Supplementary Appendix

Diagnostic accuracy of magnetically guided capsule endoscopy with a detachable string for detecting oesophagogastric varices in adults with cirrhosis: prospective multicentre study

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2. Supplementary methods

2.1 Inclusion and Exclusion Criteria

Inclusion criteria:

- Gender is not limited.
- Patients aged 18 years or older.
- Both inpatients and outpatients.
- Clinically evident or biopsy-proven liver cirrhosis.
- Able to provide informed consent.

Exclusion criteria:

- Patients aged less than 18 years.
- Patients with dysphagia.
- Patients with Zenker's diverticulum.
- Suspected or known intestinal stenosis or other known risk factors for capsule retention.
- Pregnancy or suspected pregnancy.
- Patients with active gastrointestinal bleeding.
- Patients with cardiac pacemaker or other implanted electromedical devices which could interfere with magnetic resonance.
- Patients with life-threatening conditions.
- Patients plan to undergo magnetic resonance imaging examination before excretion of the capsule.
- Patients who are participating in or have participated in other clinical trials.
- Patients who refuse to give informed consent.
- Patients with any condition that precludes compliance with the study.

2.2 Endoscopic devices and procedures of ds-MCE and OGD

1) The detachable string magnetically maneuvered capsule endoscopy examination procedure

The ds-MCE system:

The ds-MCE system included the NaviCam magnetically maneuvered capsule endoscopy system[1-3] (Supplementary figure1) and a detachable latex hollow string attachment (Supplementary figure2)[4]. The MCE system consisted of a guidance magnet robot, an endoscopic capsule, a data recorder, and a computer workstation with software for real-time viewing, two joysticks for capsule orientation control. The guidance magnet robot is a C-arm type robot, with 2 rotational and 3 translational degrees of freedom. The computer workstation with ESNavi software is designed for real-time viewing and controlling. The capsule locator is a device for activating the capsule and detecting whether it is inside the human body.

The data recorder is used for receiving image data by wireless transmission from the capsule endoscope. The capsule has a size of 27*11.8mm and a permanent magnet inside its dome. It has a battery life of more than 10 hours, offering a viewing field of 150 degrees from one end. Images are captured at an adaptive rate of 0.5-6 frames per second with a resolution of 480*480 pixels. The detachable latex hollow string is 120cm in length, with a thin latex sleeve at one end that can be attached to the CE and a thick latex sleeve at the other end that can be attached to the syringe. The capsule, which is partially enclosed within the sleeve, can be detached from the string system by using the syringe to inject air into the hollow string.

Examination procedure of ds-MCE:

The ds-MCE procedure was performed by a dedicated certified operator at each center and all operators had completed standardized training for ds-MCE examination before the enrollment. The ds-MCE operators were aware of the subject's medical history and blinded to the EGV related imaging and endoscopic findings of the enrolled subjects.

i. **Gastric and Small Bowel Preparation.** Patients were instructed to maintain a clear liquid diet for the entire day prior to the ds-MCE examination followed by a 12-h overnight fast. To improve the small bowel visualization, a purgative preparation (2L polyethylene glycol solution) or no purgative preparation was used the night before the examination according to the patient's condition. Forty minutes before the examination, patients are asked to ingest 2.5g of dimethicone (Honghe Medicine, Zigong, China) as a defoaming agent and encouraged to walk freely to maximize contact with the gastric mucosa. Ten minutes before the examination, 100ml of water was ingested to initially flush the stomach cavity. Patients would then be encouraged to drink 500ml-1000ml water as tolerated just before swallowing the capsule to fill the stomach cavity for capsule navigation. Water ingestion would be repeated to optimize gastric distension during the examination.

ii. **Capsule ingestion.** The patient swallowed the capsule with water, without any sedation.

iii. **Esophageal examination.** During esophageal examination, the capsule was actively controlled by the latex hollow string with images captured at a rate of 6 fps. After swallowing the capsule, CE was then allowed to travel down as far as the gastric cardia, from where the string was slowly pulled up to inspect the esophagus under the guidance of real-time viewing. The process was repeated for at least three passages up and down, during which participants were instructed to drink water to distend the distal esophagus and wash bubbles for better observation. Target areas of interest could be observed repeatedly as the capsule travels down with swallowed water and be pulled up by attached string. After completion of the esophageal examination, the string was separated from the capsule by injecting 5mL of air using the syringe and removed from the mouth; the capsule entered the stomach.

iv. **Gastric examination.** During the gastric examination, the capsule was actively controlled by

external magnetic field. When the capsule entered the stomach, the capsule was lifted away from the posterior wall, rotated, and advanced to the fundus and cardiac regions, and then to the gastric body, angulus, antrum, and pylorus. Of note, target areas of interest could be observed repeatedly. If distension is insufficient, water ingestion would be repeated. Stomach examination procedures was performed twice in each participant according to standardized protocol[3], and the mucosa of the gastric cardia, fundus, body, angulus and antrum were fully recorded.

v. **Small bowel examination.** After completion of the gastric examination, the capsule would be switched to "small intestine examination mode" with an adaptive capture rate of 0.5–6 fps. The capsule was then move passively under gastrointestinal peristalsis.

