestins and 6% with a LNG-IUD.
IBS and chronic pelvic pain affect a large population of women [16] and are associated with increased health care use [17] and decreased quality of life [17].
Most patients with endometriosis will experience the classic pelvic endometriosis triad of dysmenorrhoea, deep dyspareunia and dyschezia. Digestive complains such as diarrhea and/or constipation, cramping and rectal bleeding are reported in respectively 15%, 26% and 33% of the patients [18]. The cyclic exacerbation of those symptoms associated with menstruation is often found. These complaints largely overlap with those found in patients with IBS (table 1) and visa versa. In our study this phenomena was found in 80% of the patients with IBS. This may be explained by earlier observations suggesting that increased levels of prostaglandins during menstrual phase may exurb IBS symptoms [19,20].
The prevalence of IBS is approximately 32% in women with endometriosis without bowel lesions [21].
The prevalence of chronic constipation is estimated at 12-19% [22].
In our study similar results were obtained; 15% of the patients had also IBS symptoms, and in 14% functional constipation.
For patients with IBS and constipation, fibre supplementation may improve symptoms of constipation, although abdominal pain is unlikely to

change [23,24]. Our results show that in 14 (64%) of the 22 patients presented to the gastroenterologist symptoms improved after treatment with bulk-formers and/or laxatives. The 5 patients with a significant stenosis were treated with a local resection of the involved rectosigmoid which induced improvement. Of the 17 patients without stenosis, 14 (82%) had improvement of defecation complains. Pain also improved in 64%. However, improvement did not mean pain free, but a decrease of pain more than 50%. This limited response is a well-recognized problem and might be due to involvement of the nervous system, immune cells and inflammatory response to pain caused by endometriosis. For many women with endometriosis management of pain is still insufficient [25]. This observation is consistent with our results, where five of the twelve patients after treatment with fibres and laxatives still had abdominal pain after adequate regulation of defecation. It is obvious that treatment of endometriosis and IBS should be individualized according to the therapeutic goals, the extension of disease, symptoms and age of the patient.

In conclusion, gastroenterological and gynecological symptoms of endometriosis often coexist. In patients with a stenosis of rectosigmoid, local resection leads to improvement of defecation and pain. In patients without bowel stenosis, conservative treatment improved defecation in 86% and pain is decreased in 64% of the patients. Therefore, gastroenterologists and gynaecologists should collaborate in the treatment of endometriosis to evaluate overlapping symptoms so that neither accurate diagnosis is missed nor right treatment is delayed.

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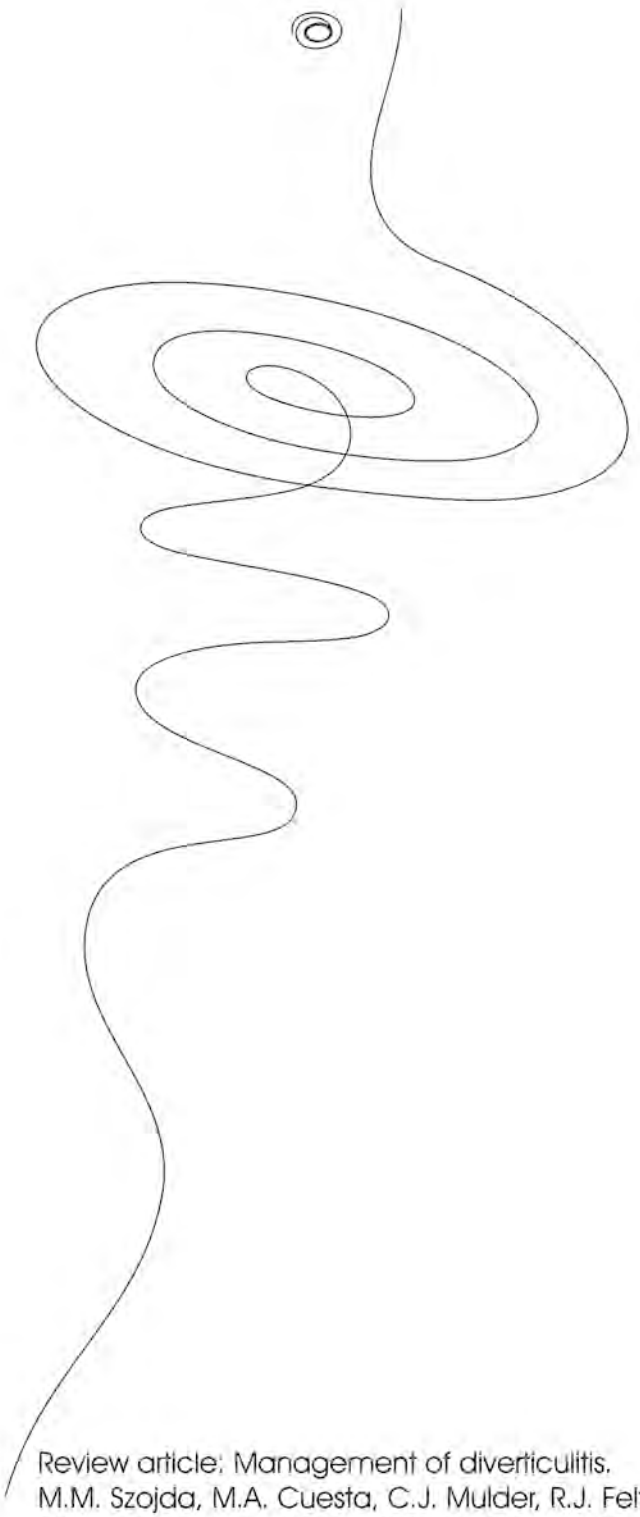

Review article: Management of diverticulitis.
M.M. Szojda, M.A. Cuesta, C.J. Mulder, R.J. Felt-Bersma
Aliment Pharmacol Ther. 2007;26 Suppl 2:67-76. Review.

Abstract

The incidence and therefore complications of (sigmoid) diverticular disease are increasing. Of all patients, 15% will develop diverticulitis, 5% complications and 5% diverticular bleeding.

Diagnosis is established with CT. Colonoscopy needs to rule out malignancy. NSAID's increase the risk of perforation; steroids, diabetes, collagen vascular disease and immune compromized are associated with complicated disease and death.

In mild diverticulitis antibiotics are recommended. In complicated disease with abscesses < 5 cm antibiotics are sufficient. Larger abscesses are drained under CT-guidance. Peritonitis forms an indication for surgery.

Diverticulitis recurrence rate is around 30%, most are uncomplicated. Recurrence after surgery is around 10%.

Elective surgery is reserved for fistula closure and obstruction. The need for elective surgery to prevent recurrence has diminished due to new insights. Important is to identify risk groups. New issues are the possible relationship between diverticulitis and cancer, segmental colitis associated with diverticulitis (SCAD), and treatment of diverticulitis with mesazaline and probiotics.

In summary, uncomplicated diverticulitis is treated medically. Complicated diverticulitis with small abscesses is treated with antibiotics while larger abscesses are drained with CT-guided puncture. Emergency surgery is reserved for peritonitis, elective surgery for fistula/stenosis. Surgery to prevent recurrence is only indicated in selected cases (immune compromised e.g.)

INTRODUCTION

Diverticulosis and therefore diverticulitis are increasing, what consequently increases complication rate. The prevalence of perforated sigmoid in diverticular disease in the western countries has increased from 2.4/100.000 in 1986 to 3.8/100.000 in 2000 [1]. Another distressing factor is that during the last 20 years, standardized annual age rates of admission and surgical intervention have increased by 16% from 20.1/100.00 to 23.2/100.000, whereas inpatient and population mortality remained unchanged [2].
The terminology of diverticular associated disease needs to be used adequately in order to avoid confusion3 (table 1).

Diverticulosis:	presence of diverticula that are asymptomatic
Diverticular disease:	diverticula associated with symptoms
Diverticulitis:	evidence of diverticular inflammation (fever, tachycardia) with or without localised symptoms or signs
Complicated diverticulitis:	perforation (into peritoneal cavity), abscess, fistula, stricture/obstruction

Table 1. Terminology of diverticulosis

Diverticulosis

Anatomy

The diverticula of diverticulosis are false diverticula, due to pulsion of herniating mucosa and submucosa through the muscle layer. This is contrast to the congenital diverticula, which contain all bowel layers. Diverticula tend to occur at 4 points around the circumference of the colon where the vasa rectae penetrate the circular muscle: each side of the mesenteric taenia, and on the mesenteric border of the 2 antimesenteric taenia [4].

Epidemiology

Although diverticulosis was noticed in the 19th century, the Mayo brothers reported the first operation for diverticular disease in the United States in 1907 [5]. The prevalence of diverticulosis in the US in the early 20th century was reported as 5% to 10% [6]. In 1969 autopsy series reported 10% to 66% presence, depending on age [7]. There is an increase in the prevalence of diverticulosis with age, from less than 10% in those under the age of 40 to 50%-70% among those over the age of 70 [8-10]. There is no clear overall difference in prevalence between women and men. Diverticula are located in 95% in the sigmoid, in 35% additionally also proximal, 7% are pancolonic [11]. There seems also to be a striking geographical variation in the prevalence of diverticulosis, since Asian nations report much lower prevalences [6,12]. One differential aspect between diverticular disease in the West and Asia is the predominant right location in the latter. A right colon location was observed in 83% of patients, whereas only 17% had lesions located exclusively in the left colon [13]. However recently, due to decreased fiber intake, both an increase in right-sided diverticulosis as well as an increase in left-sided diverticulosis has been observed in developing Asian countries [14].

Pathophysiology

The pathophysiology is related to a low fiber diet, altered motility and colonic wall resistance.

The major hypothesis concerning the propensity to form diverticula focuses on dietary fiber [9,13,15]. Most studies support a strong inverse relationship between population fiber intake and the prevalence of diverticulosis. One study of approximately 47,000 men found a relative risk of 0.58 for the presence of diverticulosis comparing the quintile with the highest average fiber intake with the quintile with the lowest intake [15]. Diverticulosis seems to become more common among groups that move to western countries or that adopt a western-style diet [16]. Moreover, other studies have also pointed to the fact that diverticulosis seems to be less common among

vegetarians [17]. The role of fiber in the pathogenesis of diverticulosis likely rests on its influence on colonic pressures. The inverse relationship between colonic diameter and pressure is explained by the Law of Laplace, in which P=kT/R (where P is the pressure, k is a constant, T is the wall tension, and R is the bowel radius). Fiber may mediate the generation of lower pressures in the sigmoid colon by increasing the bulk of stool; bulkier stools may discourage segmentation and increase the diameter of the sigmoid colon, resulting in lower pressures. Furthermore, the decrease in soluble fiber may also have important physiologic effects, altering gut flora in particular, which may have significant immune consequences central to the pathophysiology of diverticulitis [18].

Motility seems to play an important role. Most manometric studies indicate that patients with diverticula have higher resting pressures and postprandial colonic pressures than controls [10,19]. However, normal pressures have been found in another study [20]. More recent study showed that in early disease high pressures and irregular slow waves can be found, but that in late disease these features have normalized [21]. In addition, diverticular colon has exaggerated segmentation [22]. Segmentation leads to high pressure, which is the highest in the part of the colon with the smallest diameter, the sigmoid colon, which is the part most often involved by diverticulosis. Furthermore, interstitial cells of Cajal and glial cells are decreased in colonic diverticular disease, whereas enteric neurons appear to be normally represented. This finding might explain some of the large bowel motor abnormalities reported to occur in this condition [23].

Another aspect is the colonic wall resistance. The structure of colons with diverticula is often marked by myochosis, with thickened circular muscle, shortened taenia, and narrow lumens. On a microscopic level, colons with diverticulosis may have increased elastin in the taenia [24] and structural changes in collagen that mimic those seen with aging [25]. This concerns not so much the total amount of collagen, but the cross linking and an increase in type 3 fibers [19,26]. The involvement of these changes in the development

of diverticulosis is supported by the observation that diverticulosis tends to occur at younger age in patients with connective tissue diseases such as Ehlers-Danlos or Marfans syndromes [26].

Relationship with diverticulitis

Among patients with diverticulosis, approximately 70% will remain free of major diverticular complaints. Some patients with diverticulosis will complain of a variety of vague symptoms, including cramping, bloating, flatulence, or irregular defecation (diverticular disease); of these, many likely have irritable bowel syndrome. Approximately 15% to 25% of patients with diverticulosis will develop diverticulitis, and 5% to 15% will develop diverticular bleeding. Among patients with diverticulitis, approximately 75% will have simple diverticulitis and 25% will have diverticulitis complicated by abscess, obstruction, perforation, or fistula formation.

The only intervention with evidence to suggest that it reduces risk of diverticular disease and its complications is a high fiber diet, which may reduce the risk of developing diverticular disease [15,27] and may also reduce the risk of later complications among patients with diverticulosis [9].

Diverticular disease

Some patients with diverticulosis reports recurrent colicky abdominal pain, and/or changed bowel habits without any findings consistent with diverticulitis, which has been called uncomplicated symptomatic diverticulosis. Occurances of abdominal pain in these patients may be related to abnormal colon motility. In a controlled study, episodes of cramping abdominal pain were coincident with a regular colonic contractile pattern, as assessed by 24-hour colonic manometry [23].

Considering the high prevalence of irritable bowel syndrome (IBS) (5-25%) and diverticulosis (10-66%), both conditions may coexist frequently [10,28].

One study showed heightened visceral perception of the rectosigmoid (not only in the area with diverticula), not due to altered compliance of the

bowel wall [29]. This situation of hyperperception resembles IBS. In a community-based survey, a study of 261 patients with diverticulosis diagnosed by barium enema, observed that 14% met the Rome I criteria for IBS, 36% had recurrent short-lived pain, and 19% had episodes of prolonged pain lasting for 1 day or longer, which in more than 60% required emergency medical attention [30]. In more than half of the patients with prolonged pain, there was also short-lived pain as part of their usual bowel habit. The authors concluded that recurrent short-lived pain (similar to that seen in IBS) often occurs in patients who have experienced prolonged pain attributable to diverticulitis. However, the presence of colonic diverticula does not seem to change the natural history of IBS [28]. The connection and/or differences between uncomplicated symptomatic diverticulosis and IBS should be further clarified in future studies. Treatment with a high-fiber diet is recommended for patients with symptomatic uncomplicated diverticulosis [10].

Although there is theoretically no rationale for the use of antibiotics in this group of patients, this has been performed. Three Italian randomized trials comparing daily fiber supplementation alone or with cyclic administration of oral rifaximin for 12 months in 168 and 968 patients [31,32] or 24 months in 307 patients [33] showed that significantly more patients in the rifaximin group were free of symptoms, and in one of the studies the incidence of complications (mainly diverticulitis) was also reduced. Although the mechanism for such improvement is unknown, the authors postulate that it could be related to a reduction in gas production and bacterial overgrowth.

The same applies for the use of mesalazine in several Italian studies. In recent large study of 286 patients, who were randomized treated ten days a month with either rifaximine (200 or 400 mg twice a day) or Mesazaline (400 or 800 mg twice a day), the patients treated with mesazaline improved more on a global symptom score [34]. Daily prescription may even be more

effective [35]. Reduction of inflammation due to altered bacterial flora is thought to play a role.

