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Small Bowel Capsule Endoscopy: Benefits of Rereading Rather than Repeating—A Single Blinded Randomized Study

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Abstract

Objectives Small bowel capsule endoscopy (SBCE) technology detects small bowel lesions. Many factors affect its sensitivity. SBCE is also costly, and patients might not be able to repeat the test when results are equivocal. Instead of repeating the test, reading the results by two endoscopists might provide a better or a cheaper option in the right settings. We studied the sensitivity of SBCE when read by two different physicians and checked if, rather than repeating the examination, rereading the results improved its sensitivity. Furthermore, we studied the effect of small bowel transit time (SBTT) on the diagnostic yield.

Materials and Methods A retrospective cohort study on capsule endoscopies was conducted between 2018 and 2019 in a tertiary care center in Lebanon. A total of 42 patients with anemia or obscure gastrointestinal bleed were included for SBCE after a negative evaluation with upper and lower gastrointestinal (GI) endoscopy. Two specialists read the results. The second physician was blinded from the first reader's results. We compared the sensitivity of the two readings. SBTT correlation with the diagnostic yield was calculated.

Results Out of 42 patients, 18 tested positive in the first reading and 31 in the second reading. The diagnostic yield increased from 43 to 74% ($p = 0.0043$). Among the 33 patients who had a documented SBTT, longer SBTT correlated with a higher diagnostic yield (odds ratio [OR] > 1), but no statistical significance was demonstrated.

Conclusion Within the limitations of this study, we found that rereading capsule endoscopy can be more cost-effective than repeating the test.

Keywords
- capsule endoscopy
- small bowel transit time
- anemia
- obscure gastrointestinal bleed

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Introduction

Gastrointestinal bleed (GIB) is a common GI presentation.[1] Small bowel bleed specifically constitutes 5 to 10% of all GIB and cannot be detected by upper and lower endoscopy.[2] Capsule endoscopy (CE) is an advanced methodology of detecting small bowel overt and obscure GI bleeding (OGIB). It is a relatively noninvasive test that visualizes the small bowel and is considered the test of choice after adequate upper endoscopy and colonoscopy.[3,4] Small bowel capsule endoscopy (SBCE) is superior to push enteroscopy and computed tomography (CT) angiography (CE detected inflammatory lesions by 9% more than push enteroscopy in one study and it identified a bleeding source in 50 vs. 24% of patients in another study).[3,4] The technique can be improved in the future if a breakthrough is achieved with tissue sampling or therapeutic intervention. SBCE sensitivity can fluctuate between 40 and 93%.[3,4] Its sensitivity depends on several factors including bowel preparation, type of capsule used, bleeding amount, and transit time/bowel motility in addition to time from bleeding.[3,4] Furthermore, some small bowel mucosa might not be visualized because of the turbulent pathway of the capsule.

Despite its clinical significance, CE is costly. Its cost differs greatly between countries and the type of capsule used.[4,5] Its financial burden hinders the ability of patients to repeat the test once negative results are reported, even if no bleeding source was detected. This can lead to complications if the patient is discharged home without proper identification and control of the bleeding source. A possible cheaper alternative is rereading SBCE.

Reading CE is time-consuming, leading to a faster reading of the recording and possibly skipping some lesions.[6,7] Previous study protocols used the two-reader approach in their methodologies.[8,9] We study the sensitivities of SBCE when read by two different physicians in comparison with the studies repeating the test. We hypothesize that rereading SBCE improves its sensitivity, making it, at least, comparable to repeating the test, hence cost-effective. In addition, we studied the association between small bowel transit time (SBTT) and diagnostic yield. Our second hypothesis is that the longer the SBTT, the better the diagnostic yield.

Materials and Methods

This is a retrospective cohort study on capsule endoscopies conducted between 2018 and 2019 in a tertiary care center in Lebanon. A total of 42 patients with anemia or OGIB were included for SBCE after a negative evaluation with upper and lower GI endoscopy. The results were read by two physicians at different times. The second reader was blinded from the first reader's results but had access to the chief complaint, patient characteristics, and the capsule videos (single blinded study). We compared the sensitivity of the two readings and calculated the *p*-value to check for a statistical significance.

