Chapter 6

COLORECTAL VISCERAL PERCEPTION IN DIVERTICULAR DISEASE

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Abbreviations:

ADD: Asymptomatic Diverticular Disease
SUDD: Symptomatic Uncomplicated Diverticular Disease
IBS: Irritable Bowel Syndrome
MDP : Minimum Distension Pressure
GLM: General Linear Model for Repeated Measures

ABSTRACT

Background & Aims: The pathogenesis of asymptomatic diverticular disease (ADD) and symptomatic uncomplicated diverticular disease (SUDD) has not been elucidated. The aim of our study was to assess whether altered visceral perception or abnormal compliance of the colorectal wall play a role in these clinical entities.
Methods: Using a dual barostat device, sensations were scored and compliance curves were obtained using stepwise intermittent isobaric distensions during the preprandial period in the rectum and during the pre- and postprandial period in the sigmoid in 10 ADD patients, 11 SUDD patients and 9 healthy controls.
Results: In the rectum perception was increased in the SUDD group as compared to controls ($p = 0.010$) and ADD group ($p = 0.030$). Rectal compliance curves were not different between groups. In the sigmoid colon, perception in the pre- and postprandial period was increased in SUDD as compared to controls ($p = 0.018$) but not when compared to ADD.
In the rectum and the sigmoid colon, perception in the ADD group was not different from controls. Both in the rectum and in the sigmoid volume-pressure curves had comparable slopes (compliance) in all groups. However, pressure-volume curves were shifted downwards in SUDD as compared to ADD in the preprandial period ($p = 0.026$).
Conclusion: Symptomatic but not asymptomatic uncomplicated diverticular disease is associated with heightened perception of distension, not only in the diverticula-bearing sigmoid, but also in the unaffected rectum. This hyperperception is not due to altered wall compliance.

Keywords:
Diverticular disease; visceral perception; colonic wall compliance; barostat; sigmoid colon; rectum.

INTRODUCTION

Diverticular disease is a highly prevalent disorders in western countries, the incidence rising with increasing age, till 30 % above the age of 60 years. Probably 20-25% of cases go undetected, while 10-25% of patients under observation develop clinical signs of complications.[1-4] Three categories of diverticular disease can be distinguished: 1/ Asymptomatic diverticular disease (ADD), in which multiple diverticula are found at colonoscopy or barium enema, without related symptoms. 2/ Symptomatic uncomplicated diverticular disease (SUDD), in which diverticula and abdominal pain are present, with or without irregular bowel function. SUDD is also known as painful diverticular disease. 3/ Symptomatic complicated diverticular disease: diverticular disease in which hemorrhage, peridiverticulitis, abscess, perforation, fistula or bowel obstruction has developed.[5]

The pathogenesis of diverticular disease is still uncertain but is thought to be multifactorial. Patients with diverticular disease use significantly smaller quantities of dietary fibre than age-matched controls and geographic regions with low fibre intake have higher incidence rates of diverticular disease.[6-8]

Another factor thought to be involved in the pathogenesis of diverticular disease is increased phasic motility in the diverticula-bearing part of the colon, but the studies on this subject have yielded conflicting results.[9-14] A change in bowel wall structure is thought to be another component to the development of diverticular disease.[15 16] Symptoms in SUDD can be indistinguishable from those reported by patients with the irritable bowel syndrome (IBS). However, there are no data that indicate that IBS is a precursor of diverticular disease.[3 15 17] In IBS, increased visceral perception, with a decreased volume and pressure threshold for urge and or pain, was found in the rectum as well as at other intestinal levels and this abnormality is thought to be a hallmark of IBS.[18-21]

Only one study was performed that examined wall characteristics and perception in an unselected group of patients with diverticular disease. The techniques used in this 1969 study (including use of water-filled latex balloons) are now considered to be obsolete.[9] Nowadays, the barostat technique is considered to be the optimal tool to measure compliance and visceral perception, either by isobaric or isovolumetric distensions.[21-23]

The aim of our study was to assess sigmoid and rectal visceral perception as well as sigmoid and rectal wall characteristics in patients with asymptomatic and symptomatic uncomplicated diverticular disease and healthy controls.

