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Original Article

## 12-Hour SB2-EX Pillcam has Higher Diagnostic Yield Compared to the 8-Hour SB2 Pillcam

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### Abstract

**Background:** Capsule endoscopy has revolutionized the evaluation of the small bowel. The second generation capsule endoscopy that is used in clinical practice is the Pillcam SB2, which has a battery life of 8 hours. One of its main limitations is the failure to reach the cecum within the battery recording time, which may lead to missed distal small bowel lesions. Due to these concerns, a 12-hour Pillcam SB2-EX capsule was developed in 2010.

**Objective:** The primary aim was to evaluate the hypothesis that the 12-hour Pillcam SB2-EX would provide a higher small bowel completion rate compared to the 8-hour Pillcam SB2 in hospitalized patients. Secondary aims were to compare the diagnostic yield of the capsules and determine the risk factors for an incomplete small bowel examination.

**Design:** Retrospective, single-center study

**Setting:** Tertiary-care hospital

**Patients:** Hospitalized patients undergoing capsule endoscopy

**Main outcome measurements:** Completion rates, diagnostic yield, and risk factors for incomplete small bowel examination

**Results:** A total of 248 inpatient capsule endoscopies were reviewed. A higher percentage of 12-hour Pillcam SB2-EX reached the cecum, although this was not significant. More importantly, there was a significantly higher yield with the 12-hour Pillcam SB2-EX. Risk factors for an incomplete examination included older age, BMI  $\geq 18.5$ , and use of iron supplementation regardless of the type of capsule used. Diabetes mellitus was a risk factor for an incomplete study with the 8-hour Pillcam SB2, but not when the 12-hour Pillcam SB2-EX was used.

**Limitations:** Single center, retrospective study

**Conclusions:** The 12-hour Pillcam SB2-EX has a higher diagnostic yield than the 8-hour Pillcam SB2.

**Keywords:** Capsule Endoscopy; Small Bowel; Pillcam

## Abbreviations

CE: Capsule Endoscopy;

AVM: Angioectasia;

HR: Hazard Ratio;

CI: Confidence Interval;

BMI: Body Mass Index

## Introduction

Capsule endoscopy (CE) is a simple, safe, and non-invasive means to study the entire small bowel. The test is well accepted and tolerated by patients and effective in the diagnosis of small bowel disorders. However, incomplete exams due to battery depletion and/or failure to reach the cecum occur in 15-20% of cases [1,2].

The second generation CE that is used in clinical practice is the Pillcam SB2, which has a battery life of 8-hours. One of its main limitations is the failure to reach the cecum within the battery recording time [1]. The rate of incomplete examinations can be as high as 50%, with an average rate of 20% in most studies [1-3]. The risk factors for an incomplete CE examination include hospitalized patients [4] who are not mobile, older patients (age > 50 years), those with diabetes mellitus, hypothyroidism, gastrointestinal dysmotility, and patients on narcotics and other antimotility agents [5-7]. An incomplete examination may result in failure to detect small bowel lesions, especially Crohn's disease, carcinoid tumors and other lesions that have a predilection for the distal small bowel [1-3]. Due to these concerns, a 12-hour Pillcam SB2-EX (Given Imaging, Yoqneam, Israel) capsule was developed in 2010. The Pillcam SB2-EX is identical to the 8-hour-SB2 in dimensions and frames rate per second, but has an extended battery life of 12 hours, their importance is that they constitute a non-invasive method to study the entire small bowel (Table 1).

**Table 1.** 8-hour Pillcam SB2 versus 12-hour SB2-EX CE.

	<b>8-hour Pillcam SB2</b>	<b>12-hour Pillcam SB SB2-EX</b>
Dimensions	11 mm x 26 mm	11mm x 26 mm
Frame Rate	2 fps	2 fps
Operating Time	8 hours*	12 hours*
Shelf Life	18 months**	12 months**
Maximum Storage Temperature	40° C	25° C
Costs	Similar	Similar

\*Until Battery Exhaustion

\*\*From date of production

No difference in costs

To our knowledge, there has never been a published study comparing the two capsules (8-hour SB2 versus 12-hour SB2-EX).

Our primary aim was to evaluate the hypothesis that the 12-hour Pillcam SB2-EX would provide a higher small bowel completion rate compared to the 8-hour Pillcam SB2 in hospitalized patients. Our secondary aims were to compare the diagnostic yield of the capsules and determine the risk factors for an incomplete small bowel examination.

