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Original Article

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Latest possible timing for endoscopic-assisted intervention in capsule endoscopy

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Abstract

Background: Delayed upper gastrointestinal transit during small bowel capsule endoscopy (SBCE) can lead to incomplete or failed examinations but can be treated by endoscopic-assisted intervention (EAI). The aim of this study was to investigate the latest possible timing of EAI.

Methods: Patients who underwent SBCE and received EAI between July 2007 and December 2020 were retrospectively reviewed. A novel T-value was developed that accounted for the varied battery life of different generations of PillCam when determining the latest possible timing of EAI, where T is calculated as EAI time/[minimum battery life of the PillCam minus small bowel transit time (6 h)] × 100%. Patients were divided into two groups based on the cut-off value of the receiver operating characteristic curve: early EAI (group A, $T < 76.3\%$) and late EAI (group B, $T \geq 76.3\%$). The primary outcome was the completion rate (CR), and the secondary outcome was the detection rate. The latest possible timing of EAI (h) was calculated according to the T-value formula and further verified in our recent data set.

Results: This study included 108 patients. The CR was significantly higher in group A than in group B (79.2% vs 58.2%; $P = 0.018$). Late EAI was an independent predictor of incomplete SBCE (odds ratio = 2.900; 95% confidence interval, 1.193–7.053). The latest possible timing of EAI was 1.5 h and 4.6 h from the start of the examination for PillCam SB1 and PillCam SB2/3, respectively.

Conclusions: Early EAI was associated with higher CR. The latest possible timing of EAI was 1.5 h for PillCam SB1 and 4.6 h for PillCam SB2/3 from the start of the examination.

Keywords: small bowel capsule endoscopy; delayed upper gastrointestinal transit; endoscopic-assisted intervention; latest possible timing; completion rate

Introduction

The diagnosis of small bowel lesions is clinically challenging. Currently available tests such as barium meal, nuclear scans, and angiography have low diagnostic yield and poor sensitivity, which limit their utility [1–3]. As an emerging technology, small bowel capsule endoscopy (SBCE) has a superior diagnostic yield compared with other modalities used to assess the small bowel [4]. Consequently, SBCE is widely used for diagnosis and monitoring of small bowel disorders, determining locations of lesions, and evaluating treatment response [5–7]. The overall detection rate of small bowel lesions by SBCE ranges from 19% to 79% [7–12].

The diagnostic yield of SBCE can be affected by indications, bowel preparation, technical errors, view mode and frame rate during interpretation, and reviewers' experience [13]. During SBCE, the capsule offers a limited operating time of 8–15 h [14]. Risk factors for incomplete SBCE include slowed gastric transit, previous small bowel surgery, hospitalization, and moderate or poor bowel cleansing [14–17]. Delayed gastric passage of the capsule may cause 30% of incomplete SBCEs or failed SBCEs [18].

If the passage of a capsule in the upper gastrointestinal tract is delayed during SBCE, the capsule can be retrieved and placed in the duodenum or elsewhere in the gastrointestinal tract using endoscopic-assisted intervention (EAI) [19, 20]. Currently, the timing of EAI is arbitrary, with poorly timed EAI resulting in unnecessary waste of healthcare resources or incomplete SBCE. The objective of this study was to determine the latest possible timing of EAI for some different types of capsules used in SBCE.

Methods

Patients and study design

The medical records of patients aged 18–75 years who underwent SBCE (PillCam SB1, SB2, or SB3) and received EAI in Renji Hospital

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between July 2007 and December 2020 were retrospectively reviewed. Patient demographic characteristics, major indication for SBCE, and interventions were recorded. Patients with capsule malfunction and poor bowel preparation were excluded. The study was approved by the institutional review board of Renji Hospital (approval number LY2022-074-B).

In our routine clinical practice, "delay in upper gastrointestinal transit" is defined as failure of a capsule to pass through the pylorus within 1 h. Small bowel transit time (SBTT) is defined as the time required for a capsule to reach the ileocecal valve after entering the duodenum. Published literature mainly reports SBTT ranging from 4 h to 6 h [9, 21–23]. In our center, we consider an SBTT of 6 h appropriate for adequate examination of the small bowel. The lesion detection rate is defined as the ratio of the number of patients with lesions to the total number of patients.