METHODS

Study subjects

Eleven patients (five men and six women), mean age 56 years (range 43-68), with a clinical diagnosis of symptomatic uncomplicated diverticular disease (SUDD) were recruited from the outpatient clinic of the department of Gastroenterology at the University Medical Center Utrecht. This diagnosis was based on left lower quadrant abdominal pain, the presence of more than four diverticula in the sigmoid colon, as diagnosed by barium enema or colonoscopy, and the absence of inflammatory or bleeding complications of diverticula in the medical history. The selected patients had a relatively short history of abdominal symptoms (2 months – 6 years). Most of the patients fulfilled the Rome I symptomatic criteria for IBS, but two patients had had left lower abdominal pain for 2 and 3 months respectively and therefore did not meet the time limit of Rome I criteria (>6 months). Four of the SUDD patients were constipated as defined by the Thompson criteria for constipation.[24]

Ten patients (six men and four women), mean age 56 years (range 43-69), with a diagnosis of asymptomatic uncomplicated diverticular disease (ADD) were selected from the colonic polyp surveillance program. They were selected on the on the basis of having more than four diverticula in the sigmoid colon in the absence of abdominal complaints or complications of these diverticula in presence and past. None of them fulfilled the Rome I criteria for IBS and two were constipated as defined by the Thompson criteria.

Nine healthy controls (six men and three women), mean age 51 years (range 42-61), were recruited by advertisement and from our own files.

None of the subjects had signs of systemic or gastro-intestinal disease or a medical history of major abdominal surgery. All subjects, including patients, had normal bowel habits defined as a frequency of > 3 stools per week but < 3 a day and a soft to solid stool consistency.

None of the subjects used medication on a regular base. All participants were asked to stop all incidentally used laxatives and bulk agents one week before the start of the protocol.

Written informed consent was obtained from each subject and the Ethics Committee of the University Medical Center Utrecht approved the study protocol.

Barostat Device

A computer-driven volume-displacement device (Distender Series II Dual Drive Barostat, G&J Electronics Inc., Willowdale, Ontario, Canada) was used to inflate two polyethylene bags: one in the sigmoid colon and one in the rectum. The barostat device contained two independently

functioning cylinders acting as non-compliant bellows, each having a capacity of 1200 mL. Non-compliant tubes connected these reservoirs to the polyethylene bags. The barostat maintained a constant and pre-selected pressure level in the bag by an electro-mechanical feedback mechanism and continuously measured intrabag volume. In response to any change in pressure in the bag, the barostat injected or withdrew air to maintain the pre-selected pressure. Thus, the recorded changes in volume over time reflected changes in colonic tone.
The barostat apparatus included a built-in computer system that could be programmed to automatically perform distensions with fixed time-lag and bag pressure increments for both cylinders independently. At each pressure the barostat automatically calculated corrected volumes according to Boyle's law.
In this experiment we used the barostat to perform intermittent distensions, deflating the bag between each pressure-driven distension step, at an air flow rate of 1.9 L/min.

Colonic assemblies

A double-lumen non-compliant polyethylene tube (Dantec Medical, Skovlunde, Denmark) incorporating a polyethylene bag at 15 cm from the tip was used to perform distensions in the sigmoid colon. A similar polyethylene tube incorporating a polyethylene bag at its tip was used to perform distensions in the rectum. The channel for air injection and evacuation had an inner diameter of 6 mm in both catheters allowing an air flow of 35 ml/sec. The second channel had its side hole in the barostatic bag and this was used to measure the pressure in this bag. To each of the catheters a thin-walled (40 μm thick) polyethylene cylindrical bag, was attached. The maximum capacity of these bags was 800 ml, their maximum diameter was 10 cm (during table-top inflation) and their length 10 cm. Before each experiment, the bags, catheters and barostat were checked for air leaks by submerging the bags under water, while maintaining a constant pressure of 20 mmHg.