In an attempt to alter the bacterial microflora two open label prospective studies have been conducted with probiotics. One study contained 90 patients where Lactobacillus casei, mesazaline or both were given for 15 days a month. Given separately, 76% was symptom free and the patients who received the combination became in 95% symptom free after one year [36]. Another study compared an intestinal antimicrobial (dichlorchinolinol) and absorbent (active coal tablets) with the same set-up supplemented with non-pathogenic *Escherichia coli* in a prospective open trial in 15 patients administered for 1 and 5 weeks. The non-pathogenic *Escherichia coli* significantly prolonged the symptomatic remission period (14 and 2,4 months) [37].

Diverticulitis

Pathogenesis

Diverticulitis refers to a spectrum of diverticular disease ranging from subclinical inflammation to generalized peritonitis. The pathology of diverticulitis is characterized by inflammation and focal necrosis of diverticula leading to micro- or macroscopic perforation of a diverticulum. Most small perforations are walled off, although some will lead to abscess or fistula formation. The inciting agent of the inflammation was earlier thought to be fecoliths that obstructed diverticular lumens; this, however, turns out to be rare. The main culprit seems to be inspissated food that leads to mucus secretion and eventual bacterial overgrowth within the diverticulum.

Symptoms

The classic presentation of diverticulitis in the western world includes left lower quadrant abdominal pain and tenderness, constipation, fever and leukocytosis. However, the clinical features can be quite variable. Approximately 85% of diverticulitis involves the sigmoid/descending colon.

Seventy percent of patients present with left lower quadrant pain and 25-50% of patients will report having had previous episodes of diverticulitis. Although constipation is present in 50% of patients, 25% to 35% of patients may present with diarrhea, 20% to 62% may have nausea and vomiting and 10% to 15% may describe urinary symptoms [38]. Abdominal tenderness is present in most patients, and approximately 20% will have a tender mass palpable on exam [8]. Low-grade fever and leukocytosis are also characteristic, but 45% of patients will have a normal white blood cell count [39]. The presention is particularly apt to be atypical among patients with conditions such as HIV infection, organ transplantation or cancer, in which immunosuppression is common [40,41].

Not surprisingly, given the variable presentation of diverticulitis and the spatial relationship of the colon to other intraabdominal organs, the differential diagnosis for diverticulitis is broad. Potential diagnostic considerations might include appendicitis, Crohn's disease, colon cancer, ischaemic colitis, pseudomembranous colitis, complicated ulcer disease, ovarian cyst or torsion, or ectopic pregnancy. Nonetheless, the diagnosis is often relatively clear among those patients presenting with typical features.

Diagnosis

The diagnosis of diverticulitis is usually suggested by history and clinical exam. Various adjunctive tests, such as abdominal and chest x-ray, compression ultrasonography and single contrast barium enema have been and are used, although enema examinations are not much used anymore. Increasingly, computed tomography (CT) scans are the test of choice to confirm a clinical suspicion of diverticulitis. The literature has reported excellent test performance characteristics for CT scans, with sensitivity as high as 97% and specificity of up to 100% [42]. Findings on CT scans include soft tissue density in pericolic fat (present in 98%), the presence of colonic diverticula (present in 84%), bowel wall thickening greater than 4 mm (present in 70%), phlegmon and pericolic fluid (present in 35%) [43,44]. However, CT findings alone are insufficient to exclude cancer in

approximately 10% of cases [45]. Therefore, patients who have not had a colonoscopy yet should have one after resolution of the disease. CT has additional advantages of permitting classification into mild and severe categories, which may aid in predicting success of conservative therapy [46] and in selecting patients for surgery [47,48]. Diverticulitis may be complicated by abscess and fistula formation, peritonitis, or obstruction. CT may help differentiate abscesses that require drainage versus those that can be managed conservative and that behave like uncomplicated diverticulitis; the suggested size cut-off for such a distinction is 5 cm, with smaller abscess generally responding to medical treatment without drainage.

Treatment

The treatment of diverticulitis depends on the severity and extent of disease. Recommendations are available from some of the professional societies, such as the American College of Gastroenterology and the American Society of Colon and Rectal Surgeons. Many other countries conform themselves to these general guidelines with certain exceptions.

Patients (70% to 100%) with simple, uncomplicated diverticulitis will improve with conservative measures. Bed rest, only clear liquids or total dietary restriction are the first step. Antibiotics are usually, but not always given. A recent study questions the routine use of antibiotics [49]. Antibiotics are generally chosen to cover Gram negative rods and anaerobes; for example a combination of ciprofloxacin and metronidazole [50-52]. CT scans may be useful for predicting success of conservative therapy [48,53]. A critical decision is whether to hospitalise a patient; this decision may rest on such features as disease severity, ability to tolerate oral intake, age, comorbidity and availability of adequate support systems at home.

Complicated disease demands a more intense approach. One commonly used system to group patients according to severity of disease is the Hinchy classification [54] (table 2). Patients with abscesses larger than 5 cm usually require CT-guided abscess drainage. In cases of peritonitis (Hinchy 3 and 4) emergency surgery is required, where cleansing of the peritoneal cavity

and a sigmoid resection with an end-to-end procedure is preferable. Peritonitis carries a high mortality rate of approximately 6% if purulent and 35% if faecal. Fistula will be electively operated, as will patients with obstruction where malignancy cannot be excluded with colonoscopy.

Stage 1	Pericolic or mesenteric abscess
Stage 2	Walled –off or pelvic abscess
Stage 3	Generalized purulent peritonitis
Stage 4	Generalized faecal peritonitis

Table 2. Hinchy classification of peritoneal contamination of diverticulitis

Prognosis

The prognosis of diverticulitis after resolution of the acute symptoms is generally good. Approximately 30% to 40% of patients will remain asymptomatic, 30% to 40% will have episodic cramps without clinical evidence of recurrent diverticulitis and 30% will have recurrent diverticulitis [8,10,12,51]. In the past, Parks stated that recurrent attacks of diverticulitis had a high likelihood of being complicated and to be associated with higher mortality than initial attacks [8]. Furthermore, guidelines for elective surgery to prevent recurrent attacks were derived from the Parks study and newer studies were not included in these guidelines yet [55]. The older studies did not account for better medical care and new therapeutic options like CT- drainage. However, more recently it appears that recurrent attacks occur less frequently and with similar likelihood of complications as initial attacks [10,55,56]. Moreover, only about 25% of people with complicated diverticulitis have a previous attack, thus making prevention even more difficult [57-59]. Among patients who undergo surgery for diverticulitis, 15% will develop diverticula in the remaining colon [60], approximately 2% to 11% will need further surgery [60,61], and up to 27% will have postoperative pain in the same location.

Elective surgery for whom?

Indications for elective surgery remain controversial, particularly for uncomplicated diverticulitis. In view of the recent literature, a more nuancated approach may be appropriate. It seems that some subgroups are at risk for complicated disease. These are the patients with co-morbidity, like diabetes mellitus, collagenous disease and the immune compromised [55,60,61]. Also the concept that younger (male) patients are at high risk for complicated (recurrent) diverticular disease merits more critical re-appraisal. Older studies suggested indeed a higher risk in these patients [27,51,62-65], but newer studies have shown that establishing the correct diagnosis was delayed because it was not suspected. Moreover, there was a striking percentage of obesitas masking the symptoms in these patients [66]. The recurrence and complication rate were not higher then in elderly patients [67-74]. Adipositas itself forms a risk factor for diverticulitis. They have not only an increased risk to develop diverticulitis [66], but also experience more complications [75]. Obese patients have an increased mortality rate of 5.2 [76] and require a longer operation time and more post operative analgesics [77]. Thus suggested by some authors resection after 2 or after 3 episodes of uncomplicated diverticulitis therefore needs to be re-considered and should be limited to patients at risk with co-morbity like diabetes, collagenous disease and the immune compromised patient.

New Issues

Segmental colitis associated diverticulitis (SCAD)

This is defined as chronic mucosal inflammation of the sigmoid colon bearing diverticula with rectal spearing. The clinical presentation consists of rectal bleeding, occasionally left-sided abdominal pain and less frequently, bowel alterations. The endoscopic features are those of sigmoiditis (erythema, congestion and contact bleeding) with rectal sparing. The orifices of diverticula may or may not be involved. The histological

changes [78] are mostly similar to those detectable in inflammatory bowel disease (IBD): cryptic abscesses with crypt distortion, mononuclear cell infiltrate, lymphoid aggregation, epithelial cell sloughing [79] and sometimes granulomata [80,81]. On the whole, the histopathological features and rectal sparing mimic the picture of Crohn's disease rather than that of ulcerative colitis. In fact, in ulcerative colitis even when the rectum is endoscopically spared, histological involvement is always present [82].

Is segmental colitis a distinct clinical entity or coexistence of sigmoid diverticulosis and IBD? Both diverticulosis and segmental colitis usually affect elderly patients, especially men. It is also known that IBD presents a second peak of incidence in the population over the age of 60 [83]. The incidence of segmental colitis is estimated to be 0.3–3.8% [80,84-86]. The results above are too small to allow definitive conclusions to be made in terms of epidemiology. To add to the confusion, in about 10% of cases of segmental colitis, inflammation subsequently spreads to the rectum, even when this was initially histological normal, making it impossible to distinguish this condition from ulcerative colitis [80,84]. On the other hand, even when the rectum remains uninvolved and concomitant Crohn's colitis can be suspected, perianal disease is always absent [80,87]. In segmental colitis, unlike in Crohn's colitis, symptoms such as nausea, vomiting, weight loss and fever are never present and laboratory findings are usually normal, the acute-phase reactants and/or white cell count are rarely increased [85,87]. When segmental colitis is considered a distinct disorder, what are the possible causes of local inflammation? A role for bacterial flora promoted by faecal stasis has been postulated [87,88]. Other postulated factors are increased permeability to intraluminal antigens [87], focal ischaemia due to impairment of local microcirculation [89] and enhanced local production of nitric oxide and oxygen-reactive radicals [87].

Medical treatment of segmental colitis is empirical and usually carried out, in addition to a high-fibre diet, by the same pharmacological agents employed in the treatment of IBD, i.e. sulfasalazine, Mesazaline and

occasionally antibiotics [84,79]. The majority of cases are responsive to such medications [79,84,90], immunosuppressive medication is rarely required. Again, this differs from IBD in which steroids and immunosuppressants are often necessary. Patients with segmental colitis rarely require surgery [79,89] and in contrary to patients with Crohn's colitis, they seldom experience post-operative recurrences [81,91].

A differential diagnosis with IBD is important in order to optimise the treatment and long-term management of the disease. To that purpose the diagnostic workout should include accurate evaluation of the small bowel by means of ileocolonoscopy with mucosal biopsies, and or other imaging techniques.

Diverticular disease and cancer

Some studies have suggested the relationship between diverticulitis and colon cancer. In 1979 an association in 42 patients with diverticulitis in a group of 385 cases of colonic cancer was found [92]. In a retrospective study of a group of 150 patients in 1988 and 630 patients in 2002, there was a higher incidence of advanced adenomas in the sigmoid colon in patients with diverticular disease. Nevertheless, there was no higher prevalence of colorectal cancer in patients with diverticula in comparison to those without [93,94].

In a study with 7159 patients, a significantly long-term increased risk of left-sided colon cancer in patients with diverticulitis compared to those with only diverticulosis was found [95]. In contrast, a study with 512 patients with colonic resection due to diverticulitis showed a statistically significant decreased rate of advanced colonic neoplastic lesion in all age groups, but no relation with adenocarcinoma [96].

Laboratory tests are contradictory. A study in patients with diverticular disease demonstrated that hyperproliferation of the colonic mucosa was localized in the upper third of the colonic crypts [97]. This hyperproliferation of the colonic mucosa was detectable in the whole length of the colonic

crypts in the patients not only with symptomatic diverticulosis and acute diverticulitis but also in patients with asymptomatic diverticulosis [98]. This suggests that not only patients with acute diverticulitis but also those with asymptomatic diverticulosis may be at a risk of developing adenomas and colonic carcinomas. In contrast, a different matrix microenvironment was found between the colonic tissue architecture of the patients with colon cancer and those with diverticular disease, thus implying no predisposition for cancer in diverticular disease [99]. Although this is different from overt diverticulitis.

One of the feasible explanations for the association between diverticular disease and colorectal cancer is that the presence of an inflammation process increases the risk for a malignant transformation [100], since in the western population diverticular disease occurs usually in the left colon.

CONCLUSION

Diverticulosis and diverticulitis are emerging diseases. Prevention is an important factor and therefore a fibre enriched diet should be encouraged. When diverticulitis develops, uncomplicated disease can be managed conservatively. Even abscesses smaller than 5 cm can be managed with bed rest, dietary restrictions and antibiotics. Larger abscesses are punctured under CT guidance. The more serious complications require emergency surgery. New insights have shown that elective surgery to prevent recurrence should be reserved for patients at risk (co-morbidly, e.g. immune compromised). Not youth, but obesity is a risk factor for complicated disease. New therapies like mesazaline, rifaximin and probiotics merit more attention in prevention of diverticular disease and diverticulitis. Relationship with inflammatory bowel disease (SCAD) and sigmoid carcinoma needs further evaluation.

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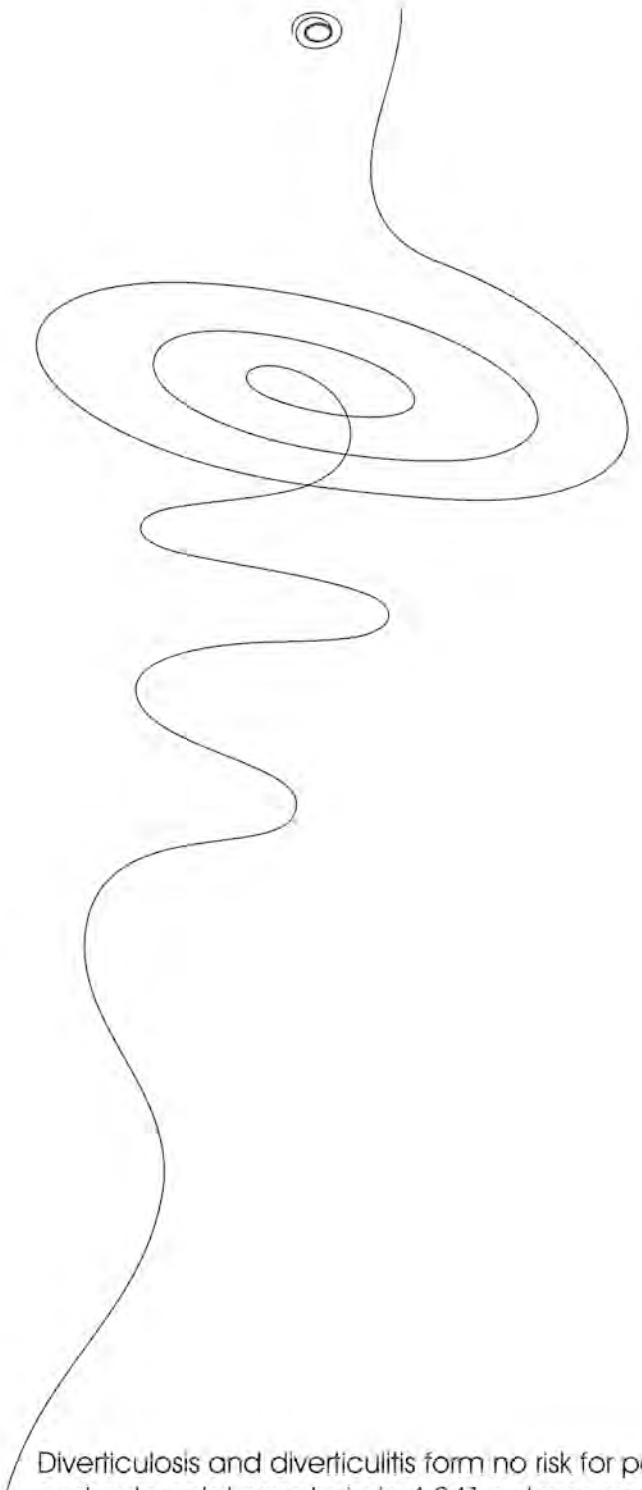

Diverticulosis and diverticulitis form no risk for polyps
and colorectal neoplasia in 4,241 colonoscopies.
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Abstract

Background and aim

There are conflicting data concerning the association between diverticular disease and colorectal carcinoma (CRC). This study was performed to determine the prevalence and association of diverticulosis, diverticulitis, polyps, and CRC.