This study used three generations of PillCam (SB1, SB2, and SB3; size: 11 mm × 26 mm) [14]. Battery life varies among the generations of PillCam (PillCam SB1 8 h, PillCam SB2/3 12 h) [7, 20]. Accordingly, we introduced a novel T-value that accounts for the varied battery life of the different generations of PillCam when determining the latest possible timing of EAI, where T is calculated as EAI time/[minimum battery life of the PillCam minus SBTT (6 h)] × 100%. T was calculated for each patient included, and T-values were normally distributed, with a mean of 71.7 ± 26.3% and a median of 77.8%. The receiver operating characteristic (ROC) curve was used to determine the latest possible cut-off T-value to distinguish high and low completion rate (CR). The ROC curve is a curve drawn with the false positive rate (1 – specificity) as the horizontal coordinate and the true positive rate (sensitivity) as the vertical coordinate, and it is a composite index reflecting the continuous variables of sensitivity and specificity, and it is used as a graphical method to show the relationship between the two degrees, and different points are generated by different boundary values, and the point that gives the largest value of the Youden index (sensitivity + specificity − 1) is calculated based on the sensitivity and specificity corresponding to the points. A point is calculated as the cut-off value. According to the ROC curve and Youden index, the cut-off value was 76.3%. Then patients were divided into two groups based on the cut-off value: early EAI (group A, $T < 76.3\%$) and late EAI (group B, $T \geq 76.3\%$).

$$T = \frac{\text{EAI time}}{\text{Minimum battery life of SBCE} - 6\text{h}} \times 100\%$$

The primary outcome was CR, defined as the ratio of the number of patients in which the capsule reached the cecum to the total number of patients after EAI. The secondary outcome was the detection rate. Factors associated with CR were explored using logistic regression analysis. The latest possible timing of EAI (h) was calculated according to the T-value formula, and the effectiveness of the latest possible timing of EAI in our study was verified in our recent endoscopic intervention operation. It means that when a delay in capsule transit occurred, we obtained satisfactory results by intervening within this time window.

Capsule placement by endoscopic-assisted intervention

SBCE was performed using the PillCam SB (Given Imaging Inc., Yokne'am, Israel); the default frame rate for SBCE is usually set at two frames per second. During SBCE, two nurses confirmed the position and orientation of the capsule by real-time monitoring. EAI was performed when passage of the capsule was delayed in the upper gastrointestinal tract. In these cases, after the patients were routinely given local anesthesia with oral lidocaine paste, endoscopists grabbed the capsule with a foreign body retrieval net, and the capsule was released into the duodenum using gastroscopy (Figure 1). EAI was performed by five experienced endoscopists, all with >10 years of experience in endoscopic operations.

Statistical analysis

Statistical analysis was performed with SPSS 26.0. Normally distributed data were expressed as mean ± standard deviation and compared using the *t*-test. Non-normally distributed data were expressed as median (interquartile range) and were compared using the Wilcoxon rank-sum test. Count data were expressed as numbers and percentages and compared using the χ^2 test. Factors associated with CR were identified using univariate logistic regression analysis. Factors with a *P*-value less than 0.05 in univariate analysis were included in a multivariate logistic regression model. Odds ratios and 95% confidence intervals were calculated. $P < 0.05$ was considered statistically significant.

Results

Demographical and clinical characteristics

A total of 108 patients were included in this study, excluding 49 patients who were excluded due to incomplete baseline information, other interventions, and other brands of capsules (of which 64, 32, and 12 patients underwent SB1, SB2, and SB3, respectively). Patient demographics and indications for SBCE are shown in Table 1. There were no significant differences in any of the demographic characteristics or indications for SBCE between group A and group B.

Primary and secondary outcomes

The CR of small bowel examinations was significantly higher in group A than in group B (79.2% vs 58.2%; $P = 0.018$). The detection rate was higher in group A than in group B [79.2% (42/53) vs 74.5% (41/55)], but the difference was not significant (Table 2). Specific pathological findings detected during SBCE are listed in Table 3.

Factors associated with CR

On univariate analysis, the timing of EAI, patient age, and the incidence of obscure gastrointestinal bleeding were significantly different between patients with incomplete and those with complete small bowel examination. On multivariate analysis, late EAI was an independent predictor of incomplete SBCE (odds ratio = 2.900; 95% confidence interval, 1.193–7.053), implying that early EAI is a protective factor against incomplete small bowel examination (Table 4).

Latest possible timing of intervention for delayed passage of a capsule through the upper gastrointestinal tract

The CR of small bowel examinations was satisfactory at $T < 76.3\%$. The latest possible timing of EAI when delayed passage of a capsule through the upper gastrointestinal tract was detected was 1.5 h ([8–6] × 76.3%) from the start of the examination for PillCam SB1 or 4.6 h ([12–6] × 76.3%) from the start of the examination for PillCam SB2/3. Our recent data verified this latest possible timing.

