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Endoscopic carbon dioxide insufflation tolerance test on the anal sphincter for anorectal hypofunction: a pilot and feasibility study

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Abstract

Background Anorectal function deteriorates with age. The diagnostic performance of the endoscopic pressure study integrated system (EPSIS), an endoscopic carbon dioxide (CO_2) insufflation stress test of the lower esophageal sphincter has been previously evaluated as a diagnostic tool for gastroesophageal reflux disease. We aimed to evaluate the applicability of EPSIS in improving anorectal function. We hypothesized that EPSIS can be applied to the diagnosis of lower gastrointestinal tract disorders.

Methods This was a pilot, single-center, retrospective study using prospectively collected data between December 2021 and March 2022. It was designed to evaluate the differences in EPSIS rectal pressure measurements between older (≥80 years) and younger (<80 years) patients. At the end of the screening colonoscopy, the colonoscope was fixed in a retroflex position. When bowel movement was observed, CO_2 was insufflated to the point where gas leakage occurred through the anus. The measured maximum pressure was defined as EPSIS-rectal pressure max (EPSIS-RP max) and compared between the groups.

Results Overall, 30 patients were included and examined. The median ages of the <80 and ≥80 years' groups were 53 (range: 27-79) and 82 (range: 80-94) years, respectively, with corresponding median measured EPSIS-RP max of 18.7 (range: 8.5-30.2) and 9.8 (range: 5.4-22.3) mmHg (P<0.001).

Conclusions Measurement of maximum rectal pressure illustrates the age-related decline in physiological anorectal function. Future studies should consider a loading test using EPSIS to quantify the decline in anorectal function and use it as a routine tool for screening and adjunctive diagnosis of anorectal hypofunction.

Keywords Anal sphincter, anorectal disorders, bowel incontinence, diagnosis, endoscopy

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Introduction

It is well-established that anorectal function deteriorates with age [1,2]. Incontinence associated with anorectal hypofunction is a common condition encountered among older people [3]; however, the psychological distress that it typically causes can result in considerably decreased quality of life. Anorectal manometry, balloon expulsion test (simulated defecation test), sphincter electromyography, and defecography are conventional methods performed to evaluate anorectal function. These diagnostic tests are essential for clarifying the pathophysiology of the disease; nevertheless, each requires a special measurement device. Therefore, it would be beneficial if physicians could easily and quickly evaluate anorectal function during routine endoscopic examinations without the need for such specialized devices.

The endoscopic pressure study integrated system (EPSIS) is a system that continuously measures the intraluminal pressure in the

digestive tract while delivering carbon dioxide (CO_2) insufflation from the endoscope. It enables continuous, real-time visual evaluation of the gastrointestinal (GI) tract movement that occurs in conjunction with CO_2 insufflation in a specific lumen. We have previously used EPSIS to perform a loading test on the lower esophageal sphincter (LES) for the diagnosis of gastroesophageal reflux disease (GERD). We have reported the diagnostic ability of EPSIS for GERD and its strong association with high-resolution manometry [4,5]. When EPSIS is used to diagnose GERD, an endoscope is inserted into the stomach. This allows the physician to observe the gastric cardia through an inverted view, at which point CO_2 insufflation is performed, and a stress test is induced to determine the air-holding capacity of the gastric cardia. In routine practice, during upper endoscopy, air leaks from the stomach in patients with GERD, as a result of impaired LES function and loosening of the esophagogastric junction. On the other hand, during colonoscopy, air leakage out of the anus is common, especially during observation of the lower rectum in retroversion. This phenomenon is similar to the mechanism of burping, in which gas in the GI lumen cannot be retained and begins to leak out. Because of the similarity between the 2 mechanisms, EPSIS may also be applied to not only the upper, but also the lower GI tract. We hypothesized that dysfunction of the LES in the pathogenesis of GERD is similar to the dysfunction of the anal sphincter, such as in fecal incontinence. Given the aforementioned hypothesis, this pilot study also aimed to evaluate the applicability of EPSIS in improving anorectal function.

Patients and methods

Study population

In this single-center, observational, retrospective study, we used the prospectively collected data of patients who had undergone colonoscopy between December 2021 and March 2022 at our institution. We included all patients who underwent colonoscopy during the study period. We excluded patients who were pregnant, or in poor general condition; those with severe dementia, who had difficulty providing informed consent; those who underwent the examination without sedation, or who underwent the examination in a near-awake state with shallow sedation; and those whose primary objective colonoscopy revealed a serious disease for which this examination was considered inappropriate. All patients gave their consent to participate in this study.

A pilot study was designed to evaluate the differences in EPSIS rectal pressure measurements between older and younger patients. The patients were divided into the following age groups: (1) those aged <80 years; and (2) those aged ≥80 years.