Materials and methods

In a cross-sectional, retrospective study, we analyzed the colonoscopy reports of complete colonoscopies and patho-histological results of all patients referred for colonoscopy in a period of 3 months in 18 hospitals in the Netherlands. Diverticulosis was defined as three or more diverticula present and diverticulitis as diverticulosis with inflammation. Polyps were also coded according to localization and size. Advanced neoplastic lesions were defined as polyps ≥10 mm in diameter and/or villous architecture and/or adenomas with high grade dysplasia and/or invasive cancer. Actual and previous described CRC were registered.

Results

A total of 4,241 patients were included in the study [1,996 (47%) male], mean age of 59 and range 18–95. Diverticula, diverticulitis, and polyps were seen in 1,052 (25%), 75 (2%), and 1,282 (30%) patients, respectively. No association was found between patients with polyps and those with and without diverticulosis (p=0.478). Invasive adenocarcinoma and adenomas ≥10 mm were most frequently observed. CRC was present in 372 (9%) patients. Negative relation between diverticulosis and CRC and invasive adenocarcinoma was observed. No association was found between polyps and CRC and patients with diverticulitis and CRC. In conclusion, there is no relation between patients with diverticulosis and higher incidence of polyps or CRC when using age-stratified analysis. No increased risk for polyps or CRC was found in patients with diverticulitis.

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INTRODUCTION

The prevalence of diverticulosis and subsequently diverticulitis is increasing in the last decades [1,2]. Diverticulosis increases with age; it is estimated less than 10% in those under the age of 40 and increases to 65–70% in those above 65 years of age [3-5]. Besides diverticulosis, the prevalence of colon cancer is also increasing in the western world [3,6]. Colorectal cancer is a leading cause of cancer mortality in the western world, with more than 1,000,000 new cases per year and with 500,000 deaths per year worldwide [7]. The estimated lifetime risk is 5–6%, where incidence rates increase sharply after the age of 50 years [8]. In the Netherlands, colorectal cancer is diagnosed in about 10,000 patients each year and causes 4,400 deaths per year [9,10]. Colorectal cancer is the third most common cancer in men and the second commonest in women in this country. Certain groups are at risk, like autosomal dominant syndromes, familial adenomatous polyposis, hereditary non-polyposis colorectal cancer (HNPCC), Peutz–Jegher's syndrome, acromegaly, and Gardner syndrome [11,12]. Patients who are at risk are included in colonosopic surveillance programs [13,14].

The relationship of diverticulosis, diverticulitis, colon polyps, and the occurrence of cancer is complicated and conflicting. There are studies in patients with diverticulosis that found an increased incidence of polyps [1,15,16] and colorectal carcinoma (CRC) [17,18], a decreased incidence of polyps [19] and colon carcinoma [1,19], or no difference in CRC [20]. In patients with diverticulitis, an increased [21] and decreased risk [19] for CRC was described. When diverticulosis and diverticulitis form an increased risk for CRC, a different view concerning colorectal screening should be taken.

The aim of this study was to establish the relationship between diverticulosis, diverticulitis, polyps, advanced neoplastic lesions (ANL), and colon carcinoma in a retrospective, cross-sectional study.

Materials and methods

Patients

In a 3-month period from September to November 2006, 4,241 outpatients who underwent colonoscopy in 18 hospitals in the region of North Holland were included. Of all the hospitals which took a part in our study, 17 were peripheral hospitals and 1 was tertiary clinic (our hospital).

The indications for colonoscopy included uncomplicated lower abdominal pain of at least 2 months' duration, hematochezia, gastrointestinal hemorrhage, unexplained changes in bowel habit, weight loss, iron-deficiency anemia, chronic obstipation without positive reaction on the treatment, chronic diarrhea, surveillance after colonic polypectomy, and screening for and follow-up of colorectal cancer. Permission was granted from the central medical ethics review board of the VUMC medical center.

Methods

The reports of 3 months complete colonoscopies and pathohistological results were entered in a database coding for age, sex, indication, medical history as present, endoscopic findings like inflammation, diverticula, polyps, CRC, and pathohistological results. Diverticulosis was defined as three or more diverticula present. Diverticulosis with inflammation was coded as diverticulitis. Any detected polyp was coded separately according to localization and size. Any described or earlier diagnosed macroscopic CRC was coded as CRC. ANL were defined as an adenomas ≥10 mm or more in diameter, >25% villous architecture and/or adenomas with a high-grade dysplasia and/or an invasive cancer. Benign polyps were defined as hyperplastic polyps and adenomas <10 mm with low/intermediate grade dysplasia.

Statistical analysis

The frequency, location, and size of polyps are described in patients with diverticulosis and diverticulitis as well as frequency of colorectal cancer.

Results are presented as mean and SD; statistical testing was done with the chi-square test, when appropriate corrected for age with the Mantel–Haenszel test (age stratified analysis in 10 years classes). Calculations were made with the SPSS program (SPSS 14.0).

RESULTS

A total of 4,241 patients were included in the study [1,996 (47%) male and 2,245 (53%) female], mean age of 59 and range 18–95. Patients with diverticulosis, polyps, and cancer were significant older than those without: mean age 69 vs. 56, 64 vs. 57, 68 vs. 58, respectively, $p<0.0001$. Diverticula were seen in 1,052 (25%), diverticulitis in 75 (2%), polyps in 1,282 (30%), and CRC in 372 (9%) patients.

In 98% of the patients, predominantly left-sided diverticulosis was found. In 21 (2%) patients, mainly right-sided diverticula were seen. The mean age of the patients with diverticular disease was 69.5 (SD 11.8) as compared with 55.9 (SD 16.8) in those without ($p<0.0001$). No gender difference existed in patients with diverticulosis.

Polyps were seen significantly more in men than in women [703 (55%) vs. 579 (45%); $p<0.0001$]. No difference in distribution of ANL was found between men and women, 348 (53%) vs. 258 (39%), respectively ($p=0.12$). ANL were seen more often in the recto-sigmoid colon than the rest of the colon, 465 (36%) vs. 386 (30%), $p=0.002$ (Table 1). Invasive adenocarcinoma and adenomas ≥10 mm were most frequently observed (Table 1).

Though unstratified analysis seemed to show an association between patients with polyps and diverticulosis and those without diverticulosis [916 (71 %) vs. 366 (29%)], however, age stratified analysis showed no relationship ($p=0.478$).

Localization of the polyps	Advanced neoplastic lesions					Benign polyps N (%)	Total N (%)
	Adenomas ≥10 mm N (%)	Invasive adenoca. N (%)	Villous adenoma N (%)	High grade displasia N (%)	Total N (%)		
Rectum	59 (37)	154 (38)	30 (79)	19 (34)	262 (40)	153 (25)	415 (32)
Sigmoid	48 (30)	131 (32)	2 (5)	22 (39)	203 (31)	233 (38)	436 (34)
Colon descendens	10 (6)	30 (7.5)	0	1 (2)	41 (6)	61 (10)	102 (8)
Transversum	9 (5)	17 (4)	1 (3)	1 (2)	28 (4)	46 (7)	74 (6)
Colon ascendens	21 (13)	36 (9)	4 (10)	8 (14)	69 (10)	82 (13)	151 (12)
Cecum	14 (9)	38 (9.5)	1 (3)	5 (9)	58 (9)	46 (7)	104 (8)
Total	161 (24)	406 (61.5)	38 (6)	56 (8.5)	661 (51.5)	621 (48.5)	1,282 (100)

Table 1. Histopatholical results and location of the polyps

A negative relation was observed between diverticulosis and CRC and invasive adenocarcinoma in age-stratified analysis (p<0.0001 and p=0.002, respectively). No association was found between polyps and CRC and patients with diverticulitis and CRC (Table 2).

	Polyps (%)	*p* value	OR	CI
Diverticulosis	916 (71)	0.478	0.94	0.8–1.1
Diverticulitis	23 (1.8)	0.695	0.87	0.5–1.4
CRC (%)				
Diverticulosis	88 (23.6)	<0.0001	0.54	0.4–0.7
Diverticulitis	3 (0.8)	0.116	0.36	1.1–1.2
Polyps	133 (35.7)	0.824	0.03	0.2–0.3
Invasive adenocarcinoma (%)				
Diverticulosis	175 (26.4)	0.002	0.66	0.5–0.8
Diverticulitis	11 (1.6)	0.43	0.66	0.2–1.5

Table 2. Relationship between diverticulosis/diverticulitis with polyps, colorectal carcinoma (CRC), and invasive adenocarcinoma

DISCUSSION

In this retrospective, cross-sectional study, we examined the relationship between diverticulosis, diverticulitis, polyps, ANL, and CRC in a group of 4,241 consecutive patients undergoing colonoscopy for various reasons.

In our study, diverticulosis was reported in 25% of patients. Underreporting and selection bias may play a role. Diverticulitis was seen in 2% of the patients, which is less than the previously reported prevalence of 5% [22]. This is probably due to the fact that, in many cases, computer tomography is performed when diverticulitis is suspected, rather than colonoscopy. Polyps were observed in 30% of the patients, of which half (51%) were ANL. The polyps and ANL were found predominantly in the recto-sigmoid colon. This finding is consistent with other studies, where the left colon is the principal site of ANL and polyps [23-25].

CRC was present in 9% of the patients. This included patients with a previously resected CRC. Since the reason for colon resection was not always reported, underreporting also might play a role here.

The prevalence of both diverticulosis and adenomas increases with advanced age [3-5,23,26] as was also shown in our results.

We have not observed any gender domination in patients with diverticulosis, ANL, and CRC. However, polyps were seen more often in men than in women. The increasing prevalence of polyps in young male patients was already observed in a recently published study [24].

We observed a negative correlation between diverticular disease and CRC as well as invasive adenocarcinoma. Furthermore, we did not find any association between polyps and CRC or diverticulitis and CRC. How can this discrepancy in the literature, including our results, be explained? Table 3 summarizes the studies regarding this subject.

Author	Year	Diverticulosis	Diverticulitis	Polyp	Carcinoma	Note
Stefanson et al. [17]	1993	+			left side ↑	mixed diverticulosis and diverticulitis
Loffeld et al. [1]	2002	+		↑	↓	many polyp surveillance
Morini et al. [15]	2002	+		sigmoid↑ ANL in sigmoid↑	=	
Kieff et al. [16]	2004	+		women ↑ distal and advanced		no previous polypectomy or surgery
Stefanson et al. [21]	2004	+			=	longitudinal, case control study
			+		4.2 ↑	
Krones et al. [19]	2006	+	+	↓	↓	only 18% diverticulosis in CRC
Soran et al. [20]	2006	+			prognosis after colonca =	10% diverticula in colonca after resection for colonca
Choi et al. [18]	2007	+			both left and right sided ↑	no previous polypectomy or surgery
Meurs-Szojda	2008	+		=	↓	many polyp surveillance
			+	=	=	

Table 3. Review of literature: relationship between diverticulosis, diverticulitis, polyps, and colon carcinoma.

ANL Advanced neoplastic lesion, *CRC colorectal cancer*

There are nine studies, including ours, concerning diverticulosis, polyps, and CRC [1,15-21]. Three studies described an increased incidence of polyps in patients with diverticulosis [1,15,16]. However, only one of these studies considered the confounding influence of age [15]. We did not find any relation between patients with polyps and incidence of diverticulosis when

using age-stratified analysis. In the light of our results, it seems vital to make an age-stratified analysis.

One study only included first time colonoscopies without prior polypectomy, colorectal surgery, or inflammatory bowel disease [16]. Although the number of included patients was only 502, selection bias was minimal. Another study [19] found a lower incidence of polyps. Since these are retrospective studies, underreporting might be due to the fact that a substantial part of colonoscopies performed, consisted of follow-up colonoscopies after polypectomy or after partial colon resection.

Eight studies, including our own, concern the relationship between diverticulosis and carcinoma [1,15,17-21]. One recent study from Korea found an increased risk of CRC in both patients with left- or right-sided diverticulosis without prior polypectomy or surgery in the affected area [18]. Three studies showed no relationship between diverticulosis and CRC, one of them being a longitudinal study [21]. The two other studies showed no prognostic difference in patients with and without diverticulitis after removal of CRC [20] and the same prevalence of CRC in both groups of patients [15]. Two studies [1,19] besides ours found less CRC in patients with diverticular disease. Again, selection bias could play a role.

There are two studies besides ours concerning the relationship between diverticulitis and CRC [19,21] and one regarding polyps [19]. Stefanson describes a longitudinal, case control study in 7,159 patients with a prior diverticulitis and a follow up of at least 20 years in which he finds an increased risk (OR=4.2) for left-sided CRC [21]. Krones et al. [19] looked retrospective at resected specimen for CRC for diverticulitis and in resected diverticulitis for ANP. In the CRC group, the incidence of diverticulosis was only 18% and ANP in the diverticulitis group only 6%, both very low numbers [23-25]. Subsequently, a negative relationship was found. Our study showed no

difference and also suffers from confounding factors like underreporting and previously removed polyps and CRC.

Although only one study [21] has demonstrated the relationship between prior diverticulitis and development of CRC, the sequence seems logic. Many patients with diverticulitis will experience recurrent attacks, and chronic inflammation can lead to overt carcinoma as is well known in patients with inflammatory bowel disease [27,28] and *Helicobacter pylori* [29].

This concept is supported by studies in vitro, although contradictory results are also found in this study. One study showed an elevated C-reactive protein concentration in blood of the persons who developed colonic cancer after several years [30]. One of the possible explanations for the association between diverticular disease and colorectal cancer is that the presence of an inflammation process increases the risk for a malignant transformation [30] since, in the western population, both diseases occur usually in the left colon. A study in patients with diverticular disease demonstrated that hyperproliferation of the colonic mucosa was localized in the upper third of the colonic crypts [31]. Hyperproliferation of the colonic mucosa was detectable in the whole length of the colonic crypts in the patients not only with symptomatic diverticulosis and acute diverticulitis but also in patients with asymptomatic diverticulosis [32]. This suggests that not only patients with acute diverticulitis but also those with asymptomatic diverticulosis are at a risk of developing adenomas and CRC. Recently, an abnormal expression of M1/MUC5AC mucin [found in (pre)cancerous lesions] in the distal colon of 26% of patients with diverticulitis was found [33]. In contrast, a different matrix microenvironment was found between the colonic tissue architecture of the patients with colon cancer and those with diverticular disease, thus implying no predisposition for cancer in diverticular disease [34].

