

Chapter 5

TONE AND PHASIC MOTILITY OF THE LEFT COLON IN DIVERTICULAR DISEASE

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ABSTRACT

Background & Aims: Asymptomatic diverticular disease (ADD) and symptomatic uncomplicated diverticular disease (SUDD) are common entities but their pathogenesis is still unclear. We aimed to assess whether rectal and sigmoid colonic tone and phasic motility play a role in diverticular disease and whether ADD and SUDD show distinct tonic and phasic motility patterns.

Methods: 9 ADD patients, 9 SUDD patients and 8 healthy controls were studied. Using a dual barostat device, tone in the rectum and sigmoid colon was recorded simultaneously before and after a 600-kCal liquid meal. Concurrently, four manometric pressure ports recorded phasic motility in the sigmoid colon.

Results: Rectal tone was not different between groups. In the sigmoid colon a trend towards lower volume at MDP+2mmHg was found in the SUDD group as compared to the ADD group ($p = 0.068$). Phasic motility, expressed as area under the curve, was higher in the ADD group than in the controls ($p = 0.020$) and marginally higher than in the SUDD group ($p = 0.056$). Both SUDD patients ($p = 0.018$) and controls ($p = 0.047$) showed an increase in motility after the meal while the ADD group did not show this phasic response.

In the SUDD group there was a significant negative correlation between sigmoid barostat volume and number of phasic pressure waves ($r_s = -0.768$, $p = 0.016$) as well as between barostat volume and AUC ($r_s = -0.723$, $p = 0.028$).

Conclusion: Patients with uncomplicated diverticular disease with and without lower gastrointestinal symptoms show differences in tonic and phasic motility in the sigmoid colon, indicating that not only symptoms but also motility is a discriminating factor in SUDD and ADD.

INTRODUCTION

Colonic diverticular disease has become increasingly prevalent among the population of economically developed countries.¹⁻⁴ Uncomplicated diverticular disease may or may not give rise to symptoms and the terms symptomatic uncomplicated diverticular disease (SUDD) and asymptomatic diverticular disease (ADD) have been used to describe these subgroups.^{5 6}

Apart from a low-residue diet, increased motility in the diverticula-bearing colon is thought to be one of the mechanisms involved in the development of these pulsion diverticula. However, manometric studies in diverticular disease have yielded conflicting results.⁷⁻¹⁶ A recent study in patients with SUDD using 24-hour manometry showed preprandial hypermotility, an abnormal colonic motor response to eating and an increased incidence of high-amplitude propagated pressure waves in the affected segments.¹⁷

A change in bowel wall structure and narrowing of bowel lumen is thought to be another component to the development of diverticular disease.^{18 19} Colonic tone may be an important factor in the development of this narrowed sigmoid lumen. Raised basal and postprandial colonic tone may increase the percentage of pressure waves causing total occlusion of the lumen, leading to progressive stress upon the colonic wall.¹³ However, no information on the role of colonic tone in diverticular disease and its relationship to phasic motility exists in literature.

In this study we evaluated colonic and rectal periprandial tone and phasic motility in patients with asymptomatic (ADD), and symptomatic (SUDD) uncomplicated diverticular disease and in healthy controls using a combined barostat-manometry technique.

METHODS

Patients

Nine patients (four men and five women), mean age 54 years (range 43-65), with a clinical diagnosis of symptomatic uncomplicated diverticular disease (SUDD) were recruited from the outpatient clinic of the department of Gastroenterology of the University Medical Center Utrecht. 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.

Nine patients (six men and three women), mean age 58 years (range 45-69), with a diagnosis of asymptomatic uncomplicated diverticular disease (ADD) were selected from the colonic polyp surveillance program, 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 their medical history.

Eight healthy volunteers (five men and three women), mean age 51 years (range 43-60), were recruited by advertisement and from our own files.

None of the subjects had signs of systemic or other gastro-intestinal disease or a medical history of abdominal surgery. All subjects had normal bowel habits defined as a stool frequency of > 3 per week but < 3 per day and a stool consistency of 2.5-3.5 on a 5-point scale. None of the subjects used medication, including laxatives, on a regular base. 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. These reservoirs were connected via non-compliant

tubes to the polyethylene bags. The barostat device continuously measured the volume of air within these bags, which were maintained at a constant and pre-selected pressure level by an electro-mechanical feedback mechanism. In response to any change in pressure measured in the bag, the barostat injected or withdrew air at a speed of 1.9 L/min. At each pressure the barostat automatically calculated corrected volumes according to Boyle's law; changes in barostat volume are thought to reflect a change in tone of the gut.