2) The OGD examination procedure

The OGD examinations were performed by experienced endoscopists using peroral conventional standard forward-viewing upper gastrointestinal video endoscopes at each center, within 48 hours after ds-MCE procedure. The OGD operators were aware of the subject's medical history but were blinded to the ds-MCE examination results. All procedures were conducted with/without sedation, according to the standard procedure of the center and the preference of the patient. During the course of the OGD, a complete evaluation of the esophagus, stomach and first and second portion of duodenum was carried out. During the examination procedure, grading of esophageal varices (when present) was performed by all endoscopists using a predefined protocol: after examination of the stomach; the OGD is then withdrawn into the esophagus, and the esophageal lumen is fully inflated. At that point, esophageal varices and red signs then were evaluated. The esophageal varices were graded as small (<5 mm) or large (≥5 mm) and, if in doubt, it was measured against the open endoscopic biopsy forceps (5 mm). The whole examination procedure was recorded on videos and the digital pictures for each participant and then evaluated at the independent imaging core-lab.

2.3 Assessment of videos and imaging of ds-MCE and OGD

The recorded videos and images of ds-MCE and OGD examinations were coded by a unique study number and then assessed by an independent imaging core-lab blinded to the patient identification information and related clinical information. All imaging core-lab members were trained and tested before the official reading in order to reduce reader variability and increase reliability. The imaging core-lab consisted of a ds-MCE group and OGD group.

In the ds-MCE group, the coded videos of ds-MCE examinations were reviewed and graded by two different independent endoscopists who were experienced in MCE and were blinded to the results of

OGD examinations. They were masked to each other's evaluations. A consensus reading was performed by a senior endoscopist experienced in MCE in case of discrepancies. They were instructed to identify and grade the esophageal varices (EV), gastric varices (GV), portal hypertensive gastropathy (PHG) to record the presence of portal hypertensive enteropathy (PHE) and the examination time of esophagus, stomach and small-bowel. The image reading of ds-MCE examination was based on the ESView software, and the percentage of the esophageal luminal circumference occupied by the EV could be measured through the software directly (Supplementary figure3).

In the OGD group, the coded videos and captured pictures of OGD examinations were reviewed and graded by another two different independent endoscopists who were experienced in OGD and were blinded to the results of ds-MCE examinations. They were masked to each other's evaluations. A consensus reading was performed by another senior endoscopist experienced in OGD in case of discrepancies. They were instructed to identify and grade the EV, GV and portal hypertensive gastropathy (PHG).

2.4 Outcome definitions

The primary outcome was the sensitivity and specificity of ds-MCE in identifying the presence of EGV in patients with cirrhosis, using detection by OGD as the reference.

The key secondary outcome was the diagnostic accuracy of ds-MCE in detection of high-risk EV, using the detection by OGD as the reference standard. Other secondary outcomes were the following: the diagnostic accuracy of ds-MCE in detection of EV, large EV, red signs of EV, GV, cardiofundal GV (GOV2 and IGV1), high-risk EGV and PHG compared with the OGD; the findings of PHE in small bowel under ds-MCE; the examination time of ds-MCE and OGD; patient satisfaction assessment and safety evaluation.

- EV identified under OGD were classified based on the Baveno III consensus to differentiate between large varices (varix diameter ≥5mm) and small varices (varix diameter <5mm)[5].
- As grading EV by OGD requires fully distention of the esophagus with air insufflation, which is lacking in CE, there has been no consensus on the standard classification of large EV under ds-MCE. In this study, based on the de Franchis method, we graded the EV under ds-MCE according to the proportion of the esophageal luminal circumference occupied by the largest EV present[6]. The Youden Index, defined as [(sensitivity＋specificity)-1], will be calculated to determine the optimal

esophageal luminal circumference percentage threshold derived from the development cohort that resulted in the best combination of specificity and sensitivity for distinguishing large EV under ds-MCE, using the results of OGD as the reference standard. Then, EVs under ds-MCE were classified into three grades: no, small or large, with the latter signifying that the esophageal varix occupied more than the "optimal threshold" (defination see statistical analysis section) proportion of the esophageal luminal circumference.

- The high-risk EV was defined as large EV or small EV with presence of red signs according to the Baveno VI consensus[7].
- GV were classified according to Sarin's classification[8]. Gastric varices could be classified on the basis of its location in the stomach and its relationship with esophageal varices during ds-MCE procedure and OGD procedure. These are divided into two groups: gastroesophageal varices (GOVs) and isolated gastric varices (IGV). GOV1 are the extension of esophageal varices which across the cardia onto the lesser curve, and GOV2 extend onto the fundus. Isolated gastric varices (IGV) are vascular protrusions without direct connection to the esophageal varices. IGV1 are located in the fundus, while IGV2 are located elsewhere in the stomach, typically in the distal body and antrum.
- Cardiofundal gastric varices including GOV2 and IGV1 are at high risk of bleeding due to the unique vascular anatomy as opposed to lesser-curvature gastric varices (GOV1).
- The high risk EGV were defined as high-risk EV or any GV[9,10].
- The PHG is classified as four elementary gastric endoscopic signs proposed by the NIEC group:1) mosaic like pattern (MLP); 2) red point lesions(RPL); 3) cherry red spots (CRS); 4) black brown spots (BBS) [11,12].
- Endoscopic findings of PHE were identified as mucosal inflammatory-like abnormalities, vascular lesions[13-15]. In addition, mucosal inflammatory-like abnormalities and vascular lesions can lead to spontaneous bleeding.
- Assessment of the examination time of ds-MCE and OGD. Examination time of ds-MCE include esophageal examination time (EET), gastric examination time (GET), gastric transit time (GTT), small bowel transit time (SBTT), and total running time (TRT). EET is defined as the time between the first esophageal image and the first gastric image. GET is defined as the time for examination of gastric primary anatomic landmarks twice. GTT is defined as the time between the first gastric image and the first duodenal image. SBTT is defined as the time between the first duodenal image

and the first cecal image. TRT is defined as the time of the last picture taken by the capsule. Capsule endoscopy completion rate (CECR) is also recorded which defined as the proportion of the capsule that has a complete visualization of the entire small bowel. Examination time of OGD was defined as the duration from the endoscope entering to exiting from the esophagus.