## Methods

At our institution, all inpatient CEs prior to 4/18/2011 were performed using the 8-hour Pillcam SB2. After that date, all inpatient capsules were performed using the 12-hour Pillcam SB2-EX. We chose to perform our study on hospitalized patients because prior studies have suggested that this population tends to have more incomplete examinations. We wanted to determine if there were any identifiable risk factors within this cohort that would result in an incomplete small bowel examination with CE.

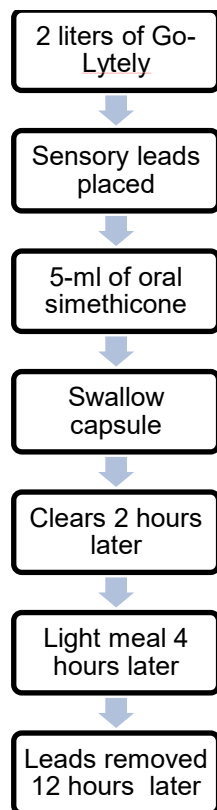
A retrospective review was conducted to collect data from all consecutive inpatient CE studies performed at Mayo Clinic Hospital in Arizona between January 1, 2009 and July 18, 2013. The study was approved by the Mayo Clinic Institutional Review Board.

Our hospital is a tertiary care center with a referral base mainly drawing from the Southwestern United States. Data were collected regarding patient demographics such as age, gender, medical and surgical history, and medication use. Additionally, information from the CE database were extracted, including indication for CE, small bowel findings, quality of the preparation, whether or not the cecum was reached and time to completion of the study. For all incomplete studies we reviewed the medical records to determine if the capsule was retained and subsequent management of those patients.

Exclusion criteria included outpatient CE, outside studies sent for interpretation at Mayo Clinic, patients with implanted electromedical devices, CE placed with endoscopic assistance and incomplete data/documentation.

## Capsule Endoscopy Procedural Protocol

Inpatients typically received 2 liters of Go-Lytely preparation on the evening prior or at least 4 hours prior to the study. A sensory array with leads was applied to the patient's abdomen and the data recorder was worn on a belt around the waist. The patient received 5-ml of oral simethicone prior to swallowing the capsule to reduce bubble formation. After the capsule was swallowed, the patient was allowed to ingest clear liquids after 2 hours and a light meal after 4 hours. The leads were removed 12 hours later or earlier if there was evidence of passage of the capsule (Flow chart 1).



**Flow Chart 1**

ffCapsule endoscopy results were pre-read by a trained gastroenterology nurse or fellow, under the supervision of one of the CE credentialed gastroenterologists, who then reviewed the video and completed the formal report. The findings on CE were documented and categorized according to standard terminology [8]. For the purposes of our study, we included clinically significant findings of angioectasia (AVM), ulcer/erosion, tumor/polyps, and strictures. The capsule study was considered complete when the cecum was reached within the recording time. If the cecum was not reached by the end of the study or if passage of the capsule was not witnessed within two weeks of ingestion, an abdominal x-ray was performed to evaluate for capsule retention.

**Statistical analysis**

Frequency distributions were evaluated for all categorical variables. Group differences were assessed using Chi-square tests or Student’s t-test as indicated by the data type. Cox proportional-hazards regression models were conducted to assess the association between covariates. Schoenfeld residuals were used to test model assumptions. The likelihood-ratio test was used to determine significant associations between predictors. Cumulative hazard functions were calculated using of the Nelson–Aalen estimator. When the association was found to be significant, a hazard ratio (HR) and 95% confidence interval

(95% CI) were reported. Models were adjusted for age, sex, co-morbidities, and other quality variables. A two-tail P-value of less than 0.05 was considered to indicate statistical significance. All analyses were performed using IBM SPSS 19.0 (IBM SPSS, Chicago, IL) or SAS 9.1 statistical software (SAS Institute, Inc., Cary, NC, USA).

**Results**

The indications and corresponding patients’ demographics were reviewed for 248 inpatient capsule endoscopies. After excluding 15 studies that did not meet the inclusion criteria, 233 were included in the statistical analyses. Mean age of the patients was 70 years (range 25-99 years) and 37% were female. Of the capsule studies, 132 were 12-hour Pillcam SB2-EX (57%) and the remainder were 8-hour Pillcam SB2 (n = 101; 43%). The most common indications for CE were obscure overt gastrointestinal bleeding (56.6%) (e.g., melena, hematochezia, or maroon stools), iron-deficiency anemia (15.8%), and suspected Crohn disease (3.4%). The remaining indications were classified as other (e.g., weight loss, abdominal pain, etc).