Colonic probes

In the sigmoid a multi-lumen non-compliant polyethylene tube assembly incorporating a 10-cm long cylindrical 40- μ m thick polyethylene bag, located 15 to 25 cm from the tip, and four manometric water-perfused sideholes was used (Dantec Medical, Skovlunde, Denmark). The four sideholes (inner diameter 0.8 mm) were located 15, 10 and 5 cm orad to the proximal end of the bag and 5 cm caudad to the distal end of the barostat balloon. The manometric sideholes were perfused with distilled water at a flow rate of 0.1 ml/min.

In the rectum a two-lumen polyethylene tube incorporating a 10-cm long polyethylene bag at its tip was used (Dantec Medical, Skovlunde, Denmark). 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. Each catheter had a second channel which ended in the bag and was connected to the pressure transducer in the barostat.

The maximal capacity of each of the cylindrical bags (during table-top inflation) was 800 ml and their maximal diameter was 10 cm. Before each experiment, the bags, catheters and barostat were checked for air leaks by submerging the bags under water, maintaining a constant pressure of 20 mmHg for 10 minutes.

Pressures and volumes in the barostat balloon were stored (after analog-to-digital conversion at 4 Hz) using computer software (Protocol Plus data scanner, G&J Electronics Inc., Willowdale, Ontario, Canada). Pressure signals recorded from the perfused sideholes were computer-stored with a sampling rate of 4 Hz (MMS, Enschede, the Netherlands).

Colonic Intubation

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, Amsterdam, The Netherlands). At 9.00 a.m. the sigmoid catheter incorporating the polyethylene bag was placed endoscopically. This procedure was performed without sedation and with minimal insufflation of air. The tip of the manometric catheter was attached to the colonoscope and introduced until the tip of the catheter reached the descending colon and the polyethylene bag was located in the sigmoid colon with the distal pressure port 20 cm proximal to the anus. Then the second probe with the polyethylene bag on the tip was introduced into the rectum without endoscopic assistance. Positions of the barostat bags were verified by fluoroscopy.

Study Protocol

After introduction of the probes, all subjects were requested to remain in a 30° supine position during the entire recording session, and they were asked not to make unnecessary movements.

One hour after placement of the sigmoid and rectal probe, the ‘minimum distending pressures’ (MDP) were defined for both rectal and sigmoid bag by recording the lowest pressure at which respiratory excursions were recorded as changes in barostat volumes. The ‘operating pressure’ was set at 2 mmHg above MDP. After another hour of accommodation, with both bags at operating pressure, a 10-min preprandial recording period was followed by ingestion of a 500 ml, 600-Kcal (35% fat, 49% glucose, 16% protein) liquid meal (Nutridrink, Nutricia, Zoetermeer, The Netherlands) that was consumed in five minutes, followed by a 20-min postprandial recording period.

Thereafter the experiment was finished and the probes were removed by gentle traction.

Parameters investigated

Manometric activity. Phasic pressure activity in the sigmoid manometric tracings, recorded 15, 10 and 5 cm proximal and 5 cm distal to the barostat bag was analyzed for one 10-min period before and two 10-min periods after the liquid meal. These three

periods will be referred to as preprandial period, postprandial period 1 and postprandial period 2, respectively. Manometric data were analyzed automatically using a dedicated computer program. The computer program calculated the mean amplitude (hPa) and mean duration (sec) of pressure waves, the number of pressure waves and the area under the curves (AUC, hPa.s) for each of the four channels in the three 10-min periods. During this periprandial period high-amplitude propagated pressure waves (HAPPWs) defined as pressure waves that propagate distally across at least three sensors, with a speed of more than 0.3 cm/s and an amplitude of at least 133 hPa in two sensors and at least 100 hPa in one other sensor, were analyzed visually.

Barostat tracings. The mean volume at ‘operating pressure’ was automatically calculated in both the rectal and sigmoid barostat bag for the three 10-min periods before and after the meal, using a computer program (Protocol Plus data scanner, G&J Electronics Inc., Willowdale, Ontario, Canada).

Correlation between manometric activity and barostat volume. In order to detect a relationship between the periprandial manometric parameters (frequency, amplitude, duration, AUC) and the periprandial sigmoid barostat volume correlation coefficients were calculated.