- For patient satisfaction assessment, patients were instructed to complete a questionnaire regarding their satisfaction of the ds-MCE and OGD after completing the endoscopies. The questionnaire is shown as follows:

  1. Did you experience discomfort during the ds-MCE/OGD procedure?

     4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

  2. Did you experience discomfort after the ds-MCE/OGD procedure?

     4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

  3. How would you rate the entire ds-MCE/OGD examination procedure?

     4 = very comfortable; 3 = comfortable; 2 = tolerable; 1 = uncomfortable; 0 = very uncomfortable

- Safety outcomes were based on adverse-event reporting. Two weeks following the ds-MCE procedure, patients were contacted to confirm excretion of the capsule and to verify that there were no changes in their wellbeing following participation in this study. An X-ray procedure was performed to confirm the capsule exit if deemed necessary by the investigator. All adverse events occurring during the study were reported to the investigators and sponsor and carefully recorded.

2.5 Sample size estimation and statistical analysis

2.5.1 Sample size estimation

As a single-arm confirmatory diagnostic accuracy study, we primarily aimed to test whether both the sensitivity and the specificity of ds-MCE for detecting EGV would be >85%, using OGD as the reference standard. With estimated sensitivity of 90%, specificity of 94%, a two-sided alpha of 5%, power of 80%, EGV prevalence of 62%, and a dropout rate of 3%, 591 patients would be needed[16].

When considering the accuracy of ds-MCE for detecting high-risk EV (key secondary outcome), the validation cohort of approximately 200 patients would provide an estimation precision (CI width/2) of <7%, with estimated sensitivity of 90% and specificity of 94%, using the optimal esophageal luminal

circumference percentage threshold derived from the development cohort, and high-risk EV prevalence of 40%.

2.5.2 Statistical Analysis Set

The analyses were performed on intent-to-diagnose (ITD)* and safety analysis set (SAS). Each analysis set summarized the number of subjects.

Diagnostic analysis set: The analysis of ITD is primary

The diagnostic analyses were based on ITD population who go through procedures of ds-MCE and OGD modalities and can be evaluated for the results of EV and GV.

Safety Set: The evaluation of safety parameters was conducted on the SAS.

SAS (Safety Analysis Set): actual data that has been inspected at least once and has safety indicators recorded.

* The modified intent-to-treat (mITT) in the statistical analysis plan was renamed as ITD. The PPS in the statistical analysis plan appeared to be the same as the ITD set.

2.5.3 Statistical analysis

The primary outcome is the diagnostic accuracy for discrimination of patients with EGV using sensitivity and specificity, along with the corresponding 95% CIs estimated using the Wilson's method. Sensitivity and specificity were compared with 85% using one-sample exact test. The accuracy, and positive and negative predictive values (PPV and NPV) were calculated as other measures simultaneously.

We assessed the diagnostic accuracy of ds-MCE for EV, red color signs in EV, GV, cardiofundal GV and PHG using sensitivity, specificity, PPV, NPV and the overall diagnostic accuracy, along with the corresponding 95% CIs estimated using the Wilson's method.

The optimal esophageal luminal circumference percentage threshold for distinguishing large EV under ds-MCE was derived from the development cohort; and the diagnostic accuracy of ds-MCE for identifying high-risk EV, high-risk EGV and large EV was assessed based on the optimal threshold (only keeping the integer portion when with decimals) in the validation cohort, using sensitivity, specificity, PPV, NPV and the overall diagnostic accuracy. The development cohort and validation cohort were divided based on centers, in the order of the first patient in (FPI). Centers with earlier FPI date were allocated to the development cohort (whose sample size should meet approximately 2/3 of the total

sample size), and the remaining centers with later FPI date were allocated to the validation cohort. The Youden Index, defined as [(sensitivity + specificity)-1], was calculated to determine the optimal esophageal luminal circumference percentage threshold derived from the development cohort that resulted in the best combination of specificity and sensitivity for distinguishing large EV under ds-MCE. The optimal threshold was internally validated with bootstrap method, with 1000 replicates.

We did a prespecified subgroup analysis of diagnostic accuracy of ds-MCE for identifying EGVs, high risk EVs and high-risk EGV in subgroups of cirrhosis stage (compensated phase and decompensated phase) and indication for endoscopy (screening and surveillance).

Descriptive statistics for continuous variables include arithmetic mean (standard deviation) or median (interquartile ranges [IQR]) as appropriate. Frequency and percentage were calculated for categorical variables. Unless otherwise specified, all significance testing was 2-tailed using $\alpha = 0.05$. Tests was declared statistically significant if the calculated p-value was <0.05. All statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc) and R, version 4.1.2 (R Foundation for Statistical Computing).