Discussion

This study investigated the latest possible timing of EAI when the passage of a capsule in the upper gastrointestinal tract is delayed

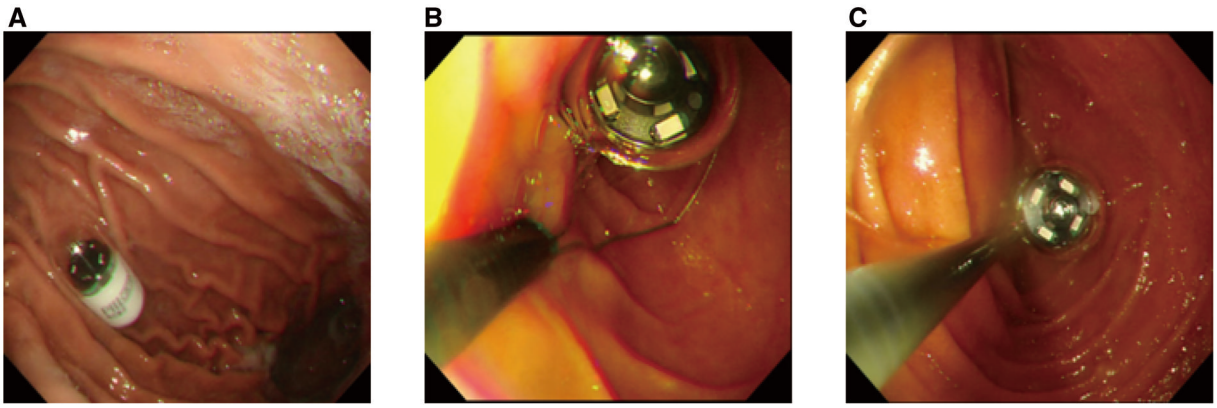

Figure 1. Endoscopic-assisted intervention (EAI) delivering capsules retained in the upper gastrointestinal tract to the duodenum. (A) The capsule was retained in the stomach. (B, C) Endoscopists grabbed the capsule with a foreign body retrieval net, and the capsule was released into the duodenum with the assistance of gastroscopy.

Table 1. Comparison of demographic and clinical characteristics between group A and group B in this study

Characteristics	Group A ($n = 53$)	Group B ($n = 55$)	P-value
Age, years, median [IQR]	56 [37.5, 64.5]	55 [39, 60]	0.751
Body mass index, kg/m^2, mean ± SD	21.6 ± 4.3	21.0 ± 2.4	0.448
Male, *n* (%)	29 (54.7%)	40 (72.7%)	0.051
Examination indications, *n* (%)			
Unexplained gastrointestinal bleeding	34 (64.2%)	37 (67.3%)	0.733
Abdominal pain/diarrhea	12 (22.6%)	11 (20.0%)	0.737
Possible inflammatory bowel disease	5 (9.4%)	3 (5.5%)	0.673
Other[a]	2 (3.8%)	4 (7.3%)	0.709

IQR = interquartile range, SD = standard deviation.
[a] Includes emesis, nausea, malignancies, etc.

Table 2. Comparison of completion rate, lesion detection rate, and SBTT between group A and group B in this study

Item	Group A ($n = 53$)	Group B ($n = 55$)	P-value
Completion rate, *n* (%)	42 (79.2%)	32 (58.2%)	0.018
Detection rate, *n* (%)	42 (79.2%)	41 (74.5%)	0.563
SBTT, min, mean ± SD	325.9 ± 134.6	281.6 ± 110.8	0.136

SBTT = small bowel transit time, SD = standard deviation.

Table 3. Comparison of classification of the findings of small bowel capsule endoscopy between group A and group B in this study

Item	Total ($n = 108$)	Group A ($n = 53$)	Group B ($n = 55$)
No abnormalities	27 (25.0%)	12 (22.6%)	15 (27.3%)
Polyps	6 (5.6%)	3 (5.7%)	3 (5.5%)
Ulcerations	17 (15.7%)	7 (13.2%)	10 (18.2%)
Mucosal lesions	7 (6.5%)	4 (7.5%)	3 (5.5%)
Active bleeding	9 (8.3%)	5 (9.4%)	4 (7.3%)
Vascular lesions	18 (16.7%)	6 (11.3%)	12 (21.8%)
Red spots	6 (5.6%)	4 (7.5%)	2 (3.6%)
Inflammatory lesions	19 (17.6%)	9 (17.0%)	10 (18.2%)
Protrusion lesions	7 (6.5%)	4 (7.5%)	3 (5.5%)
Diverticula	7 (6.5%)	4 (7.5%)	3 (5.5%)
Others	17 (15.7%)	6 (11.3%)	11 (20.0%)