Now, what should we believe? Clearly, a longitudinal study following cohorts of patients with diverticulosis or diverticulitis is the best. However, some firm conclusions can be drawn. Considering the fact that more than 60% of patients above the age of 60 will have diverticula, it is obvious that screening from this point of view is useless, even if there were a very slight increased risk.

How about diverticulitis? This is more complicated. In our group, there were not so many patients with diverticulitis (75) compared to the group of Stefanson et al. [21] (7,159), which were also followed as a cohort and found a positive relationship. But the surgical resection specimens of Krones et al. [19] were thoroughly examined, and he found less polyps and cancer. The difference could lie in the moment of endoscopy or surgery. Some find surgery mandatory after a first recurrence while others follow a more liberated policy [35]. Furthermore, additional or more adequate treatment may alter the disease and lead to less recurrences [36], thus reducing the chance for chronic inflammation. It seems that the common practice to perform a colonoscopy after a cured diverticulitis to rule out a malignancy is valuable. If any polyps are found, surveillance can occur as usual. Probably, the patient with continuous inflammation or frequent attacks of diverticulitis merit more attention.

Increasing diverticular disease and therefore diverticulitis around the world poses interesting questions regarding the long-time consequences for these patients and possible colonoscopy screening. This certainly merits more attention and research. Further longitudinal studies and awareness of underreporting are necessary, which can be overcome by standardized endoscopy reports.

In conclusion, no relationship between diverticular disease and colon neoplastic disease was found. Although some critical points can be made

about the study design, some conclusion can be drawn from this study and the existing literature. Diverticulosis probably bears no relationship with colonic neoplastic lesions. Maybe, some patients with chronic or recurrent diverticulitis are at risk. The general clinical practice that patient should have a colonoscopy after a cured diverticulitis to rule out a carcinoma holds true. Those with polyps should enter a surveillance program. Probably, the patient with recurrent attacks of diverticulitis merit more attention.

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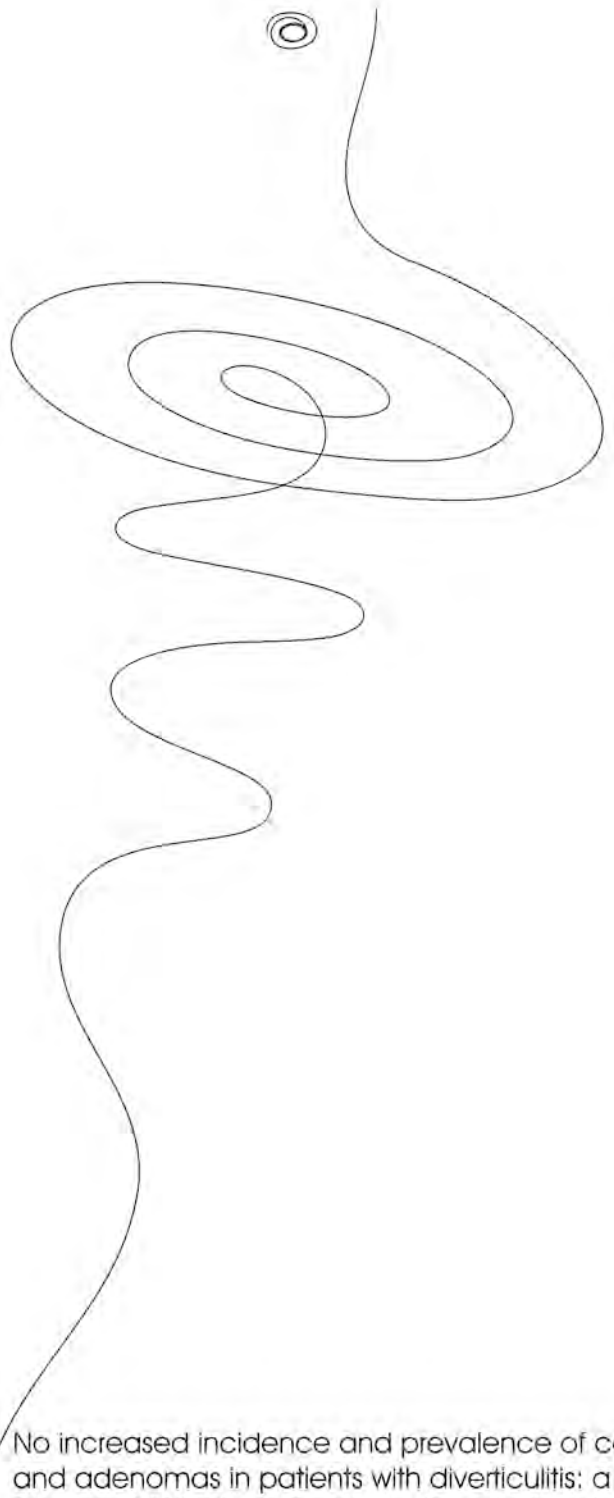

No increased incidence and prevalence of colorectal carcinoma and adenomas in patients with diverticulitis: a retrospective longitudinal study.
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Abstract

Objective

This study was designed to assess the relationship between diverticulitis and the development of colorectal carcinoma (CRC) and colonic adenomas.

Materials and methods

A retrospective study was longitudinally conducted. Patients who had been admitted to the hospital between 1990-2000 with diverticulitis were retrieved and the incidence of CRC and prevalence of colonic adenomas in these patients were determined. Data were collected from the electronic clinical and pathology records. The incidence of CRC and prevalence of adenomas in this patient cohort was compared with the general population. The patients were followed up till 2008.

Results

A total of 288 patients with diverticulitis were included (167 females [58%]). The mean age of patients at admittance for diverticulitis was 66 year (range 27-92). CRC was detected in 5 patients (1.7%) (95% CI 0.8-3.5), at a mean age of 77 year; colonic adenomas were found in 18 patients (6.3%) (95% CI 4.3-9.0), at a mean age of 62 year. The lifetime risk of developing CRC and adenomas were presumed to be 4% and 20% respectively. Calculated expected rates in our patients for CRC and adenomas were 17 (95% CI 4.0-8.6) and 69 patients (95% CI 20.1-28.3) respectively.

Conclusion

This study showed a lower prevalence of CRC and colonic adenomas in patients with diverticulitis compared to the lifetime risk, which means that diverticulitis is not a risk factor for development of CRC and adenomas. Long term colonic screening after a negative colonoscopy for diverticulitis generally performed several weeks after recovery, seems not to be justified.

Presented at UEGW October 2009 (London, England)

INTRODUCTION

The relationship of diverticular disease and colorectal cancer (CRC) remains unclear. A possible association between diverticulosis and CRC has been reported by several investigators [1-4]. In contrast, some authors failed to show any association [5] or described a decreased risk for CRC [6].

Studies have shown similar epidemiological features for both diseases. A recent report by the American Gastroenterological Association (AGA) on the burden of digestive illnesses indicates that diverticular disease represents one of the five most important gastrointestinal diseases in the Unites States and the prevalence has increased since the last century [7,8]. CRC, one of the most common malignancies in the world, has shown a similar trend. Furthermore both diseases are more frequent in developed countries and are age-dependent, as both are uncommon in those under the age of 40 [9,10]. It has been estimated that the lifetime risk of developing CRC and colonic adenomas is 2.5-6% and 10-20% respectively [11-14]. In addition, both diseases share a similar distribution. Although a gradual shift toward right-sided colonic leasion has been observed, most of them are mainly left sided [14,15]. Diverticulitis develops commonly in the left colon as well, especially in the sigmoid [16].

A possible explanation for the association between the two diseases is that they share similar risk factors. They have the same pathogenic factors, such as the Western diet, low in dietary fiber and rich in saturated fat [17]. A causal relationship between the two diseases has also been suggested [3]. In the literature several macroscopic and microscopic alterations of diverticular disease are described [18]. One of the most important is the chronic inflammation, because chronic inflammation is a risk factor for cancer. The link between chronic inflammation and cancer is well documented in patients with ulcerative colitis, gastritis, esophagitis and hepatitis [19-21].

A recurrent or chronic inflammation of the colon occurs in a number of patients with diverticulosis [18]. Moreover, 0.8 % of patients with diverticulosis

without any symptoms had sign of diverticular inflammation on the endoscopy [22].

In theory, it could be speculated that patients with diverticulitis have a higher risk of developing CRC than patient with a few outpouchings of the mucosa through the muscular layers.

The aim of the present cohort study was to evaluate a possible association between diverticulitis and CRC.

Materials and methods

Patients who had been admitted to the VU University Medical Center between 1990 to 2000 with diverticulitis were retrieved from the hospital database to determine the possible incidence of CRC and the prevalence colonic adenomas in these groups. The diagnosis diverticulitis was confirmed with CT-scan and / or surgery.

The descriptive characteristics of the study cohort were analyzed with respect to age, gender, any history of diverticulitis, preceding presence of malignancies and co-morbidities.

All patients who received a conservative treatment during their admission, were followed up by evaluating the Hospital Electronic Medical Record and the pathology reports, which are stored in the PALGA system. This system is a nationwide network and registry of histo- and cytopathology in the Netherlands.

Of all patients who underwent surgery for diverticulitis, the Hospital Electronic Medical Record and the pathology report of the resected specimen was reviewed. These patients were not followed up, because the colonic resection removed the affected post-diverticulitis colon, which excluded the development of cancer in that part.

The time of observation of patients with a conservative treatment was calculated from the date of the first admission episode with diverticulitis of the colon until death or the end of the observation period.

The Medical Ethical Commission of the VU University Medical Center granted permission.

Statistical analysis

The lifetime risk for CRC and adenomas in this patient cohort were compared to the general population with representative data from the literature. Studies described a lifetime risk variation of 2.5-6% for CRC and 10-20% for colonic adenomas [11-14]. To reduce any underreporting, the expected rates were calculated with a lifetime risk of 4% for CRC and 20% for colonic adenomas. A confidence interval was used to define the lifetime risk. Analyses were performed with the statistical software SPSS 16.0.

RESULTS

Between 1990 and 2000, a total of 288 patients with diverticulitis were admitted to the hospital (167 [58%] female). The mean age of the patients diagnosed with diverticulitis at admission was 66 years with a range of 27-92 years. The mean age at the end of the observation time was 71 years with range of 28-100 years. In total 76 patients died. Besides CRC, 39 patients (13.5%) patients were diagnosed with other malignancies (Table 1).

	Total patients n = 288	**Patients with conservative treatment n=106**	**Colorectal cancer n = 5**	**Colonic adenomas n =18**
Mean age				
years (range)	66 (27-92)	68 (29-92)	77 (66-86)	62 (38-81)
Gender				
Male n (%)	121 (42.0)	47 (44.3)	0	10 (55.6)
Female n (%)	167 (58.0)	59 (55.7)	5 (100)	8 (44.4)
Recurrence of diverticulitis n (%)	100 (34.7)	26 (24.5)	1 (20.0)	5 (27.8)
Presence of (other) malignancies n (%)	39 (13.5) - Breast - Skin - Prostate	15 (14.2) - Breast - Skin - Prostate	3 (60.0) - Breast	2 (11.1) - Breast

Table 1. Characteristics of patients

A total of 182 (63.2%) patients (of these, 53 patients first received a conservative treatment) underwent an operation as a result of diverticulitis, whereas the remaining 106 (36.8%) patients received a conservative treatment.

Of the 106 patients with conservative treatment, no further pathology reports existed for 12 (11,3%) patients. The follow-up ranged from 0 to 18 years, with a mean follow-up of 12 years. One patient died a few weeks after the conservative treatment. During the follow-up 26 (24,5%) patients in this group had a recurrent episode of diverticulitis.

CRC was detected in 5 (1.7%) patients at a mean age of 77 years, all female (Table 1). As shown in table 2 the 95% confidence interval was 0.8-3.5. The calculated expected rate for CRC was 17 (95% CI 4.0-8.6) patients (Table 2). After subclassification according to treatment, the 95% CI of patients with a conservative treatment was 0.6-5.5 and the calcuated expected rate was 8 (95% CI 4.3-12.9) patients.

In 3 (60%) cases CRC was diagnosed during the first recorded episode of diverticulitis. These patients underwent a sigmoid resection. In two cases CRC was diagnosed 4 and 15 years after their first admittance respectively. Three (60%) patients had breast cancer as co-morbidity.

Colonic adenomas were identified in 18 (6.3%) patients, at a mean age of 62 year, with 8 (44.4%) female (Table 1). The 95% confidence interval was 4.3-9.0. The calculated expected rate for adenomas was 69 (95% CI 20.1-28.3) patients (Table 2).

In 8 (44.4%) cases colonic adenomas was diagnosed during the first recorded episode of diverticulitis. In the remaining 10 cases colonic adenomas was diagnosed after 1 to 12 years with a mean of 3.4 years. Two (11.1%) patients with colonic adenomas had breast cancer as co-morbidity.

CRC	Number patients (%)	95% Confidence interval	Expected number patients (%)	95% Confidence interval
Total patients (n=288)	5 (1.7)	0.8-3.5	17 (5.9)	4.0-8.6
Conservative treatment (n=106)	2 (1.8)	0.6-5.5	8 (7.5)	4.3-12.9
Surgical treatment (n=182)	3 (1.6)	0.7-4.0	12 (6.6)	4.2-10.3
Colonic adenomas				
Total patients (n=288)	18 (6.3)	4.3-9.0	69 (23.9)	20.1-28.3
Conservative treatment (n=106)	11 (10.4)	6.5-16.3	28 (26.4)	20.0-34.0

Table 2. 95% Confidence interval of patients with CRC and colonic adenomas

DISCUSSION

This retrospective longitudinal study which included 288 patients, found no association between patients with diverticulitis and CRC and patients with diverticulitis and colonic adenomas.

This absence of an association between diverticulitis and CRC correlates with the results of two other studies. In our previous cross-sectional, retrospective study we observed a negative correlation between diverticulitis and CRC as well as with polyps in 4241 colonoscopies [23]. CRC and invasive adenocarcinoma were detected in 3 patients (4%) and 11 patients (14.7%) respectively. The retrospective study by Krones et al. involving 512 patients showed that diverticulitis was no risk factor for advanced colonic neoplasia [6].

However, this contrasts with the finding of Stefansson *et al.* [24]. The authors reported in a retrospective case control population based cohort study

involving 7159 hospitalized patients with diverticulosis and diverticulitis that there is an increased risk for a long-term left-sided CRC in diverticulitis patients.

Thus, in total 4 studies, including the present study, documented diverticulitis and CRC / colonic adenomas and are controversial (Table 3). Three showed no association and the remaining study, which included a large number of patients, found a positive relationship. The controversial findings may reflect the influence of surgical therapy as suggested in our previous study. Adequate treatment may lead to less recurrences and a reduced risk for CRC. The patients of Krones *et al.* all underwent a colonic resection for diverticulitis, which might reduce the risk of developing CRC [6]. In the study of Stefansson *et al.* no information was given about the frequency of surgical treatment [24].
It has been speculated that diverticular disease may correlate with a high epithelial cell proliferation. Morini *et al.* demonstreted hyperproliferation in the upper third of the colonic crypts of the sigmoid mucosa in patients with diverticular disease [25]. This finding has been confirmed by Tursi *et al.* [26]. They ditected an upward shifting of cellular proliferation in the whole length of the colonic crypts in the patients with symptomatic diverticulosis and acute diverticulitis. In addition, hyperproliferation was also ditected in asymptomatic patients with diverticulosis which implies that those may be at risk for developing CRC as well. In contrast, a recent study regarding the microenvironment did not support this concept. Klinge *et al.* showed group-specific differences the the colonic tissue architecture of the patients with CRC and patients with diverticulitis [27]. This suggests that there may no predisposition for cancer in diverticular disease and may explain the low rate of CRC in diverticulitis patients. However, the complex crosstalk within the cellular and extracellular matrix remains uncomplited. Further investigation is needed.