3. Supplementary Results

Table S1. Patient Enrollment per Study Center

Participating center	Number of patients recruited	Number of patients finished both ds-MCE and OGD	The date of first patient in	Site allocation (development/validation cohort)
Changhai Hospital, Shanghai, China	156(25.70%)	151(25.95%)	2021-01-07	Development cohort
Yangpu Hospital, Shanghai, China	14(2.31%)	13(2.23%)	2021-03-19	Development cohort
The Fifth Affiliated Hospital of Zunyi Medical University, Zhuhai, China	47(7.74%)	43(7.39%)	2021-03-19	Development cohort
Tongji Hospital, Shanghai, China	64(10.54%)	60(10.31%)	2021-03-23	Development cohort
Shanghai Sixth People's Hospital, Shanghai, China	25(4.12%)	23(3.95%)	2021-03-30	Development cohort
Qilu Hospital, Jinan, China	51(8.40%)	50(8.59%)	2021-04-25	Development cohort
Union Hospital, Wuhan, China	54(8.90%)	53(9.11%)	2021-04-28	Development cohort
Ruijin Hospital, Shanghai, China	21(3.46%)	20(3.44%)	2021-06-24	Validation cohort
Shanghai East Hospital, Shanghai, China	40(6.59%)	36(6.19%)	2021-06-01	Validation cohort
Zhujiang Hospital, Guangzhou, China	43(7.08%)	42(7.22%)	2021-08-17	Validation cohort
Third Xiangya Hospital of Central South University, Changsha, China	18(2.97%)	18(3.09%)	2021-07-30	Validation cohort
The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China	54(8.90%)	53(9.11%)	2021-05-11	Validation cohort
The First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou, China	6(0.99%)	6(1.03%)	2021-06-11	Validation cohort
Shanghai Pudong New Area Gongli Hospital, Shanghai, China	14(2.31%)	14(2.41%)	2021-08-09	Validation cohort
Total	607	582	/	/

Table S2. Baseline characteristics of patients included in the development cohort and validation cohort

Characteristic	Development cohort (n=393)	Validation cohort (n=189)
Age (year)，Median (IQR)	54.00 (47.00-63.00)	56.00 (49.00-65.00)
Male sex, no. (%)		
Male	265 (67.43%)	133 (70.37%)
Female	128 (32.57%)	56 (29.63%)
Body-mass index, kg/m^2 ， Median (IQR)†	23.44 (21.48-25.95)	22.60 (20.48-25.10)
Time since diagnosis of cirrhosis (yr), Median (IQR)	3.00 (0.33-7.00)	1.08 (0.10-5.00)
Etiology, no. (%)		
Hepatitis B virus infection	224 (57.00%)	116 (61.38%)
Hepatitis C virus infection	17 (4.33%)	12 (6.35%)
Alcoholic liver disease	40 (10.18%)	21 (11.11%)
Autoimmune hepatitis	39 (9.92%)	5 (2.65%)
Primary biliary cirrhosis	8 (2.04%)	8 (4.23%)
Non-alcoholic steatohepatitis	5 (1.27%)	1 (0.53%)
Cryptogenic	41 (10.43%)	19 (10.05%)
Other*	19 (4.83%)	7 (3.70%)
Child-Pugh score (points), Median (IQR)	5.00 (5.00-7.00)	6.00 (5.00-7.00)
Child-Pugh Class, no. (%)		
Class A	293 (74.55%)	109 (57.67%)

Characteristic	Development cohort (n=393)	Validation cohort (n=189)
Class B	90 (22.90%)	63 (33.33%)
Class C	10 (2.54%)	17 (8.99%)
MELD score (points), Median (IQR)	9 (7-11)	9 (8-12)
Laboratory results		
Platelet count ($\times 10^9$/L)	105 (67-158)	81 (53-121)
ALT (U/L)	26 (18-40)	25 (19-39.75)
AST (U/L)	30 (23-46)	33 (26-47.83)
GGT (U/L)	37 (21.5-72.5)	41.15 (22-81.25)
Total bilirubin (μmol/L)	18.6 (13.4-28)	18.5 (13.4-28.95)
Albumin (g/L)	40 (35-45)	36.3 (30.85-41.75)
Creatinine (μmol/L)	66.2 (58-78)	66 (56.6-79)
PT (s)	13.6 (12.7-15)	14 (12.95-15.6)
INR	1.12 (1.02-1.26)	1.20 (1.11-1.32)
Decompensated cirrhosis, no. (%)	231 (58.78%)	125 (66.14%)
Indication for endoscopy, no. (%)		
Screening	146 (37.15%)	82 (43.39%)
Surveillance	247 (62.85%)	107 (56.61%)
Clinical events, no. (%)		
Ascites	163 (41.48%)	101 (53.44%)
History of splenectomy	34 (8.65%)	7 (3.70%)

Characteristic	Development cohort (n=393)	Validation cohort (n=189)
TIPS insertion	29 (7.38%)	10 (5.29%)
History of endoscopic variceal therapy	80 (20.36%)	40 (21.16%)
History of bleeding esophagogastric varices	127 (32.32%)	62 (32.80%)

IQR, interquartile range; MELD, model for end-stage liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; PT, prothrombin time; INR, international normalized ratio

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

*Other causes of cirrhosis included schistosome infection, drug induced cirrhosis, Budd-Chiari syndrome, hepatitis C virus (HCV) and hepatitis B virus (HBV) co-infection, hepatitis B infection + alcoholic liver disease, alcoholic liver disease + schistosome infection.

Table S3. Detailed information of 14 patients with inconsistent EGV results of ds-MCE and OGD

Case	Presence of EV		Presence of GV		Final results of EGV identification by ds-MCE
	OGD	ds-MCE	OGD	ds-MCE	
1	Yes	No	No	No	FN
2	Yes	No	Yes	No	FN
3	No	Yes	No	No	FP
4	Yes	No	No	No	FN
5	Yes	No	No	No	FN
6	Yes	No	No	No	FN
7	Yes	No	No	No	FN
8	Yes	No	No	No	FN
9	Yes	No	No	No	FN
10	No	Yes	No	No	FP
11	No	Yes	No	No	FP
12	No	No	Yes	No	FN
13	Yes	No	No	No	FN
14	No	Yes	No	No	FP