Statistical Analysis

Data are expressed as mean (\pm SEM).

To analyze differences in barostat volumes during the total periprandial period between groups a General Linear Model for Repeated Measures was used. Paired t-tests for single patient comparison and independent t-tests for group comparisons were used to evaluate differences between tone or AUC in the separate periprandial periods.

In analyzing the phasic pressure waves we restricted statistical comparisons to the AUC. Pearson’s coefficient of correlation was used to examine the correlation between the sigmoid volume and phasic motility parameters. All analyses were conducted using the SPSS 7.0 statistical package.

RESULTS

Phasic motility in the sigmoid colon

ADD patients had significantly more sigmoid phasic motility, as expressed as AUC for the total periprandial period, than did the control group ($p = 0.020$). A trend towards a higher AUC was seen in the ADD group as compared to the SUDD group ($p = 0.056$). In the SUDD group the AUC was not significantly different from that in the control group.

The SUDD group ($p = 0.018$) and control group ($p = 0.047$) both showed a significant increase in phasic motility after the meal while the ADD group did not show a gastro-colonic response (Figure 1, Table 1).

During the 30-min study period, HAPPWs did not occur in any of the 26 subjects.

Table 1: Manometric findings in the sigmoid colon

		Preprandial	Postprandial 1	Postprandial 2	Total period
Number of contractions	Controls	11.4 ± 4.5	16.8 ± 4.7	15.0 ± 4.5	41.3 ± 11.2
	ADD	19.6 ± 4.2	23.8 ± 4.7	30.7 ± 4.0	74.0 ± 8.9
	SUDD	19.6 ± 6.4	26.1 ± 7.4	22.8 ± 5.4	68.4 ± 17.4
Mean amplitude (hPa)	Controls	22.8 ± 2.2	25.3 ± 1.8	24.9 ± 2.3	25.0 ± 1.5
	ADD	35.6 ± 4.5	34.0 ± 2.7	31.5 ± 2.5	33.5 ± 2.4
	SUDD	25.3 ± 1.8	29.0 ± 1.8	28.1 ± 2.2	29.0 ± 1.8
Mean duration (sec)	Controls	3.6 ± 0.8	4.3 ± 0.7	3.8 ± 0.8	4.0 ± 0.6
	ADD	5.1 ± 0.7	4.8 ± 0.6	4.6 ± 0.4	4.8 ± 0.5
	SUDD	3.0 ± 0.4	4.8 ± 1.0	3.5 ± 0.3	4.5 ± 1.0
AUC (hPa.sec)	Controls	1203 ± 538	1803 ± 511 [†]	1779 ± 798	4563 ± 1323
	ADD	3351 ± 856 [#]	3641 ± 832	4263 ± 997	11256 ± 2112 [*]
	SUDD	1240 ± 455	2416 ± 750 [‡]	2077 ± 699	5734 ± 1656

Data expressed as mean ± standard error of mean.

Statistical comparisons done for AUC only.