**Comparison of 8-hour Pillcam SB2 versus 12-hour Pillcam SB2-EX**

There were no differences in demographic information including obesity, medical history, or surgical history between the two cohorts. The only notable differences were in the use of oral calcium channel blockers and iron supplementation (Table 2).

**Table 2.** Comparison of 8-hour Pillcam SB2 and 12-hour CE SB2-EX.

	<b>8-Hour Pillcam SB2 (n = 101)</b>	<b>12-Hour Pillcam SB2-EX (n = 133)</b>	<b>p-value</b>
Sex			P = 0.554
Male	62 (26.61)	86 (36.91)	
Female	39 (16.74)	46 (19.74)	
Age			P = 0.827
20-59 yrs	18 (7.73)	25 (10.73)	
60-99 yrs	83 (35.62)	107 (45.92)	

BMI			
Obese	43 (18.45)	57 (24.46)	P = 0.926
Non-Obese	58 (24.86)	75 (32.19)	
Diabetes Mellitus			
Yes	35 (15.02)	41 (17.60)	P = 0.5625
No	66 (28.33)	91 (39.06)	
Gastroparesis			
Yes	5 (2.15)	2 (0.86)	P = 0.127
No	96 (41.20)	130 (55.79)	
Hypothyroid			
Yes	24 (10.30)	28 (12.02)	P = 0.6437
No	77 (33.05)	104 (44.64)	
Medications			
Narcotics	45 (19.3)	45 (19.3)	P = .1044
Calcium Channel Blockers	26 (11.16)	17 (7.30)	P = .0125
Beta Blockers	55 (23.61)	65 (27.90)	P = 0.4299
Oral Iron Supplementation	18 (7.73)	42 (18.03)	P = 0.014
Cholecystectomy			
Yes	21 (9.01)	19 (8.15)	P = 0.201
No	80 (34.33)	113 (48.50)	
Cecum Reached	86 (43.4)	112 (56.5)	P = 0.949
Diagnostic Yield Positive	40 (36%)	70 (63%)	P = 0.041

The proportion of 12-hour Pillcam SB2-EX that reached the cecum was higher compared to the 8-hour Pillcam SB2 (56.5% vs 43.4%, p = 0.064), but statistical significance was not obtained. However, there was a significantly higher diagnostic yield with the 12-hour Pillcam SB2-EX, as compared to the 8-hour Pillcam SB2 (12-hour 63% vs 8-hour 36%, p = 0.0001

Within the 12-hour Pillcam SB2-EX cohort, we conducted an analysis to determine whether the cecum was reached after 8-hours, and whether or not there were clinically significant findings after 8 hours. This was conducted to determine if the use of an 8-hour Pillcam SB2 in these patients would have resulted in an incomplete study and if any significant lesions would have been missed. With this analysis, 10.6% of all 12-hour Pillcam SB2-EX reached the cecum after 8 hours. Additionally, 3.7% of the clinically significant findings on the 12-hour Pillcam SB2-EX were detected after 8 hours, suggesting that the 8-hour Pillcam SB2 would have missed those findings.

**Risk Factors Analysis for Incomplete CE Examinations**

Of the 233 capsule endoscopies, 15% (n=35) were incomplete small bowel examinations and did not reach the cecum. A comparison of the demographic characteristics for patients with incomplete and complete CE is shown in Table 3. There were no differences with respect to gender, diabetes mellitus, hypo thyroidism, use of calcium channel blockers, narcotics, or beta-blockers. On univariate analysis, the predictors for an incomplete examination for all CEs included older age (≥50 years, OR = 0.351 (95% CI: 0.13, 0.98), p = 0.04), BMI ≥ 18.5 (OR = 0.466, 95% CI: .22, 1.00, p = 0.05), and the use of oral iron supplementation (OR = 0.32, 95% CI: .09, 0.87, p = 0.02) (Table 4). Diabetes mellitus was a significant risk factor for an incomplete examination with the 8-hour SB2 (OR 0.24, 95% CI: 0.03, 0.96, p = 0.04), but not with the 12-hour SB2-EX.