* TN= Ture Negative; FN=False Negative; TP= True Positive; FP=False Positive

Table S4. Diagnostic performance of ds-MCE, with OGD as the reference standard, for identifying large EV, high-risk EV and high-risk EGV using the optimal threshold of 18% based on the development cohort for internal validation (n=393)

Outcome	Sensitivity *%(95%CI)*	Specificity *%(95%CI)*	Positive Predictive Value *%(95%CI)*	Negative Predictive Value *%(95%CI)*	Diagnostic Accuracy *%(95%CI)*
Large EV based on the optimal threshold of 18%	98.30 (94.90,100.00)	97.58 (93.36,99.58)	96.81 (91.71,99.45)	98.70 (96.17,100.00)	97.71 (95.42,99.49)
High-risk EV based on the optimal threshold of 18%	97.56 (93.18,100.00)	96.09 (91.56,99.08)	95.33 (90.81,98.88)	97.93 (94.49,100.00)	96.44 (93.89,98.73)
High-risk EGV	98.67(95.96,100.00)	96.86(92.20,99.47)	97.45 (93.83,99.56)	98.37 (95.00,100.00)	97.71 (95.17,99.49)

Table S5. Subgroup analysis of the screening and surveillance population

Outcome	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value		Diagnostic Accuracy	
	%(95%CI)	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*
In the screening population										
EGV*	95.59	130/136	98.91	91/92	99.24	130/131	93.81	91/97	96.93	221/228
	(90.71,97.96)		(94.10,99.81)		(95.80,99.87)		(87.16,97.13)		(93.80,98.51)	
High risk EV based on the optimal threshold of 18%‡	91.43	32/35	95.74	45/47	94.12	32/34	93.75	45/48	93.90	77/82
	(77.62,97.04)		(85.75,98.83)		(80.91,98.37)		(83.16,97.85)		(86.51,97.37)	
High-risk of EGV‡	90.70	39/43	94.87	37/39	95.12	39/41	90.24	37/41	92.68	76/82
	(78.40,96.32)		(83.11,98.58)		(83.86,98.65)		(77.45,96.14)		(84.94,96.60)	
In the surveillance population										
EGV*	98.51	264/268	96.51	83/86	98.88	264/267	95.40	83/87	98.02	347/354
	(96.23,99.42)		(90.24,98.81)		(96.75,99.62)		(88.77,98.20)		(95.98,99.04)	
High risk EV based on the optimal threshold of 18%‡	98.33	59/60	93.62	44/47	95.16	59/62	97.78	44/45	96.26	103/107
	(91.14,99.71)		(82.84,97.81)		(86.71,98.34)		(88.43,99.61)		(90.78,98.54)	
High-risk of EGV‡	100.00	73/73	97.06	33/34	98.65	73/74	100.00	33/33	99.07	106/107
	(95.00,100.0)		(85.08,99.48)		(92.73,99.76)		(89.57,100.0)		(94.90,99.83)	

*: Based on 582 patients who finished both ds-MCE and OGD examinations (n=582).

‡: Based on the external validation cohort (n=189).

Table S6. Subgroup analysis of the compensated cirrhosis and decompensated cirrhosis population

Outcome	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value		Diagnostic Accuracy	
	%(95%CI)	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*	*%(95%CI)*	*no./total no.*
In the compensated cirrhosis population										
EGV*	90.91	80/88	98.55	136/138	97.56	80/82	94.44	136/144	95.58	216/226
	(83.07,95.32)		(94.87,99.60)		(91.54,99.33)		(89.42,97.16)		(92.05,97.58)	
High risk EV based on the optimal threshold of 18%‡	88.24	15/17	97.87	46/47	93.75	15/16	95.83	46/48	95.31	61/64
	(65.66,96.71)		(88.89,99.62)		(71.67,98.89)		(86.02,98.85)		(87.10,98.39)	
High-risk EGV‡	86.96	20/23	97.56	40/41	95.24	20/21	93.02	40/43	93.75	60/64
	(67.87,95.46)		(87.40,99.57)		(77.33,99.15)		(81.39,97.60)		(85.00,97.54)	
In the decompensated cirrhosis population										
EGV*	99.37	314/316	95.00	38/40	99.37	314/316	95.00	38/40	98.88	352/356
	(97.72,99.83)		(83.50,98.62)		(97.72,99.83)		(83.50,98.62)		(97.15,99.56)	
High risk EV based on the optimal threshold of 18%‡	97.44	76/78	91.49	43/47	95.00	76/80	95.56	43/45	95.20	119/125
	(91.12,99.29)		(80.07,96.64)		(87.84,98.04)		(85.17,98.77)		(89.92,97.78)	
High-risk EGV‡	98.92	92/93	93.75	30/32	97.87	92/94	96.77	30/31	97.60	122/125
	(94.16,99.81)		(79.85,98.27)		(92.57,99.41)		(83.81,99.43)		(93.18,99.18)	

*: Based on 582 patients who finished both ds-MCE and OGD examinations (n=582).

‡: Based on the external validation cohort (n=189).