* ADD compared to controls: $p = 0.020$; ADD compared to SUDD: $p = 0.056$

ADD compared to controls: $p = 0.057$; ADD compared to SUDD: $p = 0.045$

† Controls: postprandial period 1 compared to preprandial period: $p = 0.047$

‡ SUDD: postprandial period 1 compared to preprandial period: $p = 0.018$

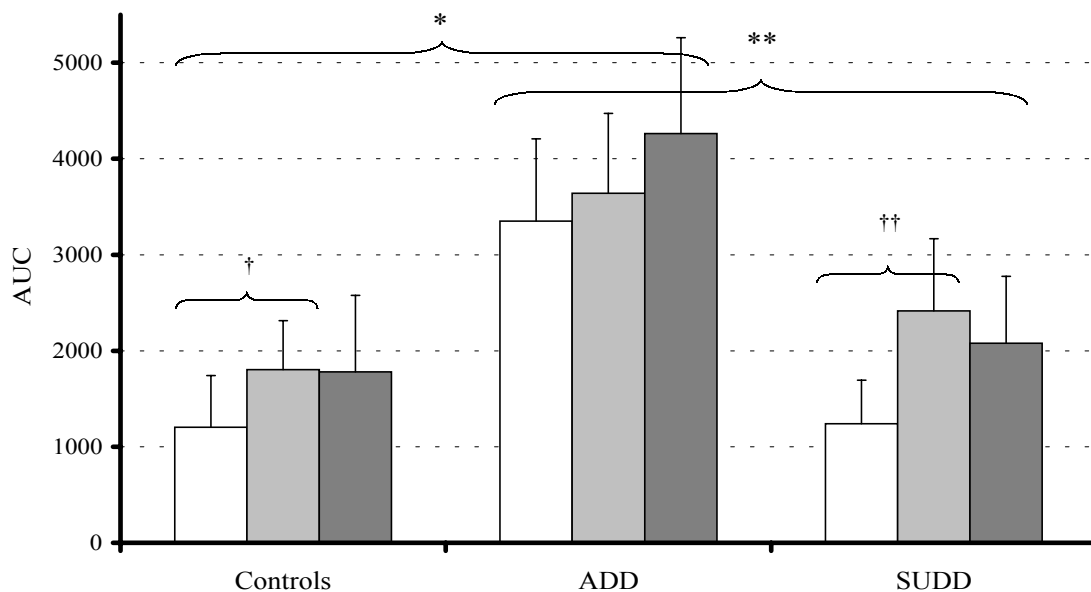


Figure 1. Area under the curve (AUC, hPa.s) for phasic motility in the sigmoid colon during the periprandial period. Preprandial (open bars), postprandial period 1 (light grey bars) and postprandial period 2 (dark grey bars).

Motility was increased in the ADD group as compared to the control group (* $p = 0.020$) whereas the difference between the ADD and the SUDD group just failed to reach statistical significance (** $p = 0.056$). Control and SUDD group showed a significant increase in motility after the meal († $p = 0.047$; †† $p = 0.018$).

Tone in rectum and sigmoid colon

The operating pressures ($MDP + 2$ mmHg) in the sigmoid colon and rectum were not significantly different between healthy controls (14.9 ± 1.3 and 18.3 ± 1.2 mmHg, respectively), ADD patients (16.8 ± 1.1 and 19.3 ± 0.9 mmHg, respectively) or SUDD patients (17.2 ± 1.2 and 20.4 ± 0.7 mmHg, respectively).

In the rectum no significant differences in tone were found between groups, neither in rectal volumes in the total periprandial period nor in the magnitude of reduction of rectal volume after the meal. In all three groups postprandial rectal volume was significantly lower than preprandial rectal volume (controls $p = 0.009$; ADD $p = 0.026$; SUDD $p = 0.002$), representing a physiologic postprandial increase in tone (Figure 2, Table 2).

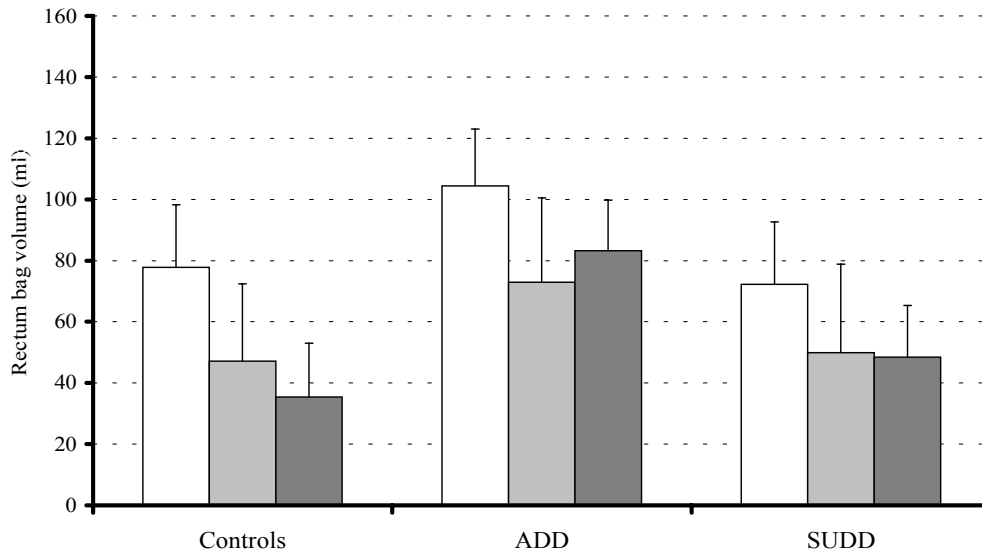


Figure 2. Barostat volumes in the rectum before the meal (open bars), and in postprandial period 1 (light grey bars) and postprandial period 2 (dark grey bars).