**Table 3.** Patient Characteristics for Complete and Incomplete CE Procedures.

	CE Complete (n = 198)	CE Incomplete (n = 35)	P
Age ≥ 50	182 (86.67)	28 (13.33)	.046
Female Sex	73 (85.88)	12 (14.12)	0.76
BMI ≥ 18.5 (Above Normal)	151 (87.79)	21 (12.21)	0.051
Diabetes Mellitus	66 (86.84)	10 (13.16)	0.576
Hypothyroidism	45 (86.54)	7 (13.46)	0.71
Narcotic Use	76 (84.44)	14 (15.56)	0.85
Calcium Channel Blocker Use	34 (79.07)	9 (20.93)	0.24

Beta-Blocker Use	105 (87.50)	15 (12.50)	0.26
Iron Supplementation Use	56 (93.33)	4 (6.67)	0.024

**Table 4.** Univariate Logistic Regression Analysis of Risk Factors for Incomplete CE ( n = 35)

	OR (95% CI)	P
Age ≥ 50	0.35 (.13-0.98)	.04
Female	1.101 (0.42-2.15)	0.96
Above normal BMI (BMI	0.466 (.22-1.0)	0.05
Presecnce of Diabetes	.80 (.34-1.71)	0.57
Narcotoc Use	1.07 (0.50-2.2)	0.85
Beta-Blocker Use	0.66 (.31-1.36)	0.26
Iron Supplementation Use	0.32 (.09-.87)	0.02
Gastroparesis	2.33 (.32-11)	.35
Hypothyroidism	.85 (.32-1.98)	.71

## Discussion

The utility of CE is limited by the potential for incomplete examinations and missed lesions in the unexamined portion of the small bowel [1-3]. The 12-hour SB2-EX with an extended battery life was developed to overcome this limitation. In this study, we compared the completion rates and diagnostic yield between the 8-hour Pillcam SB2 and the 12-hour Pillcam SB2-EX. Interestingly, while there was a trend towards more incomplete exams with the 8-hour capsule, this was not significantly different. We found a higher percentage of the 12-hour Pillcam SB2-EX reached the cecum compared to the 8-hour Pillcam SB2. There was also a significantly higher yield for small bowel findings with the 12-hour Pillcam SB2-EX. Further analysis reveals that 10.6% reached the cecum after 8 hours, and there were clinically significant findings after 8 hours in 3.7% of the studies (Table 5). We can therefore make the inference that the 8-hour capsule would have resulted in an incomplete examination and potential for missed lesions in this subset of patients.

**Table 5:** 12-hour SB2-EX findings beyond the 8 hour mark.

Case Number	Age	Sex	Finding	Time on CE
1	87	Male	AVM	08:39:12
2	86	Female	AVM, blood	08:26:22
3	37	Male	Ulcers	10:44:02
4	99	Male	Ulcers	9:31:31
5	66	Male	Blood	11:10:20

It is surprising that the completion rates were not statistically different. The rate of incomplete CEs in our study was 15%,

which is less than the incomplete rate reported in most other CE studies, and may be due to the fact that the 12-hour Pillcam SB2-EX was used in approximately half of our patient cohort [1,2,9]. Previously recognized predictors of an incomplete CE are diabetes mellitus, males, older age, hypothyroidism, and hospitalized patients [5,7]. In our cohort of hospitalized patients, older age, a BMI ≥ 18.5, and the use of oral iron supplementation were risk factors for an incomplete CE. If one tries to better understand this, older patients may have slower transit times than younger patients. Fireman et al. showed that older age (defined as ≥ 40 years) had a longer mean small bowel transit time of approximately 18 minutes more than younger patients [6]. Iron supplementation was another factor that was associated with an incomplete examination. It is known that iron can cause constipation and may slow down gut motility; this could contribute to incomplete examinations. On univariate logistic regression analysis of risk factors for an incomplete CE examination, patients with a higher than normal BMI (defined as > 18.6) were more likely to have an incomplete examination, but there was no difference when the patients were stratified as obese versus non-obese. Prior work has suggested that proximal small bowel transit may be increased in obese patients [10], which may be related to efficient nutrient absorption and subsequent lack of nutrient-induced satiety signals conveyed from the small intestine. We found that diabetes mellitus was a risk factor for an incomplete examination with the 8-hour Pillcam SB2, but not the 12-hour Pillcam SB2-EX. Whether or not a 12-hour Pillcam SB2-EX may be preferred for small bowel evaluation in diabetic patients is not yet known.

There are some limitations to our study. There are inherent biases as this was a single center, retrospective study. A larger prospective study would be helpful to compare the 8-hour Pillcam SB2 and the 12-hour Pillcam SB2-EX in separate cohorts of inpatients and outpatients undergoing capsule endoscopy.

## Conclusions

Our study showed that there was a trend towards more incomplete exams with the 8-hour capsule, however this was not significantly different. A larger prospective study would be helpful to compare them in separate cohort. One advantage of the 12-hour Pillcam SB2-EX over the 8-hour Pillcam is that it has a higher diagnostic yield.

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