Procedure (Fig. 1)

EPSIS was performed using high-definition colonoscopes (CF-EZ1500, XZ1200, and HQ290ZI; Olympus Corporation, Tokyo, Japan; 15 mm in diameter) with CO_2 gas insufflation. A CO_2 insufflator UCR (Endoscopic CO_2 Regulation Unit, Olympus Corp.) and super low-flow tube (MAJ-1816, Olympus Corporation) were used to ensure a constant flow volume of approximately 1.0 L/min. The tip of the disposable irrigation tube (AF-WT; Forte Grow Medical Corp., Tochigi, Japan) was directly connected to the working channel cap, and the other side of the tube was connected to the internal pressure measuring device (TR-W550, TR-TH08, AP-C35; Keyence, Osaka, Japan) [6]. Intravenous propofol (200 mg/20 mL) was administered in weight-converted doses in all cases. Antispasmodics were administered at the initiation of each screening test at the required dose, while taking into consideration the patient's underlying medical condition.

Pressure study

A colonoscope was initially inserted using a transanal approach to perform the intended examination, including screening for colorectal cancer, diarrhea, and bloody stools. At the end of the examination, we desufflated as much of the CO_2 gas (entering from the oral side) as possible. Subsequently, the colonoscope was inserted in the lower rectum and fixed in a position that allowed observation of the anal region in the

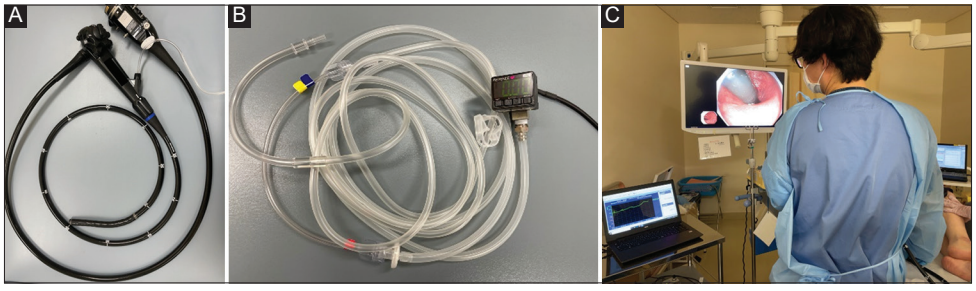

Figure 1 Setting of the endoscopic pressure study integrated system (EPSIS) in the lower rectum. (A,B) The tip of the disposable irrigation tube (AF-WT; Forte Grow Medical Corp., Tochigi, Japan) was directly connected to the working channel cap (A), and the other side of the tube was connected to the internal pressure measuring device (TR-W550, TR-TH08, AP-C35; Keyence, Osaka, Japan) (B). (C) At the end of the examination, we desufflated as much of the CO_2 gas that entered through the oral side as possible. The colonoscope was then inverted in the lower rectum and fixed in a position that allowed observation of the anal region in retroflex position. Insufflated CO_2 and intraluminal pressure were measured using EPSIS measuring instruments

retroflex position. At this point, the position of the endoscope remained fixed to avoid prying open the anus.

CO_2 insufflation was limited to the point where the pressure level produced a flat waveform or declined due to gas leakage from the anus, or when the patient awoke from sedation because of discomfort. The measured maximum pressure was defined as EPSIS-Rectal Pressure max (EPSIS-RP max) and compared between the 2 age groups: <80 years and ≥80 years.

Statistical analysis

Normality was assessed using the Kolmogorov-Smirnov test. The mean value ± standard deviation was used to report variables with a normal distribution and the median and range were used for variables with a skewed distribution. Differences between the groups were analyzed using the chi-square test, and Fisher's exact test was performed to analyze categorical data. Student's *t*-test was performed to compare the mean values of continuous data. All statistical analyses were conducted using JMP 16 (SAS Institute Inc., Cary, NC, USA).

Ethical considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki, and it was approved by the Institutional Review Board of Showa University Koto Toyosu Hospital (21T5003). Written informed consent was obtained from all participants.

Results

A total of 30 patients were examined, and their data were analyzed. The patients' clinical characteristics are summarized in Table 1. The median ages of the <80 and ≥80 years' groups were 53 (interquartile range [IQR] 27-79) and 82 (IQR 80-94) years, and the number of patients who used antispasmodics during screening colonoscopy were 18 (90%) and 9 (90%), respectively. Episodes of incontinence and diaper use were more common in the ≥80 years' group. The pressure waveforms drawn during the EPSIS examination demonstrated 2 major patterns: flat and uphill (Fig. 2, Supplementary Video). Flat waveforms, in which air was expelled from the anus and internal pressure showed no increase, were observed in 5 (25%) patients in the <80 years' group and 7 (70%) in the ≥80 years' group. The remaining patients exhibited an uphill waveform. For each waveform, the highest value that could be measured was noted. The measured EPSIS-RP max had median values of 18.7 mmHg (IQR 8.5-30.2) and 9.8 mmHg (IQR 5.4-22.3) (P<0.001) in the <80 and ≥80 years' groups, respectively. Evidently, it was significantly lower in the ≥80 years' group. In the latter group, the EPSIS-RP max values in 3 patients with symptoms of incontinence were 8.2, 5.6, and 5.4 mmHg, considered relatively low.