There were no significant differences between groups. In all three groups rectal volume decreased significantly after the meal (controls $p = 0.009$; ADD $p = 0.026$; SUDD $p = 0.002$).

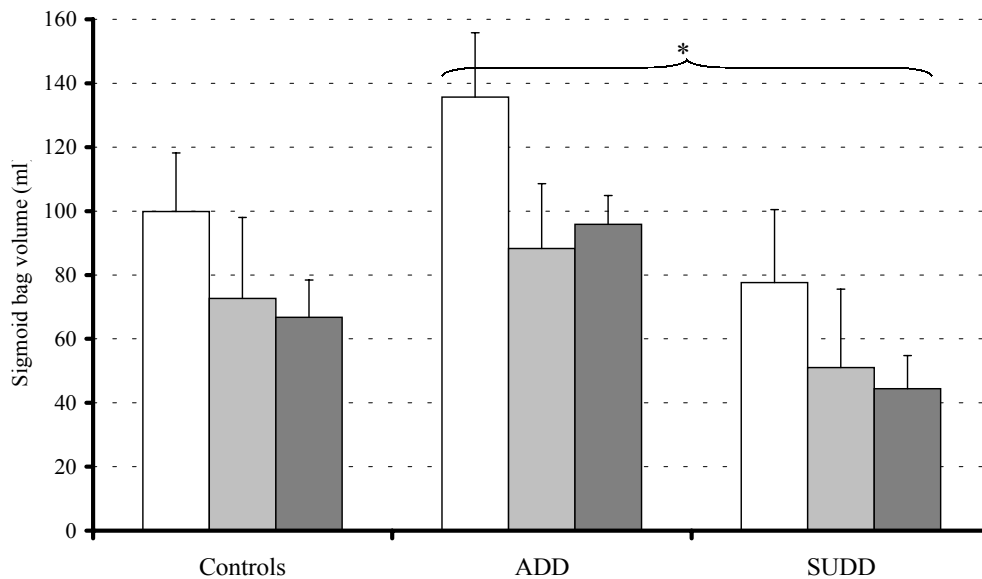


Figure 3. Barostat volumes in the sigmoid colon before the meal (open bars), and in postprandial period 1 (light grey bars) and postprandial period 2 (dark grey bars). Periprandial barostat volumes in the ADD group tended to be higher than in the SUDD group (* $p = 0.068$). In all three groups sigmoid volume decreased significantly after the meal (controls $p = 0.001$; ADD $p = 0.002$; SUDD $p = 0.004$).

In the sigmoid colon barostat volumes in the total periprandial period did not differ significantly in any of the patient groups as compared to the control group. However, a trend towards decreased sigmoid barostat volumes, was found in the SUDD group as compared to the ADD group ($p = 0.068$).

All groups had a prompt and highly significant decrease in sigmoid barostat volumes after ingestion of the meal (controls $p = 0.001$; ADD $p = 0.002$; SUDD $p = 0.004$). The volume reached in postprandial period 1 was maintained in the postprandial period 2. The magnitude of the volume reduction was not significantly different between groups, representing a postprandial tonic response in all three groups (Figure 3, Table 2).

Table 2: Volume in sigmoid colon and rectum; differences between groups

		Preprandial	Postprandial 1	Postprandial 2
Volume sigmoid colon (ml)	Controls	99.9 ± 18.2	72.7 ± 20.1	66.7 ± 22.8
	ADD	135.7 ± 25.3*	88.3 ± 20.2	95.9 ± 24.5#
	SUDD	77.7 ± 11.7	51.0 ± 9.0	44.4 ± 10.4
Volume rectum (ml)	Controls	77.8 ± 20.5	47.2 ± 18.6	35.4 ± 20.5
	ADD	104.4 ± 25.2	72.9 ± 27.5	83.3 ± 28.9
	SUDD	72.2 ± 17.9	49.9 ± 16.5	48.4 ± 16.9

Data expressed as mean ± sem

* Preprandial period: ADD compared to SUDD: $P = 0.061$

Total periprandial period: ADD compared to SUDD: $P = 0.068$

Correlations between sigmoid volume and phasic motility

In the SUDD group a significant negative correlation between the sigmoid barostat volume and the number of phasic pressure waves ($r_s = -0.768$, $p = 0.016$) was found during the total 30-min period, as well as a significant inverse correlation between the barostat volume and AUC ($r_s = -0.723$, $p = 0.028$). No correlations were found between sigmoid barostat volume and periprandial phasic motility parameters in the control or ADD group.