Table S7. Small bowel findings of portal hypertensive enteropathy detected by ds-MCE

Lesions	The entire small bowel‡ (n=510)	Proximal small bowel* (n=510)	Middle small bowel* (n=510)	Distal small bowel* (n=510)
Presence of PHE	333 (65.29%)	274 (53.73%)	229 (44.9%)	243 (47.65%)
Inflammatory-like lesions	273 (53.53%)	227 (44.51%)	121 (23.73%)	131 (25.69%)
villous edema	185 (36.27%)	166 (32.55%)	63 (12.35%)	55 (10.78%)
erythema	204 (40.00%)	146 (28.63%)	86 (16.86%)	84 (16.47%)
erosion	39 (7.65%)	23 (4.51%)	12 (2.35%)	15 (2.94%)
ulcerations	19 (3.73%)	6 (1.18%)	3 (0.59%)	14 (2.75%)
polypoid lesions	13 (2.55%)	6 (1.18%)	7 (1.37%)	6 (1.18%)
Vascular lesions	252 (49.41%)	122 (23.92%)	175 (34.31%)	189 (37.06%)
red spot	123 (24.12%)	56 (10.98%)	54 (10.59%)	64 (12.55%)
angioectasia	58 (11.37%)	21 (4.12%)	29 (5.69%)	23 (4.51%)
varices	180 (35.29%)	60 (11.76%)	126 (24.71%)	149 (29.22%)
Spontaneous bleeding	3 (0.59%)	1 (0.20%)	1 (0.20%)	1 (0.20%)

‡: Among 582 cirrhotic patients, a total of 510 patients finished the whole small bowel examination under ds-MCE.

*The entire small bowel was divided into three parts based on transit time: the proximal, middle, and distal small bowel.

Table S8. Examination time of ds-MCE and OGD procedures

Characteristic	Examination times
ds-MCE	
Esophageal examination time (min), Median (IQR)	4.74 (3.12–7.15)
Gastric examination time (min), Median (IQR)	15.78 (8.57-23.70)
Gastric transit time (hour), Median (IQR)	1.12 (0.68-1.85)
Small bowel transit time (hour), Median (IQR)	5.30 (4.13-6.78)
Total recording time (hour), Median (IQR)	12.83 (11.66-13.63)
OGD	
Total examination time from the OGD entering to exiting from the esophagus (min), Median (IQR)	5.50 (4.50-7.00)

IQR, interquartile range

Table S9. Procedure satisfaction of ds-MCE and OGD without sedation (n=279)

Item	ds-MCE [points,median (IQR)]	OGD [points,median (IQR)]
Discomfort score during procedure	4 (3-4)	3 (2-3)
Discomfort score after procedure	4 (4-4)	4 (3-4)
Overall satisfaction score	3 (3-4)	2 (2-2)

IQR, interquartile range

Table S10. Procedure satisfaction of ds-MCE and sedated OGD (n=303)

Item	ds-MCE [points,median (IQR)]	OGD [points,median (IQR)]
Discomfort score during procedure	4 (3-4)	4 (3-4)
Discomfort score after procedure	4 (4-4)	4 (3-4)
Overall satisfaction score	3 (3-4)	3 (2-3)

IQR, interquartile range

Figure S1. The NaviCam magnetically maneuvered capsule endoscopy system. It consists of a guidance magnet robot and a computer workstation (A), a magnetic capsule endoscope (B); a capsule locator (C); ESNavi software (D); and a data recorder (E).

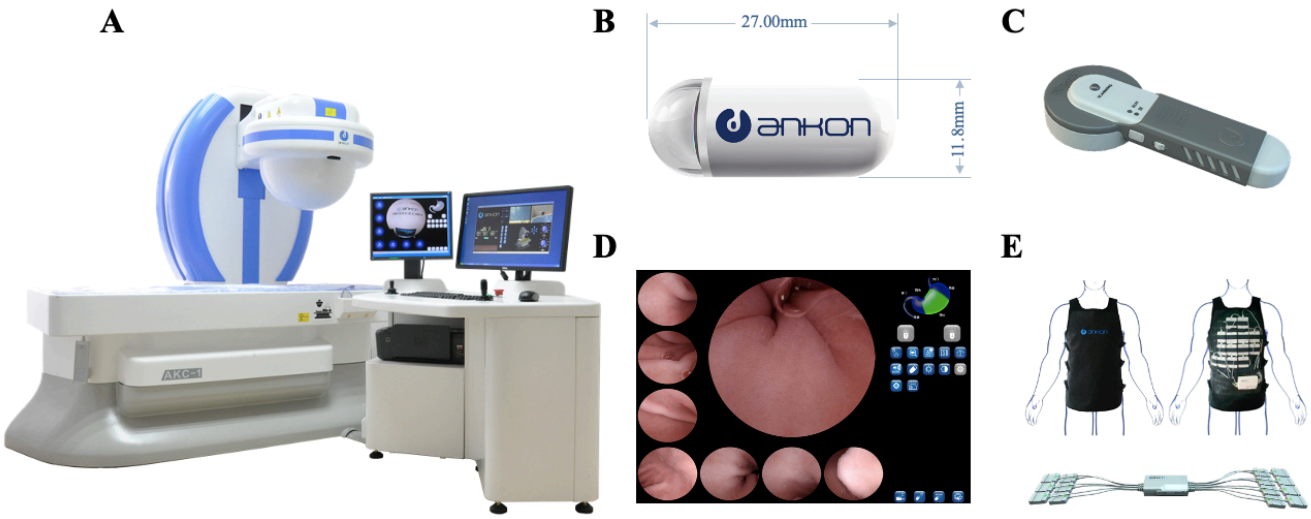


Figure S2. The detachable latex hollow string attachment. A, the string system; B, enclosing the capsule within the sleeve; C, injecting air into the hollow string with the syringe; D, the detachment of the capsule and the string.