Discussion

Pressure measurement using EPSIS is a loading test in which CO_2 is delivered from an endoscopic system into the digestive tract lumen. Subsequently, the highest pressure at which the dilated lumen can be maintained is measured. In other words, it indirectly assesses the function of a specific sphincter. Using EPSIS, we have previously reported the diagnostic utility and relevance of CO_2 stress testing on the LES in the pathogenesis of upper GI tract-related GERD and GERD-related conditions [4,7,8]. In addition, by evaluating patients with GERD, we confirmed a close association between EPSIS measurements and high-resolution manometry and reported that EPSIS can evaluate LES function [5]. In this study, we assumed that by following the same procedure in

Table 1 Patients' clinical characteristics (n=30)

Characteristics	Age < 80 years (n=20)	Age ≥ 80 years (n=10)	P-value
Male sex, n (%)	7 (35%)	3 (30%)	>0.99
Body mass index (kg/m^2)	22.8 (19.5-31.6)	20.8 (17.1-28.1)	0.13
Episodes of incontinence, n (%)	0	3 (30%)	N/A
Able to walk independently, n (%)	20 (100%)	8 (80%)	0.03
Past illness history, n (%)			
Cerebral neurological diseases	0	2	N/A
Dementia	0	2	N/A
Anorectal surgery	2 (Hemorrhoid, rectal cancer)	1 (Rectal prolapse)	>0.99
If female, fertile	0	0	N/A
Daily use of constipating agent, n (%)	2 (10%)	4 (40%)	0.06
With antispasmodics during screening, n (%)	18 (90%)	9 (90%)	>0.99
EPSIS-RP max (mmHg), median (range)	18.7 (8.5-30.2)	9.8 (5.4-22.3)	<0.001
Waveform pattern (flat pattern)	5 (25%)	7 (70%)	0.0177

EPSIS-RP, endoscopic pressure study integrated system rectal pressure max

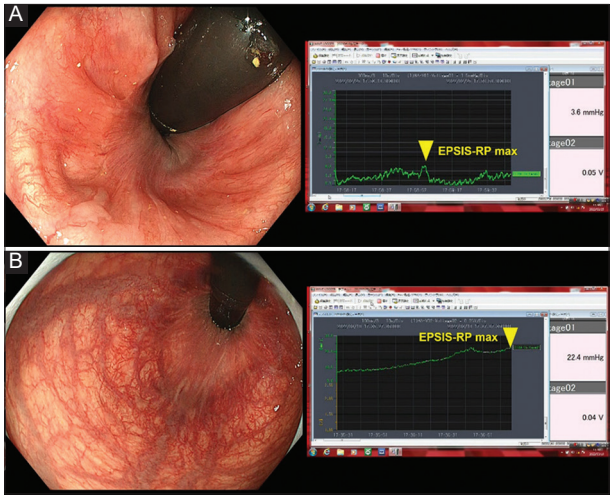

Figure 2 Screening during the endoscopic pressure study integrated system (EPSIS) inspection (actual pressure waveform observed). The waveforms of measured pressure drawn during the examination showed 2 major patterns. For both waveforms, the highest value that could be measured was noted. (A) Flat waveform; CO_2 leakage occurred below 10 mmHg, resulting in a flat pattern. The measured EPSIS-rectal pressure max (RP max) in this case was 6.0 mmHg. (B) Uphill waveform; the patient could hold >10 mmHg, and gas leakage occurred at a certain value. The measured EPSIS-RP max in this case was 22.5 mmHg

the lower rectum, load testing on the anal sphincter would be possible using CO_2 gas under endoscopic visualization.

Anorectal function has been reported to deteriorate with age [1,2], and during routine colonoscopy of older patients, observing the lower rectum is often made difficult by air leakage as a result of a loosened anus. This study attempted to translate and quantify anorectal function into pressure measurements. EPSIS-RP max was lower in the ≥80 years' group, especially among those with incontinence symptoms. The low value reflects the reduced ability of the rectum to retain air due to the decreased function of the anal sphincter muscle. This result parallels the well-studied association between age and decline in physiological anorectal function. Therefore, a loading test using EPSIS has the potential ability to quantify the decline in anorectal function. In addition, the pattern of pressure waveforms recorded during the examination was similar between the anorectal function in the present study and the LES function reported previously. We have previously reported that a flat pattern is related to GERD, a condition resulting from LES dysfunction [7]. In the present study, a higher proportion of patients with a flat pattern was observed in the group with low EPSIS-RP max and impaired anorectal function. In other words, anal sphincter function, similarly to LES function, may be evaluated more simply by using waveform patterns.