Study Protocol

At 8.00 a.m. participants were admitted to the clinical research center after overnight fasting. The colon was cleaned by a 1.5-L enema of polyethylene glycol and electrolytes (Klean-Prep, Norgine, Utrecht, the Netherlands). At 9.00 a.m. the sigmoid catheter incorporating the barostatic bag was placed endoscopically. The tip of the catheter was attached to the colonoscope and introduced until the tip of the catheter reached the descending colon and the bag was located in the sigmoid colon. The procedure was performed without sedation and with minimal insufflation of air. Then the second probe with the polyethylene bag at the tip was introduced

into the rectum without endoscopic assistance. Positions of the barostat bags were verified by fluoroscopy.

After introduction of the probes, all subjects were in a 30^{o} supine position during the entire recording session, and they were asked not to make unnecessary movements.

One hour after placement of the probes, the 'minimum distending pressure' (MDP) was defined for both rectal and sigmoid bag by recording the lowest pressure at which respiratory excursions were regularly recorded as changes in barostat volumes.

After another hour of baseline recording, with both bags at MDP + 2 mmHg, a series of 8 stepwise intermittent isobaric distensions (maintained for 2 min) were performed with 4-mmHg increments, deflating the rectal barostat balloon to MDP between two distensions during 2 min. The maximal pressure reached was 32 mmHg above MDP (distension step 8) or the pressure at which the subject perceived the maximal tolerable pain. After this rectal series and a 40-min baseline period at operating pressures, the same series as described above was performed in the sigmoid colon, with maximal pressure reached 28 mmHg above MDP (distension step 7) or the pressure at which the subject perceived the maximal tolerable pain, followed by a 10-min stabilizing period and a 20-min preprandial baseline recording.

Then a 600-kCal (16% protein, 49% glucose, 35% fat) liquid meal (Nutridrink, Nutricia, Zoetermeer, the Netherlands) was consumed in 5 min, followed by a 20-min postprandial period. Subsequently the same sigmoid distension procedures were carried out as described for the preprandial period.

Both during rectal and sigmoid distension the intensity of sensation to each distension step was scored. Prompted by a red light one min after the start of each distension, the subjects were asked to rate their sensation by pushing one button of an array of 7. Button 1 indicated "no sensation" and button 7 "maximal tolerable pain".

During distension of the rectum or sigmoid bag the pressure in the other bag (sigmoid and rectal respectively) was maintained at operating pressures. The subjects were instructed that they had the option to deflate the bags instantaneously at any time of significant discomfort by pressing a button on their electronic control panel. Subjects had no visual or auditory clues to anticipate the type or course of distensions.

After fluoroscopic control of the catheter position, the experiment was finished and the probes were removed. The duration of the experiment from probe placement until their removal was about 5 hours.

Parameters investigated

Perception score. The mean sensation score was assessed for every distension step.

Compliance. The volumes measured at 1 min after the onset of each of the distensions were used to construct the pressure-volume curves. The dV/dP relationship was analyzed by calculating the slope of the pressure-volume curve by means of linear regression analysis resulting in a compliance coefficient.

Statistical Analysis

Data are expressed as mean (SEM). To analyse differences in compliance curves and perception intensity curves between groups and between the pre- and postprandial state within groups, a General Linear Model (GLM) for Repeated Measures was used. Paired t-tests for within-patient comparison and t-tests for group comparisons were used to evaluate differences between compliance coefficients. All analyses were conducted using the SPPS 7.0 statistical package.

RESULTS

All subjects completed the experiment. None of the subjects used the emergency button on the control panel to deflate the balloon because of unbearable discomfort. None of the barostat bags was dislocated during the experiment, as checked by fluoroscopy.