Author	Stefansson [24]	Krones [6]	Meurs-Szojda [23]	Lam
Year	2004	2006	2008	2009
Study	case control cohort	retrospective	retrospective cross-sectional	retrospective cohort
Patients with diverticulitis n	7159 patients with diverticulose and diverticulitis	512	75	288
diverticulitis patients with colonic neoplastic lesion n (%)	46 diverticulitis patients with CRC in total 64 cases with cancer and 123 controls	28 (6) advanced colonic neoplastic lesion	3 (4) CRC 11 (14.7) invasive adenocarcinoma	5 (1.7) CRC 18 (6.3) adenomas
mean follow up years (range)	no information (±6 - ±26)	9 (3-17)	not applicable	12 (0-18)
therapy n (%)	no information	all resection	not applicable	182 (63.2) resection
conclusion	increased risk	reduced risk	no increased risk	no increased risk

Table 3. Review of studies concerning association between diverticulitis and colonic neoplastic lesions.

Moreover, studies concerning the association between diverticular disease and CRC are also controversial. In the literature, nine studies were reported

regarding this subject. One study demonstrated an increased incidence of CRC in patients with diverticulosis [3], two studies showed no difference in CRC [24,28] and three studies found a decreased incidence [5,6,23]. Regarding the polyps, three studies showed an increase of prevalence [2,4,5], one study no difference [23] and one study a decrease [6].

Surprisingly, in this study the diverticulitis patients who developed CRC were all female. Gender has not been established as a risk factor for CRC. However, in the literature the incidence of CRC is even slightly higher in men. Nevertheless, the incidence rates for cancer have increased particularly in women, because of the increased carcinogenic habit of smoking cigarettes [29]. Unfortunately, smoking habit was not recorded in the present study.

Nonetheless, there are some limitations in our study that should be considered when interpreting these findings. The first limitation is the observation time. Although the present results may be due to a short follow up compared with the study if Stefansson *et al.* [24], the study population has reached a mean age of 66 years at first admission. Since incidence rates increase sharply after the age of 50 years [30], it could be considered that our mean age finding would not lead to an underestimation of CRC. Furthermore, a previous episode of diverticulitis was only recorded if the patients were investigated at our hospital. Regarding the lack of information bias in the collection the first episode of diverticulitis, the approach of calculating the duration of diverticulitis and developing CRC, may underestimate the actual transition duration.

Secondly, the included patients are a hospital-based population. Patients with diverticulitis without admission to the hospital were not included, which may cause an underriporting of diverticulitis. A sublinical diverticulitis inflammation could be presented [22]. However, in theory, patients who were admitted, have a more significant illness episode of diverticulitis than those who were not. A more severe diverticulitis usually requires surgical intervention, which can cause a bias. Both diseases are mainly located in

the left colon [14-16]. Therefore, colonic resection due to diverticulitis could eliminate the chance of developing CRC, which means that the association between severe diverticulitis and CRC has not been ruled out. Thirdly, there could be an underreporting of the prevalence rate of neoplasia and polyps. This seems especially the case with polyps, since they rarely give complaints. Small sized CRC usually only cause mild complaints, which might lead to underreporting as well, but larger CRC will generally give clinical symptoms and even in the very old or debilitated patients the diagnosis would have been established.

Fourthly, as table 1 showed, 3 patients with CRC (60%) had breast cancer as co-morbidity. Therefore, CRC may be caused by inherited genetic predispositions which leads to breast cancer and not by diverticulitis. Brose *et al.* showed an increased risk of cancer of the colon in patients with breast cancer [31].

The last limitation is that a preceding simultaneous presence of two diseases was not ruled out. CRC can develop simultaneous in diverticulitis patients. However, the incidence of CRC was still low in diverticulitis patients and did not meet the calculated expected rates for CRC.

In conclusion, the present study found no association between diverticulitis and CRC, and diverticulitis and colonic adenomas. Therefore, there is no need to justify any screening procedures for early detection of cancer in patients with a history of diverticulitis. However, this should be interpreted with caution. Regarding the fact that in 3 of the 5 patients CRC was detected during the first episode of diverticulitis, it is maybe worthwhile to perform a colonoscopy to rule out any concomitant presence of CRC after a cured diverticulitis as is the current strategy.

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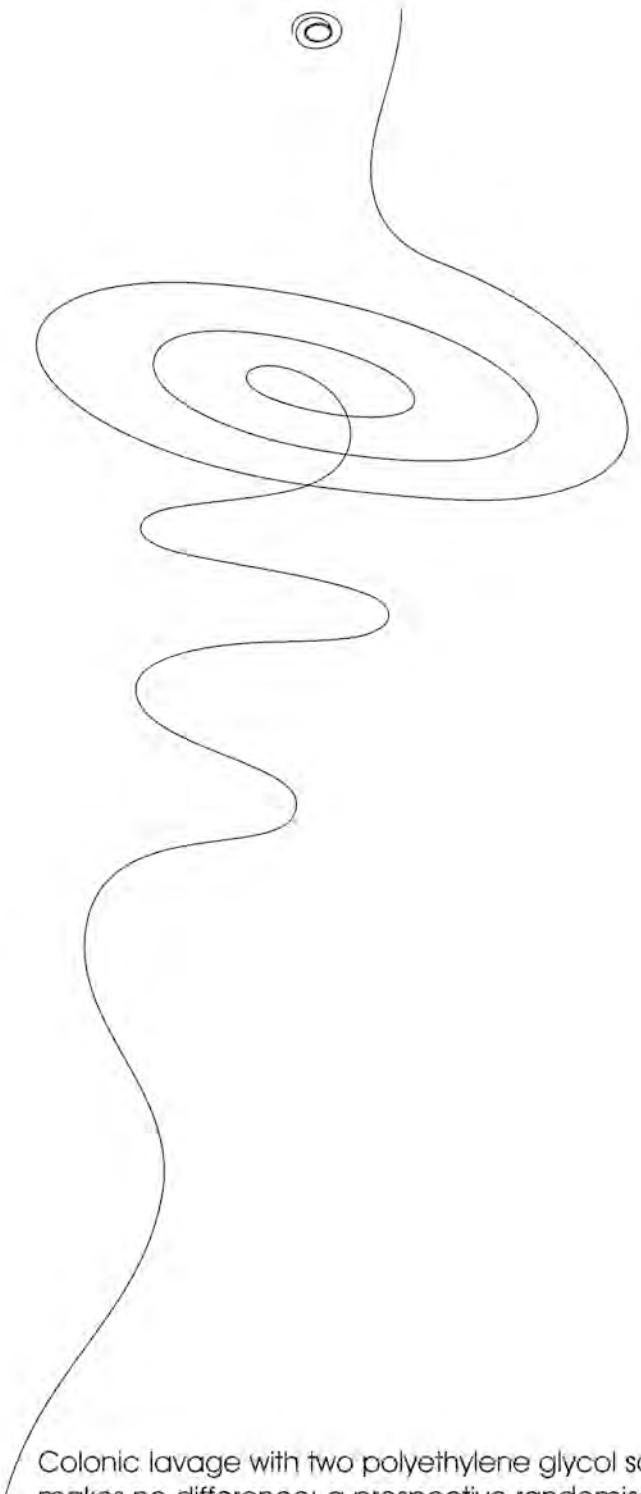

Colonic lavage with two polyethylene glycol solutions prior to colonoscopy makes no difference: a prospective randomised controlled trial.
M.M. Szojda, D.J. Kuik, C.J. Mulder, R.J. Felt-Bersma
Scand J Gastroenterol. 2008;43:622-6.

Abstract

Objective

It is suggested that bowel preparations for colonoscopy are easier to tolerate when a smaller volume of solution with a more pleasant taste is used. The aim of this study was to establish equivalence between a 3-l sulphate-free polyethylene glycol solution (SF-PEG) and a 4-l PEG solution in effectiveness, patients' acceptability and tolerability.

Material and methods

The study comprised 110 patients scheduled for elective colonoscopy and randomized to receive either SF-PEG or PEG. Before colonoscopy, the patients completed a questionnaire on stool frequency, medication, concomitant diseases, the amount of solution ingested, willingness to retake it, volume of other fluid taken and tolerance of bowel preparation, taste of the laxative and occurrence of abdominal cramps. Three experienced endoscopists, blinded to the type of preparation, assigned bowel-cleansing scores using a validated 5-point scale to assess cleansing effect.

Results

Data were available for 102 patients (44 male (40%), mean age 53 years, range 23-83 years). No significant differences were found in cleansing the rectosigmoid (p=0.71) or complete colon (p=0.79). Diverticulosis, constipation, gender and body mass index (BMI) did not influence cleansing. There was no significant difference in compliance between the two groups (p=0.61). No differences were found for tolerance, taste and abdominal cramps. Patients who received SF-PEG had a preference for the same preparation next time in comparison with patients who had PEG cleansing (17 (33%) versus 4 (8%), respectively) (p=0.03).

Conclusions

Both preparations are comparable in their cleansing effect and toleration. However, patients prefer cleansing with a smaller volume of solution. Improving the acceptability of colonic preparation could improve willingness to undergo colonoscopies in the future.

INTRODUCTION

Colonoscopy is an essential procedure for the detection and treatment of colonic lesions. Therefore, cleansing the bowel for adequate visualization of the colonic mucosa during the procedure is important. Elective colonoscopy is of major importance in screening and surveillance programs for patients with colorectal cancer, which is a leading cause of cancer mortality in the Western world [1,2]. Inadequate preparation can result in missed polyps and other lesions [3-6] and can prolong the insertion time, as well as increasing the risk of complications and patient discomfort [7,8]. Colonic cleansing is generally done with solutions containing high molecular-weight polyethylene glycol (PEG), sodium phosphate, magnesium citrate, or bisacodyl [9-13]. PEG solutions are considered to be the gold standard for bowel cleansing in many countries and their efficacy and safety have been well established in more than 50 controlled trials. However, many of these solutions require intake of large volumes of fluid, which is disadvantageous to their use and reduces acceptability in patients [11]. Some studies comparing different regimens and solutions in precolonoscopy bowel cleansing suggest that regimens with larger amounts of colonic fluid are poorly tolerated by patients [6,14-21]. Patients are often unable to ingest sufficient quantities of the solution, which leads to inadequate colon cleansing, amounting to 10-75% in randomized controlled trials [7,13,18,22]. Poor bowel preparation has been associated with patients' characteristics such as a history of constipation, use of antidepressants and non-compliance with cleansing instructions [8,23,24]. Safe and effective colonic cleansing is crucial for a correct diagnosis, which often decides on efficient treatment without unnecessary delay. The importance of patient acceptability is often underestimated and is not seriously considered, despite it being responsible for poor compliance with the cleansing regimen. In this study we compared the effectiveness, patient acceptability and physical tolerability of a sulphate-free (SF) 3-l PEG solution (SF-PEG) versus 4-l PEG solution for bowel preparation prior to colonoscopy.

Material and methods

From November 2006 to February 2007, 110 patients scheduled for elective colonoscopy in our outpatient clinic were enrolled in this study. Eligible patients who had given informed consent were prospectively randomized to receive either 3-l SF-PEG, or 4-l PEG. The two bowel-preparation schedules were also randomized. Exclusion criteria included gastrointestinal obstruction, bowel perforation, obstructive or paralytic ileus, pregnancy, immobility of the patient, unstable angina or other disease that might interfere with the study. Patients who were not able to consume enough of the preparations safely to initiate colonoscopy were also excluded from the study.

Demographic characteristics such as age, gender, weight, height, stool frequency per week, previous bowel preparation, bowel surgery and additional medical history were obtained for all patients. Both preparations were administered in compliance with the prescription information. For a morning procedure, patients started with ingestion of 3-l SF-PEG or 4-l PEG the evening before the procedure. For an afternoon procedure, patients began ingestion of the prescribed solutions the morning of the day of the procedure. During and after lavage, patients were restricted to a fluid-only diet.

On the day of presentation for colonoscopy, patients were requested to complete a detailed questionnaire. The questions concerned the amount of PEG preparation the patient actually ingested, time between fluid intake and colonoscopy, volume of other fluid taken before colonoscopy, taste of the preparation (1=very unpleasant taste and 4=very good taste), tolerance of bowel cleansing (1=very bad, 4=very good), abdominal cramps (1=severe, 4=none) and the willingness of the patients to retake one of the solutions in the future. Three experienced endoscopists, blinded to the type and quantity of the preparations, assigned a bowel-cleansing score using the Aronchick 5-point scale [25] to assess bowel cleansing in each segment of the colon and for overall examination. For clinical purposes, we

mention only bowel cleansing in the rectosigmoid and overall colon since, in our clinical experience, the rectosigmoid is often not clean while the rest of the colon is. Diverticula, polyps or other endoscopic lesions found during the procedure were noted.

The caecum was detected and defined endoscopically. The study protocol was approved by the VU University Medical Centre Ethics Commission.

Statistical analysis

To decide on the size of the study sample, we carried out a power analysis beforehand. Assuming a standard deviation of 1.0 for the Aronchick scale, we needed an overall sample of 99 patients, in order to show an equivalence between the two groups defined by a difference in mean Aronchick scale of less than 0.5 (α=0.05, β=0.8). To guard against a 10% dropout, we included 110 patients in the study. Medians were calculated and compared where appropriate with the Mann-Whitney test; χ^2 tests and trend tests were used to compare percentages (GraphPad InStat Software, San Diego, Calif., USA).

RESULTS

Data were available for 102 patients (44 (40%) male, 66 (60%) female, mean age 53 years, range 23-83 years). Eight of the patients were excluded because of failed bowel preparation (3 in the 3-l SF-PEG group and 5 in the 4-l PEG group). There were no differences in demographic findings between the two study groups (Table 1).

	3-l SF-PEG	4-l PEG	
Demographic characteristics	**n=51 (%)**	**n=51 (%)**	**p-value**
Age, mean±SD (range)	52±13.7 (24-83)	53±12.6 (23-81)	0.605
Gender			
Male	18 (17.6)	22 (21.6)	0.490
Female	33 (32.4)	29 (28.4)	
BMI			
Small (BMI <21)	6 (5.9)	3 (2.9)	0.270
Medium (BMI: 21-24)	15 (14.7)	20 (19.6)	
Large (BMI >24)	30 (29.4)	28 (27.5)	
Sigmoid resection	2 (4)	3 (6)	0.812
Hysterectomy	1 (1)	4 (3.9)	0.362
Diabetes on medication	6 (5.8)	4 (3.9)	0.740
Regular laxatives	2 (1.9)	4(3.9)	0.677
Earlier colonoscopy	28 (55)	26 (51)	0.723
Bowel movements per week			
≤3	4 (3.9)	0	0.516
4-7	33 (32.3)	34 (33.3)	
8-14	7 (6.9)	11 (10.8)	
>14	7 (6.9)	6 (5.9)	
Findings at colonoscopy			
Polyps	7 (6.8)	9 (8.8)	0.786
Diverticular disease	15 (14.7)	24 (23.5)	0.102
Colorectal cancer	0	4 (3.9)	0.117
Inflammatory bowel disease	5 (4.9)	3 (2.9)	0.715
Haemorrhoids	5(4.9)	4 (3.9)	1.00

Table 1. Demographic characteristics.