There are 3 advantages of utilizing and establishing this technique. First, it can be easily performed during routine screening colonoscopy. During a thorough examination for abnormal anal function, a functional test using special equipment—such as a catheter-based internal pressure measurement and defecation test, the current gold standard—and a screening test using a colonoscope to rule out organic abnormalities are performed. However, functional tests require specialized equipment and can only be performed at specific facilities. In addition, some tests, especially defecation tests, are associated with embarrassment to the patient.

In contrast, EPSIS is performed during the first colonoscopy as a screening test and can be performed at non-specialized facilities, without the need for special equipment. It can also be easily repeated. Secondly, because the examination is performed using an endoscope, the area of interest can be directly visualized during the examination. While catheterization is performed under non-visualized conditions, EPSIS allows direct observation of bowel and anal movements linked to fluctuations in internal pressure while viewing images in real-time. Thirdly, CO_2 stress testing can be performed. This serves the same purpose as the balloon stress test but is simpler and superior in that evaluation can be performed simply by insufflating CO_2 without insertion of a device; CO_2 insufflation is now commonly used in endoscopy and is said to cause less postoperative discomfort [9], making it minimally invasive. Thus, EPSIS is a simple and safe examination method that allows real-time evaluation via endoscopy.

The main limitation of this study is that we were unable to confirm its consistency with existing tools, such as rectal manometry, but we aim to continue the study assuming the conditions described in this paper. Other limitations of this study can be summarized as follows. The study was based on a limited sample size. Since the amount of CO_2 migrating to the sigmoid colon cannot be quantitatively evaluated, the morphology and size of the bowel may have affected the measurements, but this was corrected by standardizing the body position to the left lateral recumbent position. Furthermore, this study included not only healthy subjects, but also patients with comorbidities. Patients who were administered antispasmodics at the start of colonoscopy insertion were also included, which could have affected the results, but there was no difference between the 2 groups in the percentage of usage, and the effect was minimized as much as possible by performing the measurement at the end of the primary examination. In this study, it was difficult to distinguish the type of fecal incontinence, i.e., fecal incontinence or gas incontinence, based on the questionnaire, because some patients had dementia or other conditions that prevented detailed information from being obtained. In addition, there may be differences in sensory thresholds depending on age; however, their influence was minimized by administering sedatives to all patients for the test. Future studies need to investigate their effect, which has the potential to significantly improve the quality of life among older individuals.

Herein, we report a pilot, feasibility study of age-dependent trends in anorectal pressure measured by EPSIS. EPSIS is the first to integrate existing assessment tools; endoscopic imaging findings, and endoscopic stress testing. This tool has the potential to be considered a breakthrough, not only in the diagnosis of GERD, but also in functional endoscopy of the entire GI tract. We believe that EPSIS will emerge as a tool for the screening and supplementary diagnosis of anorectal hypofunction cases that can be easily and safely performed during routine colonoscopy at facilities without specialised equipment. Furthermore, as a functional endoscopic tool, it will help elucidate the pathogenesis of several functional diseases of the lower GI tract.

Summary Box

What is already known:

- Anorectal function deteriorates with age
- Existing tests of anorectal function require special equipment and are often associated with embarrassment to the patient
- The endoscopic pressure study integrated system (EPSIS) is a device that measures intraluminal pressure during endoscopy, and it has been evaluated to assess lower esophageal sphincter function in gastroesophageal reflux disease
- EPSIS is easy to use and can integrate existing assessment tools, endoscopic imaging findings, and endoscopic stress testing

What the new findings are:

- Rectal pressure measured using EPSIS correlated with age-related decline in anorectal function
- EPSIS can also be used to evaluate rectal-anal function
- Compared to existing tests that require special equipment or involve embarrassment, EPSIS is simple and can be repeated, beneficial to both patients and physicians
- There has never been an internal pressure measuring device that can also perform loading tests in conjunction with real-time endoscopic video; therefore, new insights may be obtained with EPSIS

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Supplementary material

Supplementary Video Video visually summarizes the actual events, endoscopic view, and measuring and recording equipment used during measurement using the endoscopic pressure study integrated system (EPSIS). Intraluminal pressure measured over time using EPSIS is displayed as a waveform. By simultaneously displaying the EPSIS waveform and the endoscope's real-time image on the same screen, the 2 can be compared and evaluated

You can see: https://youtu.be/KF--EIk7qnw