Inclusion criteria: Patients with anemia and/or OGIB were included. Documentation of capsule reaching the cecum was required.

Exclusion criteria: Patients with Crohn's disease, small bowel obstruction, pacemakers, and implantable defibrillators were excluded.

The participating outpatients were cleared by their cardiologists or primary physicians to hold their anticoagulation/antiplatelet medications if any. However, due to the subjective nature of this study, there was no direct control of their medications.

All the patients fasted for 8 hours prior to capsule ingestion and were prepared with a total of two sodium picosulfate sachets followed by 4 L of water given in split doses (1 sachet followed by 2 L the evening before and 1 sachet followed by 2 L the morning of the procedure). Alverine citrate/simethicone was also given the night before capsule ingestion and the morning of the procedure. Patients were instructed to resume clear liquids 2 hours after capsule ingestion.

The type of the capsule used was a CapsoCam Plus, which provides a 360-degree panoramic view of the small bowel mucosa using four cameras at a sequential of 90-second intervals in its midsection, allowing a better visualization of the small bowel mucosa, thus improving the diagnostic yield.[9] It is able to capture images at variable rates between three and five frames per second per camera with an operating time exceeding 15 hours depending on its transit speed.[10] The capsule video was read at a maximum speed of 10 frames per second, per single view mode, as per the European Society of Gastrointestinal Endoscopy (ESGE) quality recommendation.[11] Both endoscopists have more than 10 years of experience in SBCE. Informed consent was obtained from all participants.

Patients were compared for positive findings, SBTT, bowel cleanliness, age, and sex. The findings of the SBCE were classified according to the small bowel results. Findings were considered positive when ulcer, erosion, arteriovenous malformation, diverticula, bleed, prominent vessel, or small bowel lesions were detected. Findings were labeled negative when normal results were found. To note, only positive findings in the small bowel contributed to positive results and positive diagnostic yield.

Results

In this study, out of a total of 42 patients, the first reading detected 18 positive tests compared with 31 in the second reading. Comparing the sensitivity of the two readings, the first reader had a 43% diagnostic yield, while the second had a 74% diagnostic yield (►**Table 1**). Using the Mann–Whitney *U* test, *p*-value was statistically significant at 0.0043 (►**Table 1**). For the first reader, out of the 18 positive tests, 17 (94.44%)

Table 1 Sensitivity of the two readings

	Positive results	Negative results	*p*-value
First reading	43%	57%	0.0043
Second reading	74%	26%	

Table 2 New findings detected in the second reading

Case number	Indication	First reader	Second reader
1	Anemia	Normal	AVM + ulcer
2	Anemia	Normal	Large AVM + active bleed
3	Anemia	Normal	Ulcer
4	Anemia	Normal	Ulcer
5	Anemia	Normal + poor preparation	Ulcer
6	Anemia + melena	Normal	Ulcer
7	Anemia	Normal	Hemangioma
8	Anemia	Normal	Erosions + hemangioma
9	Anemia	Normal	AVM
10	Anemia	Normal	Ulcer + AVM + active bleed
11	Anemia	Normal	Erosions + AVM/hemangioma
12	Anemia	Normal	Ulcer + AVM
13	Anemia	Normal	Ulcer
14	Anemia	Normal	Ulcer

Abbreviation: AVM, arteriovenous malformation.

Table 3 Number of patients according to their small bowel transit time (SBTT)

SBTT (h)	Number (%)
0–2	2 (6%)
2–4	7 (21.2%)
4–6	11 (33.3%)
6–8	8 (24.2%)
>8	5 (15.2%)

were detected again by the second physician. In addition, the second reader reported 14 (33.33%) new tests to be positive (►**Table 2**).