Perception score

In the rectum perception scores in the distension series were significantly higher in the SUDD group than in controls ($p = 0.010$) and ADD group ($p=0.030$). No difference in perception scores were found between ADD and controls. (Fig. 1)

In the sigmoid colon, preprandial perception scores in the distension series were significantly higher in the SUDD group than in controls ($p = 0.018$) but not as compared to the ADD group.

Postprandially, in the sigmoid colon, comparable results were found with perception scores being significantly higher in the SUDD group than in controls ($p = 0.018$) but not significantly different from ADD. There were no significant differences in perception scores between ADD and controls, neither pre- nor postprandially. (Fig. 1)

Compliance

The operating pressures for the barostat bags in the sigmoid colon and rectum were not significantly different between controls (15 ± 1.3 mmHg and 18 ± 1.2 mmHg respectively), ADD (17 ± 1.1 mmHg and 19 ± 0.9 mmHg respectively) and SUDD patients (17 ± 1.2 mmHg and 20 ± 0.7 mmHg respectively).

Neither in the rectum, nor in the sigmoid there were differences between the three groups in the slope of the volume-pressure curves (dV/dP) (Fig. 2; Table 1). However, in the sigmoid colon, the preprandial volumes in SUDD patients were significantly lower than in the ADD patients ($p = 0.026$), due to a lower volume at MDP in the SUDD group. In the postprandial period a trend towards the same phenomenon was found ($p = 0.079$).

Ingestion of the meal had no significant effect on compliance (Fig. 2; Table 1)

DISCUSSION

In this study we have investigated two groups of patients with uncomplicated diverticulosis of the colon: one with asymptomatic diverticular disease (ADD) and one with symptomatic uncomplicated diverticular disease (SUDD), also called painful uncomplicated diverticular disease. We wished to examine whether visceral perception of the distension stimulus is different in these clinically distinct entities, and, if so, whether the differences could be explained by differences in compliance of the rectosigmoid. In the sigmoid colon, perception in the pre- and postprandial period was increased in SUDD patients as compared to controls. Rather unexpectedly we also observed increased perception scores in the rectum of SUDD as compared to ADD and controls. As will be discussed below, this increase in pain perception in the SUDD group was not due to a change in rectal wall characteristics.

Thus, in SUDD, increased perception appears to be present not only in the diverticula-bearing sigmoid colon but also in the unaffected rectum. This observation gives rise to the suggestion that patients with SUDD are in fact Irritable Bowel Syndrome (IBS) patients who also happen to have diverticulosis. Increased visceroperception in the rectum as well as in other parts of the alimentary canal is a well known feature of IBS. [18 20] It can be argued that some clinical observations suggest that IBS and SUDD are two distinct conditions without progression of one to the other. IBS patients often have a long history of abdominal complaints, starting at young adult age, whereas in many patients with symptomatic uncomplicated diverticular disease the onset of abdominal pain is shortly before the discovery of their diverticula.[3 15 17] However, these

observations do not take away the possibility that IBS patients with late symptom onset whose pre-existent diverticulosis is incidentally discovered during diagnostic work-up, are erroneously labeled as SUDD patients.

In our patients with uncomplicated diverticular disease bowel wall compliance was normal, not only in the rectum but also in the sigmoid, i.e., the resistance to distension was similar in ADD, SUDD and health. This also is an unexpected finding since a change in bowel wall structure is thought to be one of the components for the development of diverticular disease. In diverticular disease the amount of elastin in taeniae coli is increased, causing a shortening of taeniae and "upbunching" of muscle, mesentery and mucosa. The lumen narrows, the muscle layer seems increased and the gut is shortened.[15 16] One would expect that these changes could lead to a decreased compliance of the gut wall. However, in our study the SUDD group had significantly lower volumes on every pressure step as compared to the ADD group, without a change in wall compliance. A change in basal tone may explain this, and results in an increased lengthening of circular smooth muscle cells on every pressure distension in SUDD as compared to ADD at similar dV/dP when started at a lower sigmoid volume.