PEG=polyethylene glycol; BMI=body mass index; SD=standard deviation.

Assessment of bowel cleansing

The caecum was reached in 91 patients (90%). Six times in the 3-l SF-PEG group and 5 times in the 4-l PEG group the caecum was not reached. We showed equivalence between the two preparations (Table 2). The endoscopists scored the effect of the colonic lavage of the rectosigmoid

with the 3-l SF-PEG and 4-l PEG solutions as "excellent" or "good" in 40 patients (78%) versus 35 patients (69%), respectively (p=0.71). For cleansing of the complete colon this was 34 (68%) and 33 (69%) patients, respectively (p=0.79).

The computed confidence intervals for the Aronchick scale were -0.340, 0.498 and -0.485, 0.372 for the rectosigmoid and overall colon, respectively. Neither of the intervals contained +0.5, so equivalence of the 3-l SF-PEG solution and 4-l PEG solution has been shown.

	3-l SF-PEG	4-l PEG
Quality of cleansing	**n=51 (%)**	**n=51 (%)**
Rectosigmoid	**p=0.71**	
Excellent	22 (43)	19 (37)
Good	18 (35)	16 (31)
Adequate	6 (12)	13 (26)
Poor	2 (4)	2 (4)
Inadequate	3 (6)	1 (2)
Overall colon	**p=0.79**	
Excellent	17 (34)	16 (33)
Good	17 (34)	17 (36)
Adequate	11 (22)	11 (23)
Poor	2 (4)	3 (6)
Inadequate	3 (6)	1 (2)

Table 2. Quality of bowel-cleansing preparation in patients. One overall colon result is missing in the 3-l PEG group and three results in the 4-l PEG group.

SF=sulphate-free; PEG=polyethylene glycol.

There was no difference in effectiveness of the bowel preparation between colonoscopies performed in the morning or in the afternoon and between the 3-l SF-PEG and 4-l PEG groups, although there was a small tendency towards overall colonoscopy, which failed to reach statistical significance (morning "excellent" or "good" in 50 out of 67 patients (75%) versus

afternoon 19 out of 33 (57.5%) patients, p=0.10). Diverticulosis was diagnosed in 39 patients (38%); no difference in the cleansing effect of the rectosigmoid (p=0.26) and complete colon (p=0.22) was found overall and in the 3-l and 4-l PEG groups. The demographic and other endoscopic findings did not influence the cleansing results.

Patients' acceptability and preference

There was no significant difference in patient compliance between the group that ingested a 3-l SF-PEG solution and the group that ingested a 4-l PEG solution: 41 (82%) and 38 (76%), respectively (p=0.61) (Table 3). Mean time from the last preparation intake to colonoscopy was shorter in the group prepared with 3-l SF-PEG: 10.6 h versus 15.5 h (p <0.0001), and the mean volume of other fluids consumed before colonoscopy was smaller: 475 ml versus 850 ml (p=0.0002). No significant difference was found in taste, which was assessed as "very good" 4 (3.9%) versus 2 (1.9%) times and "not good, but tolerable" 19 (18.6%) versus 15 (14.7%) times in the groups prepared with 3-l SF-PEG and 4-l PEG, respectively (p=0.11). Both groups of patients found that the bowel preparation was easy to tolerate, no differences in frequency or intensity of the abdominal cramps being detected between the two PEG solutions (p=0.62). No abdominal cramps were reported in 29 (28.4%) versus 32 (31.3%) patients and mild cramps in 17 (16.6%) versus 14 (13.7%) patients prepared with 3-l and 4-l PEG, respectively.

	3-l SF-PEG	4-l PEG	p-value
Amount of ingested PEG (%)	100	100	0.6097
Volume of other fluids consumed before colonoscopy (ml)	300	1000	0.0002
Time between bowel preparation and colonoscopy (h)	12	17	0.0000

Table 3. Medians of bowel preparation parameters.

SF=sulphate-free; PEG=polyethylene glycol; h=hours.

Patients who received a 3-l SF-PEG lavage preferred the same preparation for future colonoscopy as compared with those who received a 4-l PEG lavage; 17 (33%) and 4 (8%), respectively (p=0.03).

DISCUSSION

Adequate bowel preparation for colonoscopy is essential and has a considerable impact on the quality of colon cleansing and diagnostic yield of colonoscopy. In this study we sought to determine whether a small volume of SF solution provides better efficacy and better toleration than a large volume of PEG solution, as was suggested in some studies [18,22,26]. No difference was found in the quality of the bowel preparation between patients who received a 3-l SF-PEG or 4-l PEG solution. Our findings are consistent with the results of another study, which demonstrated equally good effectiveness and toleration of these two preparations [27]. Those results are in contrast to the findings of another study, which demonstrated superior cleansing with a solution of 4-l PEG compared with 3-l SF-PEG for elective colonoscopy [10]. However, these investigators used a divided two-step preparation in accordance with the schedule of colonoscopies: a half dose in the afternoon on the day before the examination and the other half in the morning before the colonoscopy. The timing of the bowel preparation is suggested to play a role in the effectiveness of bowel cleansing prior to colonoscopy. In some studies it was found that the quality of cleansing was significantly better when preparation was done on the same day as the colonoscopy rather than when the whole preparation was carried out the day before the examination [6,23,28]. In another study an identical regimen was used for bowel preparation the evening before, irrespective of the timing of the colonoscopy, and no difference in bowel cleansing was found [29]. Although we adapted the bowel preparation according to the time of the procedure, we did not find any difference in efficacy of the bowel preparation between morning and afternoon sessions.

Despite consumption of more additional fluids before colonoscopy and more time being given between completion of bowel preparation and colonoscopy (allowing more fluid loss) in the 4-l PEG group, no significant difference was found in the quality of colon cleansing between the two groups.

In one study it was suggested that older age, female gender, a body mass index (BMI) ≤25, diverticular disease and constipation correlated with a difficult colonoscopy [30]. Although the clinical experience is that in patients with diverticula characteristic faecal material can sometimes be seen, we could not demonstrate any difference in cleansing between patients with or without diverticula, as was shown in a previous study [15].

Patients with constipation have a longer colon transit time than healthy volunteers [24] and could therefore have a less clean colon. We did not find a relationship between defecation frequency and a clean colon.

In this study we found no difference in compliance between entire bowel-cleansing preparation in patients prepared with 3-l SF-PEG and 4-l PEG solutions.

However, patients preferred the 3-l SF-PEG cleansing, with 33% of patients saying they would be willing to use the same preparation again, compared with only 8% in the 4-l PEG group. This has already been suggested elsewhere [31].

Our results showed no significant differences in taste, abdominal cramps and overall tolerance between the two PEG solutions. This is in agreement with an earlier study, which did not find any statistical difference in the overall acceptability, taste and cramping between the two solutions [32].

In summary, both preparations proved to be comparable in their cleansing effectiveness and are well tolerated by patients. However, patients prefer a preparation with a smaller volume of solution. Improving the acceptability of colonic preparation could improve patients' compliance and the quality of the colonoscopy.

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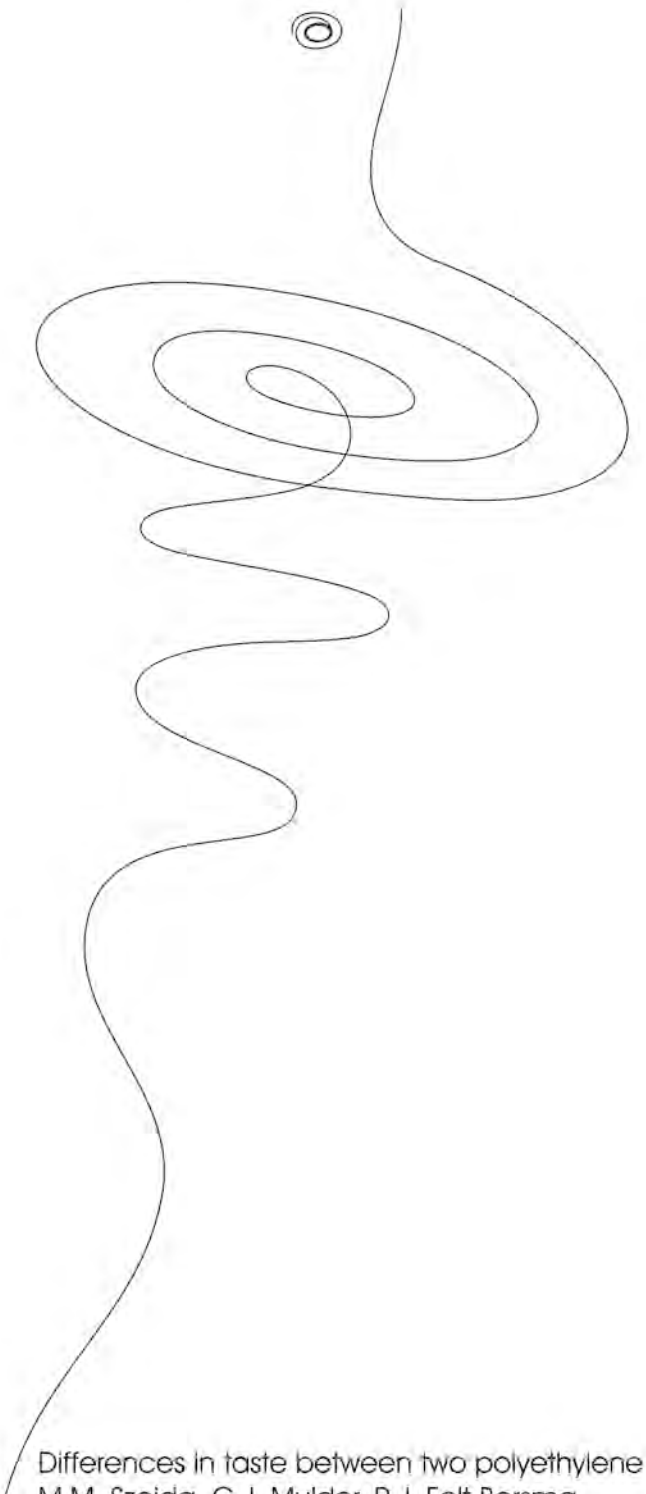

Differences in taste between two polyethylene glycol preparations.
M.M. Szojda, C.J. Mulder, R.J. Felt-Bersma
J Gastrointestin Liver Dis. 2007;16:379-81.

Abstract

Background and aims

Polyethylene glycol preparations (PEG) are increasingly used for chronic constipation in both adults and children. There are some suggestions that PEG 4000 with orange flavour *(Forlax®)* tastes better than PEG 3350 which contains salt *(Movicolon®).* Poor taste is an important factor for non-compliance and is one of the leading causes of therapy failure. The aim of the study was to compare the taste of two commonly used polyethylene glycol preparations, PEG 4000 and PEG 3350

Methods

A double-blind, cross over randomised trial. Hundred persons were recruited by advertisement. All tasted both preparations without swallowing. After tasting each of the preparations, the mouth was rinsed. Then a score on a 5-point scale was given for both preparations.

Results

100 volunteers were included (27 males and 73 females, mean age 36). The taste score for PEG 4000 (mean 3.9, SD 0.7) was significantly better than for PEG 3350 (mean 2.7, SD 0.7) ($p<0.0001$, Wilcoxon matched pairs test). No difference in gender or age was observed. The volunteers which tasted PEG 3350 first appreciated it more than when tasted second ($p<0.0001$). The order in which volunteers tested PEG 4000 had no influence on the taste results.

Conclusion

PEG 4000 tastes better than PEG 3350. This may have implications for patient compliance and effectiveness of treatment in patients with chronic constipation.

INTRODUCTION

Constipation is one of the most common health problems, with a negative impact on quality of life. The frequency of constipation is not exactly known, it varies from 2-4% for infrequent defecation to more than 10% for excessive straining and up to 20% in nursing homes [1]. The overall incidence of constipation in adults in the Western world is estimated at 15% [2].

The most common causes for chronic constipation are general causes like low fibre diet, low fluid intake and physical inactivity [3-6]. Medication (anticholinergic, antidepressants, opioid analgetics, NSAID) [7], neurological and psychiatric disorders and idiopathic chronic constipation are other common causes [8]. There are also socioeconomic, sex, regional and national differences in prevalence of constipation [9,10]. Constipation significantly impairs health-related quality of life and only 66% of the patients consider their treatment as sufficient [11]. Functional constipation is defined according to the Rome III criteria, were both slow transit and difficult evacuation are considered [12].

Mild constipation can be managed with non-pharmacological intervention like fibre-enriched diet which increases faecal bulk, increased fluid intake (>2 litters) and a more active lifestyle. Further physiotherapy, biofeedback and yogic breathing can be helpful in relaxing the pelvic floor and thus promoting defecation and evacuation. More severe constipation requires treatment with laxatives. There are several types of laxatives: bulk-forming, osmotic and stimulant [13]. Bulking agents include methylcellulose, psyllium and polyethylene glycol.

Patients suffering from severe chronic functional constipation require a long-term, regular therapy with laxatives. Although the literature is very scarce on this subject we know that the taste of laxatives is often not appreciated by patients [14,15]. Many patients find it difficult to deal with poor tasting medication when prescribed. This counts especially for geriatric and paediatric patients with chronicle medication use. Such problems result in

high incidence of non-compliance which is one of the leading reasons of therapy failure [15,17].

Polyethylene glycol based products (PEG) are iso-osmotic solutions, which are effective [18-21], safe [22-14] and increasingly used in chronic constipation in both adults and children. It has been suggested that the taste of PEG 4000 was appreciated by the patients [15].

The aim of the study was to compare the taste of two commonly used polyethylene glycol preparations, PEG 4000 *(Forlax®)* and PEG 3350 *(Movicolon®)*.

Methods

Study design

A total of 100 healthy volunteers recruited by advertisement were included in a double blind, randomized cross over study. All volunteers were invited to taste both preparations. After tasting the first 25ml without swallowing, the mouth was rinsed and the second preparation was tasted without swallowing. Then a score on a 5-point scale was given (1=very bad taste, 5=very good taste) for both preparations. It was investigator initiated study. Permission nr 06/081 was granted from the central medical ethics review board of the VU University Medical Centre.

Polyethylene glycol preparations

PEG 4000 *(Forlax®)* consists of 10g macrogol 4000 per sachet, is an orange-grapefruit flavoured, gentle acting osmotic laxative. It contains no extra salt and electrolytes. It is neither absorbed nor metabolized. PEG 3350 *(Movicolon®)* contains 13.125g macrogol 3350, sodium hydroxide carbonate 178.5mg, sodium chloride 350.7mg, potassium chloride 46.6mg and citron aroma. The extra electrolytes cause taste of this laxative.

Each dosis of the preparations was dissolved in 150 ml of cold water conform the instructions.