SBTT is defined as the time from first duodenal image to first cecal image.[12] In our study, we excluded nine patients who did not have a documented SBTT. Therefore, 33 of 42 patients were included and stratified into five groups (0–2, 2–4, 4–6, 6–8, and >8 hours). The results were as follows. The majority (11 patients) had an SBTT between 4 and 6 hours (►**Table 3**). The average SBTT was 5.48 hours. We studied the association between SBTT and the detection of positive findings reported by either reader, as shown in ►**Table 4**. Odds ratio (OR) and the corresponding *p*-values were calculated to see if a correlation exists between the two entities. The 0- to 2-hour group was our control. We concluded that all groups had a positive OR ($OR > 1$) suggesting a positive correlation between a longer SBTT and a higher diagnostic yield, but no clinical significance was demonstrated ($p > 0.05$).

The results in ►**Table 4** clearly show the increment of OR in association with the longer SBTT, being the highest in the time group of greater than 8 hours.

In ►**Table 5**, we studied the association between SBTT, age, and sex. Among the 33 patients who had a documented SBTT, the average transit time was the same (~5 hours) for both males and females and across all age groups except for the 40- to 60-year age group who had a small sample size and a longer SBTT with a statistical significance ($p < 0.05$).

Discussion

In a previous retrospective report, Svarta et al[13] studied 676 patients, of which 82 patients (12%) had repeat CE with a diagnostic yield of 55%. Comparing the data, we had a 74% diagnostic yield for rereading CE and one-third (33.3%) of the previously negative tests were found positive in the second reading. Rereading CE was statistically significant ($p = 0.0043$). These results were comparable, if not higher than, to the sensitivity of repeating CE in the study conducted by Svarta et al.[13]

Table 4 Association between small bowel transit time and reader detection of a positive finding

Small bowel transit time (h)	Odds ratio (OR)	95% confidence interval	*p*-value
4–6	2.66	0.12–57.62	0.26
6–8	3.00	0.12–73.64	0.25
>8	4.00	0.11–136.95	0.22

Table 5 Association between SBTT, age, and sex

	Age (y)/sex	Number	Average SBTT (h)	*p*-value
Age (y)	<40	19	5:12:28	0.67
	40–60	2	10:10:21	0.016
	>60	12	5:44:37	0.74
Sex	Females	13	5:23:45	0.49
	Males	20	5:54:12	0.89

Abbreviation: SBTT, small bowel transit time.

In contrast, Blanco-Velasco et al[14] applied a two-reader approach on 100 SBCEs of various indications (48 tests for small bowel bleeding and 52 for other indications); a non-significant increase of 6.3% in the diagnostic yield was obtained after a second reading of the small bowel bleed subset. Nonetheless, our findings suggest that having two readers interpret the CE provides a significant alternative to repeating this costly test. However, it is evident that rereading CE might not be useful in cases of bad preparation, capsule retention, and if some significant mucosal visualization was missed because of the turbulent capsule pathway. In our study, poor bowel preparation or active bleed might explain the difference in the positive findings between the two endoscopists, hence the nonconcordance. Therefore, emphasis on bowel cleanliness is advised. However, recent systematic reviews and meta-analyses evaluating the effect of bowel preparation on SBCE results showed no clear advantage.[15–17] Moreover, intestinal bleeding is usually intermittent, and in certain cases, physicians need to repeat the test to better localize the bleeding focus and decide on therapeutic interventions (in case of rebleed, overt bleeding, or if blood transfusion is needed).

Furthermore, the time from bleeding can greatly affect the sensitivity of CE. The closer the study is to the bleeding episode, the higher the sensitivity, dropping within 1 week to 66.6% and to less than 10% in 2 weeks.[18] In patients with occult bleeding who had CE on the same day or the day after fecal immunochemical test (FIT) turned positive, the prevalence of small bowel disease was significantly higher.[18]

SBTT is defined as the time from first duodenal image to first cecal image.[12] Evidence is growing regarding the positive correlation between a slower SBTT and a higher diagnostic yield. However, there is still some controversy regarding the specific SBTT that is defined appropriate to have the best diagnostic yield.