No alteration in compliance was observed in this study, whereas in diverticular disease, only one other distension study using water filled latex balloons was performed before, in which a decreased resistance to stretch of the sigmoid wall was found.[9] Pressure in a latex balloon, filled with progressive volumes of water was found to increase to a maximum, after which further increments of volume did not cause any further increase in pressure. The maximum was called the critical pressure. In patients with diverticular disease critical pressure was found to be half of the critical pressure of controls.[9] Postmortem distension studies yielded the same results.[25] It is now also accepted that latex balloons are far from ideal for studying colonic wall characteristics. First, a latex balloon has a compliance of its own that has to be corrected for. Secondly, at certain critical pressures, a latex balloon looses its elastic properties and becomes plastic, resulting in a balloon that can accommodate large volumes with little increase in pressure. In a rigid tube this may occur at a lower "critical pressure" than in a non-rigid tube.[23 26] Therefore, the results of our study cannot be compared with those obtained with a latex balloon.

In summary, the present study shows that patients with symptomatic uncomplicated diverticular disease (SUDD) show heightened visceral perception of distension stimuli applied to rectum and sigmoid colon which is not found in asymptomatic diverticulosis (ADD). The hyperperception is not due to an altered compliance of the gut wall. A study on perception and wall characteristics in SUDD patients as compared to age-matched patients with a long history of IBS without diverticula may resolve remaining questions.

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Table 1 Compliance (ml/mmHg) in rectum and sigmoid

	CONTROLS	ADD	SUDD
Rectum	7.5 ± 0.1	7.1 ± 0.7	9.2 ± 0.9
Sigmoid preprandial	4.1 ± 0.5	3.7 ± 0.5	4,1 ± 1.2
Sigmoid postprandial	4.7 ± 0.7	4.6 ± 0.9	3.9 ± 0.9

Data expressed as mean ± SEM.

LEGENDS

Fig. 1 Perception (score 1 = no sensation, score 7 = maximal tolerable pain) on stepwise isobaric distensions of the rectum and sigmoid colon during the preprandial period and in the sigmoid colon during the postprandial period in healthy controls (squares), ADD group (circles) and SUDD group (triangles).
* In the rectum the SUDD group had increased perception scores as compared to the control group (GLM: $p = 0.010$) and ADD group (GLM: $p = 0.030$).
# In the sigmoid colon in the pre- and postprandial periods, the SUDD group had increased perception scores as compared to the control group (GLM: $p = 0.018$).

Fig. 2 Volume-pressure curves in the rectum and sigmoid colon during the preprandial period and in sigmoid colon in the postprandial period on isobaric distensions in healthy controls (squares), ADD group (circles) and SUDD group (triangles).
Preprandially, the SUDD curve was shifted downwards as compared to the ADD curve (* GLM: $p = 0.026$).