during SBCE. Results showed that the CR of small bowel examinations was significantly higher in patients who underwent early EAI compared with late EAI. Logistic regression analysis identified early EAI as an independent predictor of complete SBCE. The latest possible timing of EAI when passage of a capsule in the upper gastrointestinal tract is delayed during SBCE was no later than 1.5 h or 4.6 h from the start of the examination for PillCam SB1 or PillCam SB2/3.

Since 2001, SBCE has become the first-line diagnostic modality for small bowel lesions [17, 24–26]. CR is one of the most important quality indicators in SBCE [16], with prolonged gastric transit time an independent risk factor for incomplete SBCE [15, 18]. Several approaches have been used to improve the CR in SBCE, including monitoring progress using an external real-time viewer, which increased the rate of positive findings and the CR of SBCE [27]; oral administration of polyethylene glycol and intramuscular injection of metoclopramide, which increased the CR [28]; and maintaining patients in the right lateral position, which improved the CR by reducing the gastric transit time [29]. One study showed that endoscopic delivery of a capsule that was initially retained in the stomach to the duodenum using a retrieval net improved the rate of entire small bowel observation [19]. Our center reported that EAI is an effective and safe method to reduce gastric transit time and increase the CR of SBCE [20]. However, the current timing for endoscopic intervention is arbitrary. Performing EAI too early may result in unnecessary wastage of medical resources. At the same time, considering that EAI is an invasive intervention with certain risks, patients' acceptance may not be high. On the contrary, if intervention is delayed, even with EAI, the capsule may not reach the cecum within the specified time, leading to an incomplete examination of the small intestine. This not only wastes medical resources but also hinders patients from obtaining satisfactory examination results. Our present study extends these previous findings and informs management of patients with delayed upper gastrointestinal transit during SBCE, showing patients can be

Table 4. Univariate and multivariate analysis of factors associated with completion rate of SBCE after EAI

Variables	*P*-value for univariate analysis	Multivariate analysis	
		P-value	Odds ratio (95% confidence interval)
Sex	0.755		
Age (<55 years vs ≥55 years)	0.020	0.058	2.427 (0.970–6.072)
Body mass index	0.970		
Obscure gastrointestinal bleeding (no vs yes)	0.047	0.169	2.046 (0.738–5.675)
Abdominal pain or diarrhea	0.262		
Suspicion of inflammatory bowel disease	0.256		
Intervention timing (T < 76.3% vs T ≥ 76.3%)	0.020	0.019	2.900 (1.193–7.053)

SBCE = small bowel capsule endoscopy, EAI = endoscopic-assisted intervention.

monitored at a single time point rather than continuously. SBCE is associated with substantial healthcare resource utilization and costs. Bowel preparation for SBCE is common practice but may cause patient discomfort [30]. Optimizing EAI and improving CR may be associated with cost savings to healthcare systems and increased patient satisfaction.

This study was associated with several limitations. First, this was a retrospective study; therefore, there was potential for selection bias and recording errors. In particular, clinical decision making around EAI was not random. Second, the relatively small sample size and variations in small bowel preparation may explain why there was no significant difference in detection rates between group A and group B. Third, we did not include diabetes, history of abdominal surgery, drugs, and other relevant factors in the analysis, which may have some influence on the conclusion of the study. Finally, only Medtronic capsules were used, which may limit the generalizability of these results. Findings should be verified in a large multicenter study.

Conclusions

The endoscopist should intervene no later than 1.5 h or 4.6 h from the start of SBCE with PillCam SB1 or PillCam SB2/3 in patients with delayed upper gastrointestinal transit. This allows time for the capsule to be propelled through the gastrointestinal tract; however, EAI can be performed in a timely manner, if needed, while achieving complete examination of the small bowel.

Authors' Contributions

X.H. was responsible for study design, methodology, statistical analysis, and drafting of the manuscript; Y.S. was responsible for data acquisition and compilation and methodology; Y.F. was responsible for data acquisition, statistical analysis, and methodology; Z.G. was responsible for study design, data acquisition, and compilation; H.X. was responsible for study design, drafting and revision of the manuscript, and supervision; H.C. was responsible for study design and methodology, drafting and revision of the manuscript, and supervision. All authors have read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare that there are no conflicts of interest in this study.

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