In a retrospective study of 212 patients with anemia or OGIB, Buscaglia et al[19] showed a twofold increase in the diagnostic yield in patients with an SBTT longer than 6 hours.

In a prospective study including 1,433 patients with OGIB, Girelli et al[20] also concluded that a longer SBTT was associated with a higher detection rate of significant lesions. This is probably related to better visualization with slower transit time. However, they did not stratify the SBTT into groups to check for the specific time above which there was statistical significance for a higher diagnostic yield. But the mean transit time for the group who had significant findings was 4.7 ± 1.75 hours compared with 4.48 ± 1.63 hours for the group who had normal or negligible findings, and this was statistically significant ($p < 0.05$). This was comparable to the average transit time in our study (~5 hours; ►**Table 5**). We found a positive OR in all the following SBTT stratification groups: 4 to 6, 6 to 8, and >8 hours (►**Table 4**). We noticed that OR increased in association with a longer SBTT (>8 hours) although no statistical significance was obtained (►**Fig. 1**). Due to the small sample size, the range of the 95% confidence interval (CI) was wide (►**Table 4**). Further studies and larger samples are needed. There is also no difference in the SBTT between both sexes and between different age groups.

This study has its limitations. First, a retrospective study limits the availability of additional patient information or test data (e.g. documentation of SBTT). The small sample size (42 patients) might not increase the statistical power. The preparation for CE in an outpatient setting is sometimes suboptimal, decreasing the diagnostic yield. All patients with Crohn's disease were excluded. Also, we were unable to further stratify the OGIB as overt or occult. In addition, there was a variable time span between the two reads, and at times it was up to 18 months, explaining why there is no effect of the findings of the second read on the clinical management, and making the second physician more prone to detect or overread the findings. Another prospective study where two independent readers translate the data to the treating physician will be ideal, making the results and their effects more applicable to clinical situations.

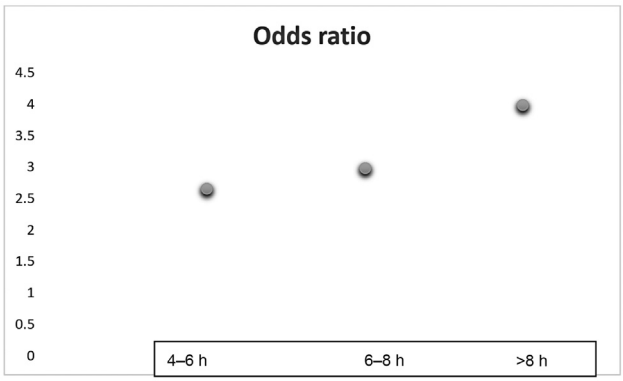

Fig. 1 Graph of odds ratio forest plot of small bowel transit time (SBTT) and sensitivity.

Conclusion

For patients with an initial negative SBCE, a second evaluation of the test is recommended to increase its diagnostic power and provide a cheaper alternative to repeating the test. Our rereading-based study results were comparable/superior to both the repeating-based study conducted by Svarta et al.[13] and the two-reader approach adopted by Blanco-Velasco et al.[14]

A longer SBTT is possibly correlated with a higher diagnostic yield. However, more data with higher recruitment numbers and further group stratification according to transit time should be implemented in future studies.

We also suggest adding "time from bleeding" in case of overt bleed and studying the usefulness of the FIT test in case of occult bleeding.

Author Contributions

A-N.A. and A.T. contributed equally to designing the research, collecting and analyzing the data, and writing the manuscript. N.O. assisted in the design of the research, collection and analysis of data, and wrote a part of the article. A.C. contributed to data processing and analysis. J. M. and S.F. were the readers of the CE tests and the pioneers of the initial idea of the project. S.F. was the treating physician and the main investigator.

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Conflict of Interest

None declared.

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