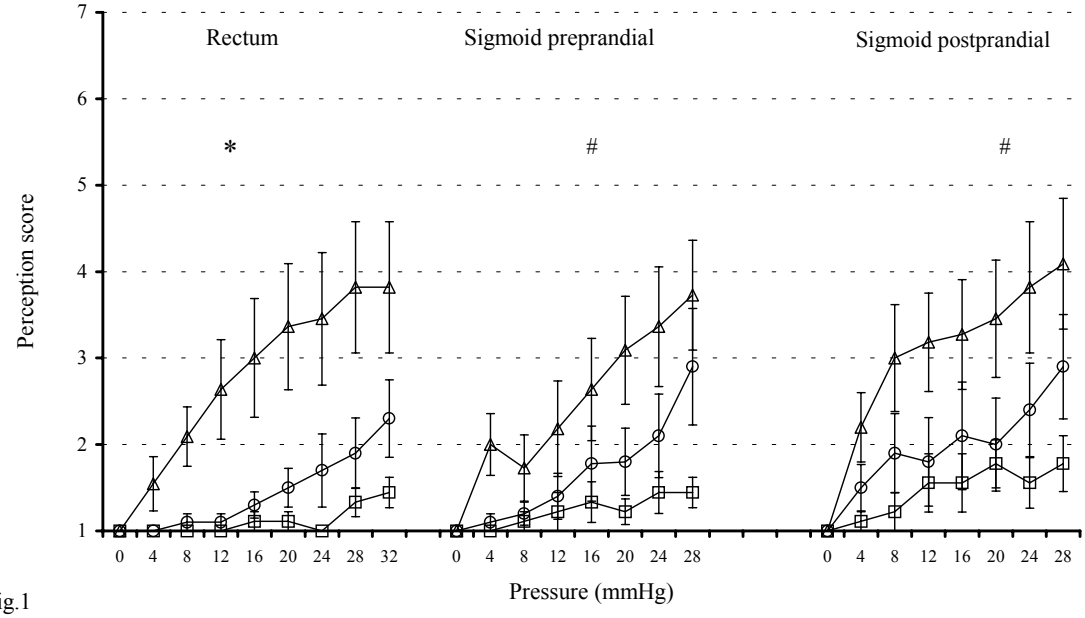
Rectum
Sigmoid preprandial
Sigmoid postprandial
*
#
#
Perception score
Pressure (mmHg)

Fig.1

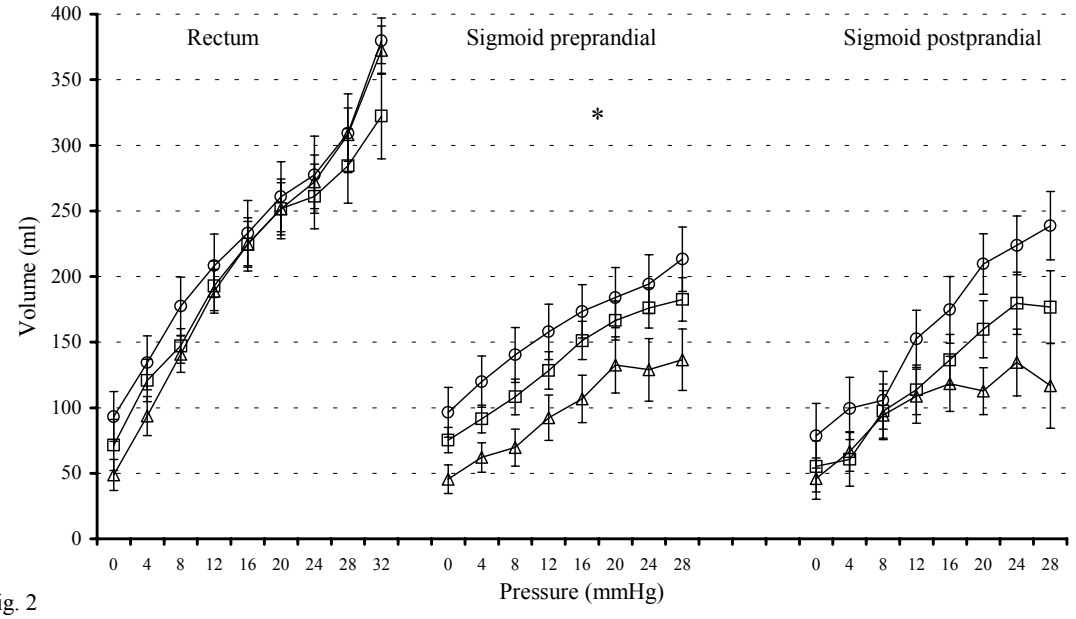
Rectum
Sigmoid preprandial
Sigmoid postprandial
*
Volume (ml)
Pressure (mmHg)

Fig. 2