DISCUSSION

In this study we compared patients with asymptomatic diverticular disease (ADD) and patients with symptomatic uncomplicated diverticular disease (SUDD), with healthy controls. A dual barostat device enabled us to measure simultaneously rectal and sigmoid volume as well as phasic motility in the sigmoid. When intraluminal pressure is kept constant, changes in colonic tone caused by contraction or relaxation of the colonic smooth muscle cells lead to sustained changes in luminal cross-sectional area and circumference. Since colonic surface area cannot easily be measured directly *in vivo*, it is assumed that the colon and rectum roughly behave like cylindrical structures, implying that variations in volume as measured by the barostat reflect fluctuations in colonic diameter, and are thought to reflect variations of tone of the bowel wall.²⁰

In our study rectal volume at MDP+2 mmHg and the postprandial increase in rectal tone were not significantly different between groups. Therefore we believe that it is doubtful that tone in the rectum plays a major role in the pathophysiology of diverticular disease. Sigmoid colonic volume tended to be lower in the SUDD group than in the ADD group. Although the ADD group had a comparable postprandial decrease in sigmoid volume, the postprandial sigmoid volume in ADD was still higher than the preprandial volume in the SUDD group. These findings suggest that the sigmoid of SUDD has a higher tone than that of ADD patients. If we assume that the sigmoid is cylindrical in both groups, the sigmoid of our patients with SUDD tended to be narrower than the sigmoid of the ADD patients, both before and after a meal.

Manometric detection of phasic contractions of the gut wall requires lumen occlusion. One would therefore expect that manometry would have detected more and stronger phasic contractions of the sigmoid in the SUDD patients than in the ADD patients, since the latter have a wider sigmoid. However, the opposite was found. We found that phasic motility, expressed as AUC, was significantly higher in the ADD group than in the control group and tended to be higher than in the SUDD group. The SUDD group and controls, but not the ADD group, demonstrated a postprandial increase in phasic motility. In the SUDD group exclusively, a significant negative correlation between the

sigmoid barostat volume and phasic motility was found which means that a decrease in sigmoid volume, i.e. an increase of tone, indeed is expected to stimulate phasic motility in this patient group.

In 5 of the 6 earlier studies on sigmoid motor activity in diverticular disease an increased phasic motility was found.^{10-12 21-23} However, all of these studies were performed in patients with various subtypes of diverticular disease grouped together. More recently, some studies investigated subgroups of diverticular disease. A study by Weinreich and Andersen found an exaggerated response to prostigmine in SUDD patients as compared to ADD patients and controls.¹⁴ Trotman and Misiewicz found increased motility before and after a meal in patients who were asymptomatic at the time of the experiment.¹⁵ In a study by Cortesini et al. 60 % of SUDD patients had increased motility indices as compared to ADD patients and controls. The maximum amplitude of pressure waves was significantly higher in SUDD than in ADD and controls during the 6-hour registration period, with peaks frequently exceeding 120 mmHg. No differences were found between ADD and controls.⁵ Katschinski et al performed a combined myoelectric and manometric recording study of the sigmoid in SUDD, mixed IBS patients and controls. He found no significant differences in motility characteristics between groups using objective computer analyses.¹⁶ A recent prolonged manometric study by Bassotti et al. in SUDD patients found a higher motility index only in the period before and not after a meal in the left colon. An increased number of HAPPWs contributed to the increased motility indices of SUDD patients.¹⁷

We could not confirm the increased periprandial phasic motility in the SUDD group, as found in some earlier studies, and rather found increased motility in ADD. This discrepancy might well be explained by the fact that, due to a relatively short observation period no HAPPWs, which usually have a great impact on motility indices or AUC, were observed in our study.

In conclusion, we have shown that sigmoid motor activities in patients with symptomatic uncomplicated diverticular disease differ from those in patients with asymptomatic diverticulosis. In SUDD the volume of the sigmoid colon tends to be lower than in ADD and phasic motility of the sigmoid tends to be decreased as compared to ADD. These observations indicate that not only symptoms but also motility in the sigmoid colon is a discriminating factor in these two groups of patients with uncomplicated diverticular disease.

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