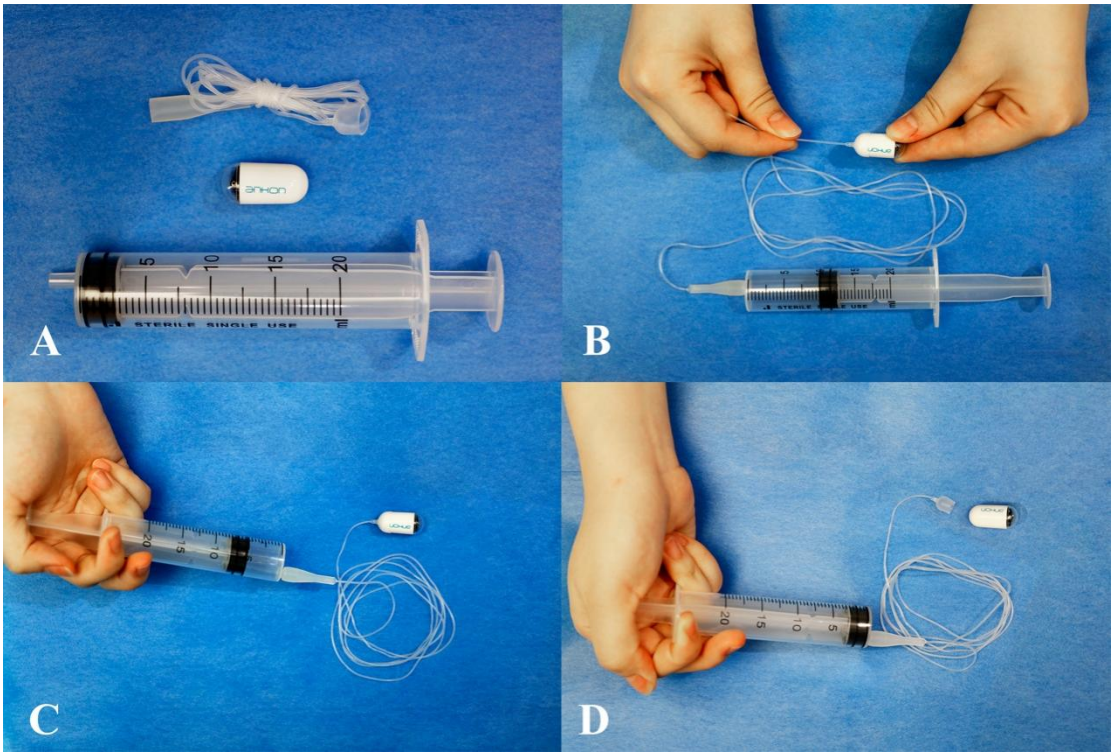


Figure S3. The interface of ESView software for calculating the percentage of the esophageal luminal circumference occupied by EV.

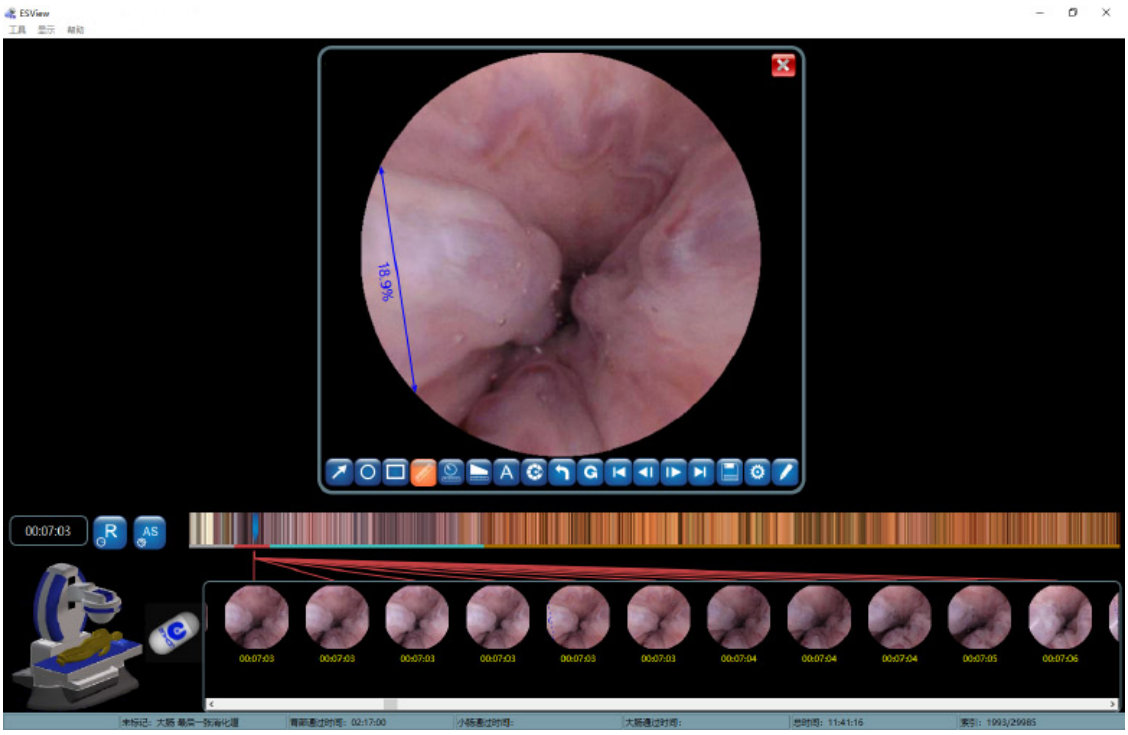


Figure S4. Receiver operating characteristic curve of ds-MCE based on the development cohort (n=393). An optimal esophageal luminal circumference percentage threshold of 18.45% for discrimination of the large EV using ds-MCE was calculated from the maximum Youden's index at 0.948.