Statistics

All results were analyzed in Wilcoxon matched pairs test (GraphPad InStat Software, SanDiego, Ca, USA).

RESULTS

All 100 volunteers were included (27 males and 73 females, mean age 36, range 18-65). Eighty-four volunteers preferred the taste of PEG 4000, 9 found no differences in taste between the two preparations and only 7 preferred the taste of PEG 3350. The taste score for PEG 4000 (mean 3.9, median 4, SD 0.7) was significantly better than PEG 3350 (mean 2.7, median 3, SD 0.7) ($p<0.0001$) (Figure 1). There was no difference in gender or age observed.

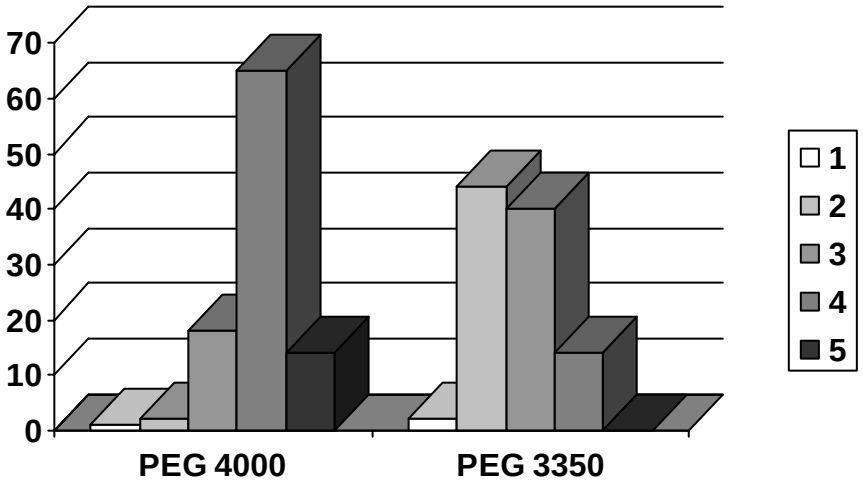

Figure 1. Taste scores (1=very poor taste, 5=very good taste) for PEG 4000 and PEG 3350 given by the volunteers ($p<0.0001$).

The volunteers who tasted PEG 3350 first appreciated the taste significantly more than persons which tasted it second ($p<0.0001$). The order in which volunteers tested PEG 4000 had no influence on the taste results of this preparation
(Table 1).

scores	PEG 4000 first tried	PEG 4000 second tried	PEG 3350 first tried	PEG 3350 second tried
1	0	1	0	2
2	0	2	5	39
3	9	9	32	8
4	34	31	13	1
5	7	7	0	0
mean	3.96	3.82	3.16	2.16
p	**0.3161**	**0.3161**	**<0.0001**	**<0.0001**

Table 1. Taste scores according to the sequence of tasting of the PEG solutions.

DISCUSSION

This study showed that PEG 4000 tastes better in comparison to PEG 3350, independent of gender or age. In addition, PEG 3350 was even less appreciated when PEG 4000 was tasted first. The sequence of tasting did not differ for PEG 4000. In spite of rinsing the mouth, the PEG 3350 was overall less appreciated.

Causes of non-compliance in long-term medical treatment are the medications´ taste and dosage frequency. It would be helpful to switch to another better tasting preparation when patients dislike the taste. However, this study has only demonstrated a preference for PEG 4000 during a single intake of 25 ml of fluid. Weather this difference is so outspoken after months or years is unknown. We chose for this method without swallowing since taste was the issue and not the volume load; the volume of PEG as a laxative is only 150-300 ml daily. The odour of the preparation may also influence the judgement of the volunteers.

We could expect however that PEG 4000 should be more appreciated by the patients and as a result may be more effective in long-term treatment. At the other hand, mixing with other fluids might also compensate for poor taste.

In conclusion, the taste of PEG 4000 is generally more appreciated then the taste of PEG 3350. When patients complain about the taste of their PEG preparation switching may be an alternative.

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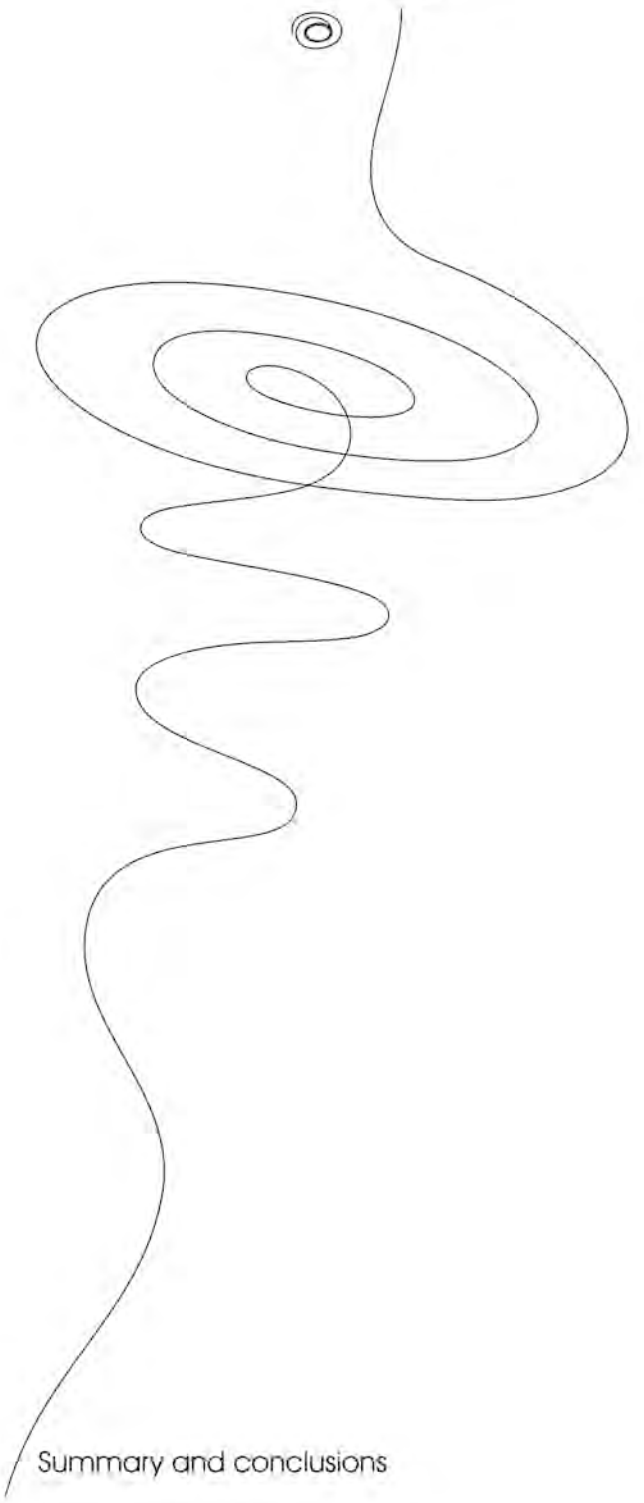


Summary and conclusions

Summary and conclusions

The aim of the work in this thesis was to study the epidemiology, diagnostic procedures and therapy of anorectal and colorectal diseases. Several topics were studied to approach this goal. Some studies analyzed acceptability and tolerability of the investigations and treatments, since patient compliance is important for a successful result.

Anorectal complaints are debilitating and form a frustrating problem for both patients and their doctors. Patients are often referred for anorectal function evaluation (AFE). The aim of the study in **chapter 2** was to determine which referrals of the patients with anorectal symptoms for AFE were indicated to establish a diagnosis with subsequent therapeutic consequences. In a retrospective study from 216 referred patients, only 65% of referrals were indicated. AFE has therapeutic consequences for some diagnoses like in faecal incontinence without diarrhea, 3rd degree sphincter rupture, pre-operative for stoma or re-anastomosis, fistula, fissures and sometimes constipation. Anal ultrasound is always indicated in patients with fistula, manometry and rectal compliance only when impaired continence reserve is suspected. In 80% the advice was followed: in 35% of the patients the complains were improved and 57% of the patients was reassured. The effect of advices was also studied and consisted of dietary, physiotherapy, medications and surgery. On a VAS scale (1 to10) complains improved an average of 3.2 points. Most patients tolerated AFE very well and perceived minimal discomfort during AFE. It is important to provide better information for referring doctors about diagnostic possibilities of the AFE to ensure the most optimal advantage of indicated referrals.

Therapy for faecal incontinence remains a difficult issue and is often inadequate. Temperature–controlled radiofrequency energy (SECCA) is a therapy with favorable results in few open studies. In **chapter 3** we report

the promising results of this relatively new therapeutic method. The mode of action of this treatment seems to be the increased rectal sensitivity.
We treated 11 women with long existing faecal incontinence complains. In three months time, 6 of them improved and this improvement persisted during the follow-up of 1 year. Anal manometry and rectal compliance showed no significant changes between those who improved and those who did not. The treatment was well tolerated and side effects such as local haematoma, minor bleeding, pain persisting 1-3 weeks and laxatives-related diarrhea during 1-3 weeks were acceptable. However, more investigations and placebo-controlled studies are warranted with a larger number of patients and longer follow-up.

Irritable bowel syndrome (IBS) is an invaliding common functional disorder. IBS has a wide range of symptoms, though specific symptoms are lacking. In this way IBS can easily mimic other diseases in the (lower) abdomen, thus causing delay in establishing the right diagnosis and giving the appropriate treatment. We have studied these difficulties in **chapter 4**. Hundred and one patients with proven endometriosis were included from the gynecological outpatients clinic. By means of a questionnaire patients who complied with Rome III criteria were referred to our gastroenterological outpatient clinic. Fifteen percent of the patients had additional IBS and 14% had functional constipation without IBS. Of the 22 patients finally presented to the gastroenterologist, 5 had a significant stenotic rectosigmoid and underwent surgical resection of the involved bowel segment with primary anastomosis. Four of the operated patients improved clinically and had no symptoms, the fifth had a stenotic anastomosis and was successfully dilated. The remaining 17 patients were treated conservatively with laxatives and fiber. Defecation symptoms improved in 86% and pain was reduced in 64%. For many women with endometriosis and additional IBS or chronic constipation good cooperation between gynecologist and gastroenterologist is essential

and can give symptom relief in a shorter time. However, for many women with endometriosis management of pain is still insufficient.

The prevalence of diverticulosis and subsequently diverticulitis is increasing the last decades. Diverticulosis increases with age. It is estimated less than 10% in those under the age of 40 and increases to 65-70% in those above 65 years of age. Therefore, diverticulitis is also increasing. Predominant western lifestyle increases this pathology, with all their complications and consequences. In **chapter 5** we review the literature concerning the pathogenesis, prevalence, diagnostic procedures and therapeutic options of diverticulitis.

In the literature the relationship between diverticular disease and colorectal cancer has been suggested. Considering the increasing prevalence of diverticular disease and incidence of colorectal cancer in younger patients, this might have consequences for colorectal cancer surveillance. In **chapter 6** we studied the possible risk for colorectal neoplasia or polyps in 4,241 colonoscopies of patients with diverticulosis and diverticulitis. Diverticula, diverticulitis, and polyps were found in 25%, 2% and 30% of the colonoscopies, respectively. However, no association was found between patients with polyps and those with or without diverticulosis. Colorectal cancer was found in 9% of the patients. We observed a negative relation between diverticulosis and colorectal cancer and invasive adenocarcinoma. We could not find any association between polyps, diverticulosis or diverticulitis and increased risk for colorectal cancer. A drawback of the study was the underreporting of polyps and their possible earlier removal as well as the lack of long term follow-up.

In **chapter 7** the relationship between diverticulitis and colorectal carcinoma was studied in a retrospective, longitudinal study. In 288 patients the colonoscopies and pathology registry PALGA of the patients admitted

to our hospital with diverticulitis were analyzed. Colorectal cancer and colonic adenomas were detected in 1,7% and 6,3% of the patients, respectively. However, again this study showed a lower prevalence of colorectal cancer and colonic adenomas in patients with diverticulosis. Underreporting is possible due to the retrospective character. More attention and further prospective, longitudinal studies are warranted about this subject. So far, a strong relationship does not seem likely.

Patient compliance is an important factor for successful establishing a diagnosis or following a therapy. Colonoscopy is still the most important tool in screening and surveillance programs of patients with colorectal disease. Adequate preparation of the colon is important for good quality and safety of the examination. **Chapter 8** refers to a prospective, randomized study comparing the effectiveness of two preparation in 110 patients referred for elective colonoscopy with 3 litre sulphate-free polyethylene glycol solution (SF-PEG) or 4 litre PEG. Data was analyzed with respect to stool frequency, medication, concomitant diseases and diverticular disease diagnosed during the investigation. No differences were found between two regimes of preparation in cleansing the rectosigmoid or complete colon. Moreover diverticulosis and constipation had no influence on quality of cleansing. Both preparations had comparable acceptability and tolerability of the colon cleansing, however patients preferred cleansing with a smaller volume of solution. This can improve the compliance of the patients and improve their acceptance for colonoscopy.

Treatment of chronic constipation is not always easy and usually life-long. Laxatives often do not have an encouraging taste to use it for a long time. For this reason poor compliance and effectiveness of the treatment is only in 66% of patients sufficient. **Chapter 9** describes a study, which compared the taste of two polyethylene glycol preparations for patients suffering from constipation. In a double blind, cross over, randomized trial 100 volunteers

tasted both preparations. They gave score on 5-point scale of taste. The taste score for PEG 4000 was significantly better than for PEG 3350. Whether this results in long-term better compliance for PEG 4000 can not be established from these data.

Conclusions

This thesis allows several conclusions on epidemiological, diagnostic and therapeutic field of anorectal and colorectal diseases.

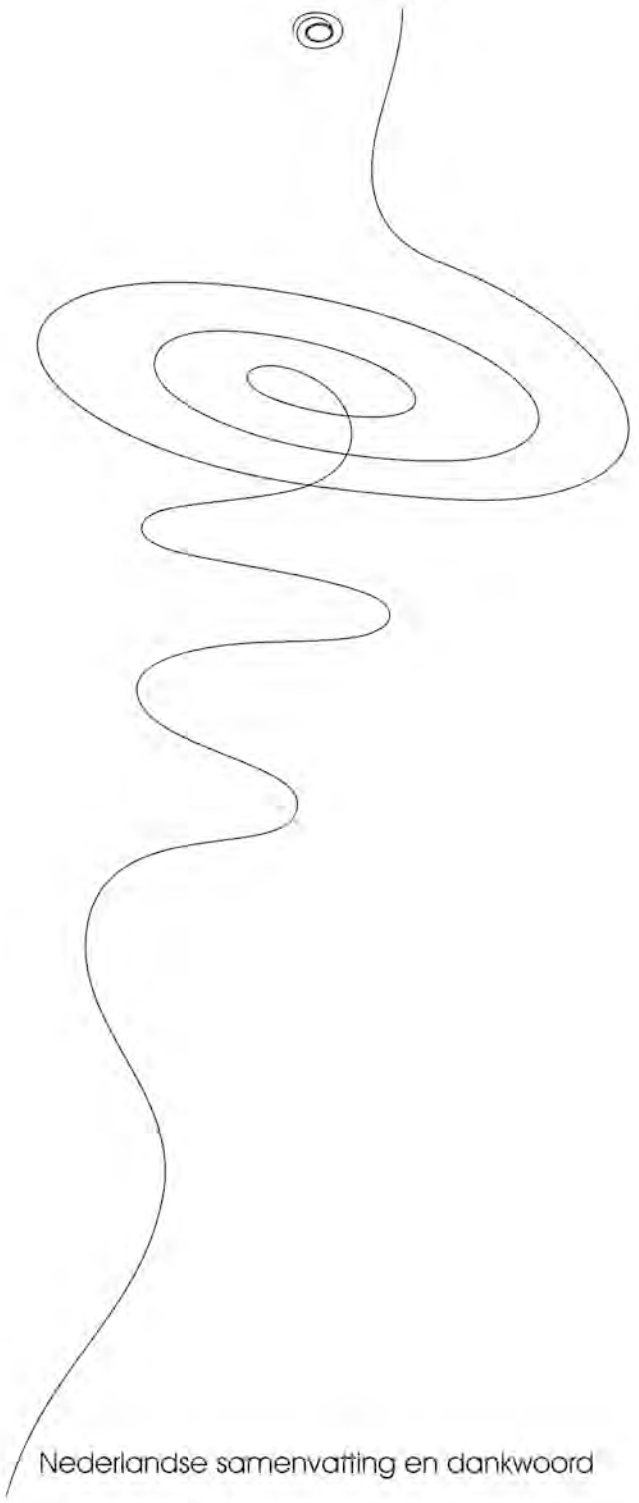
1. The anorectal function evaluation has therapeutic consequences only for some diagnoses. Good education and awareness of anorectal diseases is important for prompt treatment and / or indicated referral.
2. Temperature–controlled radiofrequency energy can be a new therapy for faecal incontinence in the near future.
3. In patients with endometriosis and in addition IBS or chronic constipation gastroenterological consult can contribute to better symptom relieve. The gynaecologist is also an important partner for the gastroenterologist.
4. Diverticulosis and diverticulitis form no increased risk for colorectal cancer.
5. Success in treatment depends on good compliance of the patients, so palatability and amount of volume intake are important issues.

Implications

More education in anorectal disorders is necessary and problem orientated pelvic floor units will be developed.
New therapies for faecal incontinence will emerge, since none of the existing ones are adequate. SECCA may be one of them. This method has shown a promising effect in USA, where this treatment has already 5 years

follow-up and there are many new studies published. We have already started prospective, longitudinal, randomised study.
Interest in diverticular disease and diverticulitis is growing, since the disease is so widespread and can have a (life) threatening course. More longitudinal, prospective studies are warranted concerning different aspects of diverticulitis.
At last, patient compliance is a very important issue which will receive even more attention in the future. Not only taste, but also other life style issues will be introduced.

11



Nederlandse samenvatting en dankwoord

Samenvatting

Het doel van de studies in dit proefschrift was de epidemiologie, diagnostiek en therapie van anorectale en colorectale aandoeningen te onderzoeken. Om dit doel te bereiken hebben wij een aantal onderwerpen bestudeerd. In enkele studies hebben wij de acceptatie door patiënten van de onderzoeken en behandelingen geanalyseerd, aangezien dit belangrijk is voor een succesvol resultaat.

Anorectale klachten zijn buitengewoon hinderlijk en kunnen sociaal isolerend zijn. Zij vormen een bron van frustratie voor zowel patiënten als artsen. Veel patiënten worden verwezen voor anorectaal functie onderzoek (AFO). Het doel van de studie in **hoofdstuk 2** was vast te stellen welke van de verwijzingen voor AFO van patiënten met anorectale klachten daadwerkelijk geïndiceerd zijn, teneinde een diagnose te kunnen stellen met vervolgens therapeutische consequenties.
In een retrospectieve studie met 216 verwezen patiënten, waren slechts 65% van de verwijzingen geïndiceerd. AFO heeft therapeutische consequenties voor een aantal diagnosen zoals faecale incontinentie zonder diarree, 3e graads sfincter ruptuur, preoperatief voor stoma of re-anastomose, fistula, fissuren en sommige vormen van obstipatie. Anale endoechografie is altijd geïndiceerd bij patiënten met fistula. De manometrie en rectale compliantie zijn alleen geïndiceerd bij verdenking op een verminderde continentie reserve. Tachtig procent van de gegeven adviezen werden opgevolgd: bij 35% van de patiënten waren de klachten verbeterd en 57% van de patiënten waren tevreden. Het effect van de adviezen werd ook bestudeerd. De adviezen bestonden uit dieet, fysiotherapie, medicatie en/of chirurgie. Op de VAS schaal (1 tot 10) waren de klachten gemiddeld 3.2 punten verbeterd. De meeste patiënten hadden AFO goed verdragen en er was nauwelijks sprake van ongemak tijdens het onderzoek. Het verstrekken van betere informatie over de

diagnostische mogelijkheden van AFO is belangrijk voor verwijzende artsen teneinde geïndiceerde verwijzingen te garanderen.

De behandeling van fecale incontinentie vormt een groot probleem en is vaak teleurstellend. Temperatuur-gecontroleerde radiofrequente energie (SECCA) is een behandeling met gunstige resultaten in een aantal open studies. In **hoofdstuk 3** melden wij de veelbelovende resultaten van deze relatief nieuwe therapeutische methode. Een verhoogde rectale gevoeligheid lijkt het werkingsmechanisme van deze behandeling te zijn. Elf vrouwen met lang bestaande fecale incontinentie klachten werden behandeld. Drie maanden na de behandeling waren bij 6 patiënten de klachten verbeterd en dat effect hield aan gedurende de hele periode van de 1 jaar follow-up. Anale manometrie en rectale compliance lieten geen significante veranderingen zien tussen de verbeterden en zij die niet verbeterd waren. De behandeling werd zeer goed verdragen en enkele bijwerkingen (locaal hematoom, wat bloedverlies, lokale pijn met aanhoudende duur van 1-3 weken en laxantia gerelateerde diarree van 1 tot 3 weken) waren acceptabel. Echter, verder onderzoek en placebo gecontroleerde studies met een groter aantal patiënten en langere follow-up zijn nodig.

Irritable bowel syndrome (IBS) is een invaliderende veel voorkomende functionele aandoening. IBS heeft een groot spectrum van symptomen, maar heel specifieke symptomen ontbreken. Hierdoor kan IBS heel gemakkelijk andere ziektes simuleren in de (onder)buik, en zo vertraging veroorzaken in de diagnostiek en juiste behandeling. Deze problemen hebben wij onderzocht in **hoofdstuk 4**. Van de polikliniek gynaecologie werden 101 patiënten met bewezen endometriose geincludeerd. Met behulp van vragenlijsten werden patiënten die voldeden aan de Rome III criteria voor IBS en/of obstipatie naar onze polikliniek maag-, darm- en leverziekten verwezen. Vijftien procent van de patiënten hadden IBS en

14% had functionele constipatie zonder IBS. Uiteindelijk werden 22 patiënten gezien door de maag-, darm- en leverarts. Vijf hadden een significante stenose in het rectosigmoid en ondergingen een chirurgische resectie met primaire anastomose. Vier van de geopereerde patiënten waren klinisch verbeterd en hadden geen klachten, de vijfde ontwikkelde een naadstenose en werd succesvol gedilateerd. De andere 17 patiënten werden conservatief behandeld met laxantia en vezels. De defecatie klachten verbeterden in 86% en de pijn verminderde in 64%. Goede samenwerking tussen gynaecoloog en maag-, darm- en leverarts is onmisbaar voor de vele vrouwen met endometriose en bijkomende IBS of chronische obstipatie. Dit kan verlichting geven van de klachten in kortere tijd. Echter, voor veel vrouwen met endometriose is behandeling van de pijn nog steeds onvoldoende.

De prevalentie van diverticulose is de laatste decennia gestegen. Diverticulose neemt toe met de leeftijd en wordt geschat op minder dan 10% onder de 40 jaar en neemt bij toe bij 65 plussers tot 60-70%. Hierdoor neemt de prevalentie van diverticulitis ook toe. Een predominant westerse levensstijl verhoogt het risico voor deze pathologie, met al zijn complicaties en gevolgen. **Hoofdstuk 5** geeft een literatuuroverzicht betreffende pathogenese, prevalentie, diagnostiek en therapeutische mogelijkheden.

In de literatuur wordt een relatie tussen diverticulose/diverticulitis en colorectaal carcinoom gesuggereerd. Gezien de stijgende prevalentie ook bij jongere mensen kan dat consequenties hebben voor surveillance. In **hoofdstuk 6** hebben wij het mogelijke risico onderzocht voor colorectaal carcinoom of poliepen in 4241 colonoscopieën bij patiënten met diverticulose en/of diverticulitis. Divertikels, diverticulitis en poliepen werden respectievelijk in 25%, 2% en 30% van de colonoscopieën gevonden.
Er werd geen associatie tussen patiënten met poliepen en aan afwezigheid van diverticulose gevonden. Colorectaal carcinoom werd bij 9% van de

patiënten gevonden. We zagen een negatieve correlatie tussen diverticulose met colorectaal carcinoom en met invasief adenocarcinoom. Wij konden geen associatie vinden tussen poliepen, diverticulose of diverticulitis en een verhoogde risico voor colorectaal carcinoom. Een nadeel van de studie was zowel de onderreportage van poliepen als mogelijke eerdere verwijdering hiervan, naast een onvoldoende lange follow-up.

In **hoofdstuk 7** werd de relatie tussen diverticulitis en colorectaal carcinoom in een retrospectieve, longitudinale studie onderzocht. De colonoscopie verslagen en het pathologie register PALGA van 288 patiënten die opgenomen waren in het ziekenhuis wegens diverticulitis werden geanalyseerd. Colorectaal carcinoom en adenomen van het colon werden respectievelijk in 1.7% en 6.3% van de patiënten gevonden. Echter, ook deze studie liet een lagere prevalentie zien van colorectaal carcinoom en adenomen in patiënten met diverticulitis.
Onderreportage is mogelijk gezien het retrospectieve karakter van de studie. Meer aandacht en verdere prospectieve, longitudinale studies zijn nodig. Tot nu toe lijkt een sterk verband tussen diverticulitis en colorectaal carcinoom niet aanwezig.

Goede medewerking van de patiënten is een belangrijke factor voor succesvolle diagnostiek en behandeling. De colonoscopie is het voornaamste instrument in screening en surveillance programma's voor patiënten met colorectale aandoeningen. Adequate voorbereiding van het colon voor een goede kwaliteit en veiligheid van het onderzoek is belangrijk. **Hoofdstuk 8** betreft een prospectieve, gerandomiseerde studie, die de effectiviteit van twee preparaten vergelijkt, 3 liter sulfaat-vrij polyethyleen glycol en 4 liter polyethyleen glycol, bij 110 patiënten verwezen voor electieve colonoscopie. De data werden geanalyseerd met betrekking tot defecatie frequentie, medicaties, andere ziekten en

diverticulose gediagnosticeerd tijdens de colonoscopie. Er werd geen verschil in kwaliteit van voorbereiding van rectosigmoid of colon gevonden tussen beide schema's. Bovendien hadden diverticulose en obstipatie geen invloed op de kwaliteit van de voorbereiding. Beide preparaten waren vergelijkbaar qua acceptatie en tolerantie voor colon voorbereiding, hoewel patiënten de voorkeur hadden voor voorbereiding met een kleinere hoeveelheid vloeistof. Dit kan de compliantie en acceptatie van de patiënten voor colonoscopie verbeteren.

De behandeling van chronisch obstipatie is niet altijd gemakkelijk en meestal levenslang. De smaak van laxantia nodigt meestal niet uit tot langdurig gebruik. Dit is een reden van lage compliantie en waardoor de effectiviteit van behandeling slechts in 66% effectief is. **Hoofdstuk 9** beschrijft een studie die de smaak vergelijkt van twee polyethyleen glycol (PEG) preparaten voor patiënten met obstipatie. In de dubbel-blind, cross over, gerandomiseerde studie proefden 100 vrijwilligers beide preparaten. De smaak-scores werden op een 5-punts schaal aangegeven. De smaak-score voor PEG 4000 was significant beter dan voor PEG 3350. Of deze resultaten op langere termijn zorgen voor een betere compliantie betreffende PEG 4000, kan met deze data niet beoordeeld worden.

Conclusies

Uit dit proefschrift kunnen enkele conclusies getrokken worden betreffende epidemiologie, diagnostiek en therapie van anorectale en colorectale aandoeningen.

1. Anorectaal functie onderzoek heeft alleen therapeutische consequenties voor sommige diagnosen. Goede educatie en kennis van anorectale aandoeningen is belangrijk voor de juiste behandeling en/of geïndiceerde verwijzing.

2. Temperatuur gecontroleerde radiofrequente energie (SECCA) kan in de nabije toekomst een nieuwe therapie vormen voor fecale incontinentie.
3. Bij patiënten met endometriose en IBS of chronische obstipatie kan een consult bij de maag-,darm-, en leverarts in een verbetering van de klachten resulteren.
4. Diverticulose en diverticulitis vormen geen risico voor colorectaal carcinoom.
5. Succes van behandeling is afhankelijk van goede compliantie van patiënten; zowel smaak als volume van de medicatie zijn belangrijk.

Implicaties

Meer educatie over anorectale aandoeningen is noodzakelijk en probleem gerichte bekkenbodemcentra zullen verder ontwikkeld worden.
Nieuwe therapeutische opties voor fecale incontinentie nemen toe, daar geen van bestaande behandelingen echt voldoende zijn. SECCA kan een van die opties zijn. Deze methode liet positieve effecten zien in de VS, waar deze behandeling al 5 jaar follow-up heeft en enkele nieuwe studies gepubliceerd zijn. Wij zijn al begonnen met een longitudinale, prospectieve, gerandomiseerde studie.
Interesse in diverticulose en diverticulitis neemt toe, aangezien deze ziekte vaak voorkomt en een (levens)bedreigend beloop kan hebben. Meer longitudinale, prospectieve studies zijn nodig met betrekking tot verschillende aspecten van diverticulitis.
Tenslotte is de compliantie van de patiënten een heel belangrijk punt en zal in de toekomst nog meer aandacht krijgen. Niet alleen smaak en hoeveelheid, maar ook andere levensstijl aspecten zullen een rol spelen bij diagnostiek en therapie.

Dankwoord

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Curriculum Vitae:

The author is born on September 16, 1976 in Katowice, Poland.
After graduating from high school (No3 A. Mickiewicza) in Katowice in 1995, she proceeded with her medical study at the Silesian University of Medicine in the same city, where she obtained her degree as a medical doctor (MD) in 2001.
During the period of internship from 2001 to 2002 she worked in the Department of Internal Medicine of the General Hospital in Katowice; in March 2003 she started her fellowship in internal medicine in the General Hospital in Siemianowice Śląskie.
In November 2005 she immigrated to the Netherlands to expand her medical training specifically in her main field of interest: gastroenterology. She started her work as research physician in Department of Gastroenterology (prof. dr. C.J.J. Mulder) in February 2006 under supervision of dr. R.J.F. Felt-Bersma at the Vrije Universiteit Medisch Centrum in Amsterdam, which resulted in this thesis.
After her fellowship in the Department of Internal Medicine that started in January 2008, she will continue her fellowship in gastroenterology in January 2010.
She is married with Frank and they are expecting their first child.