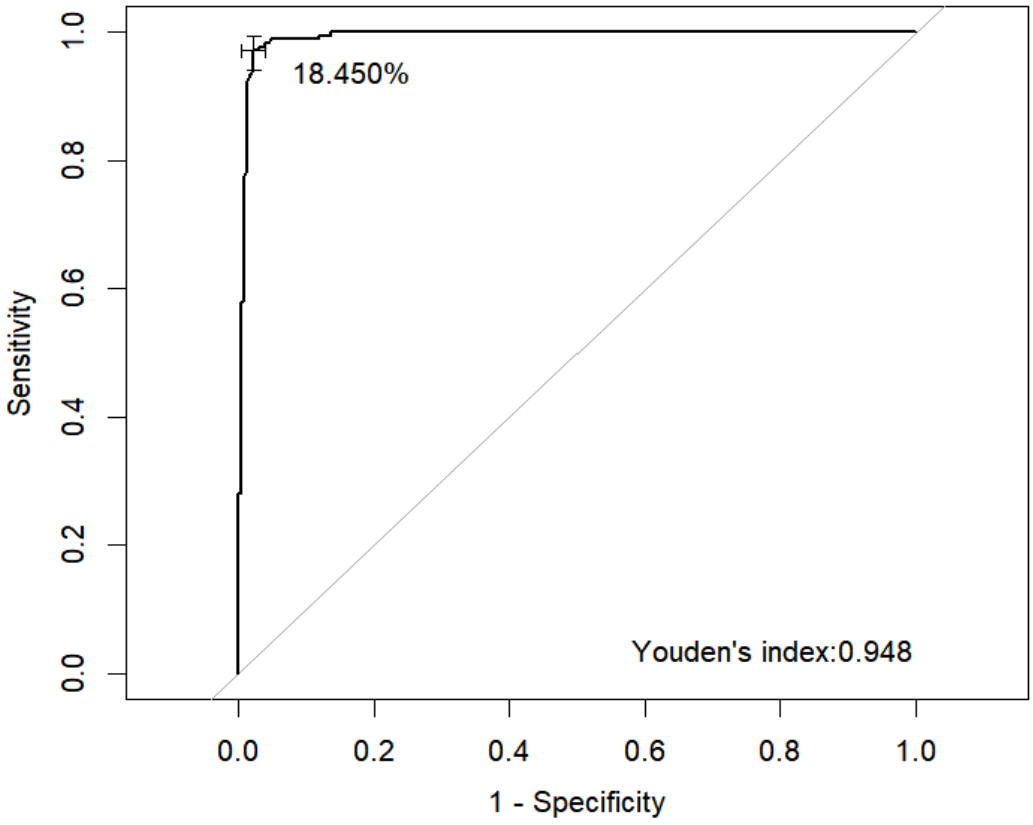
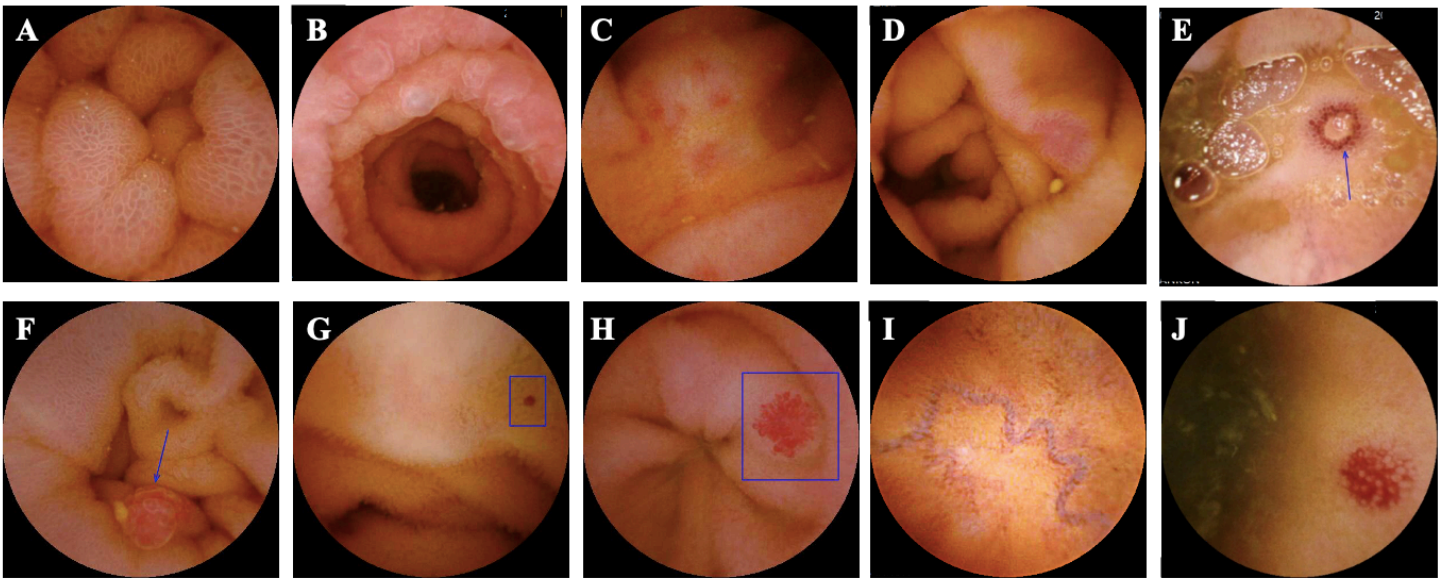


Figure S5. Representative lesions of portal hypertensive enteropathy observed on ds-MCE. Villous edema (Panel A and B), erythema (Panel C), erosion (Panel D), ulcerations (Panel E), polypoid lesions (Panel F), red spot (Panel G), angioectasia (Panel H), varices (Panel I), spontaneous bleeding (Panel J) are shown.



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