Small Bowel Capsule Endoscopy Performance in Octogenarians: A Case–Control Study

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Background and Study Aims. Capsule endoscopy is a high-sensitive tool for the investigation of suspected small bowel disorders, but its effectiveness in elderly patients is unknown. We sought to determine capsule endoscopy feasibility and diagnostic yield in octogenarians.

Patients and Methods. Records of patients ≥80 years old (Group A) were retrieved from a database of 827 consecutive capsule endoscopy performed on as many patients. Capsule endoscopy failures, complications, diagnostic yield, and findings were recorded and compared with those of patients younger than 80 (Group B), randomly extracted from the same database in a 2:1 ratio.

Results. Group A consisted of 79 patients, 84 ± 6 years old and Group B of 188, 44 ± 11 years old (p < .0001). We visualized the entire small bowel in 59 (74.6%) patients of Group A and in 169 (89%) of Group B (odds ratio = 0.33, 95% confidence interval: 0.16–0.66, p = .0025), mainly for capsule failures in reaching the duodenum; this event occurred in 10 patients of Group A and in 3 of Group B (odds ratio = 9, 95% confidence interval: 2.4–33.4, p = .0048). The rate of adverse events and diagnostic yield did not differ between the two groups. Inflammatory and neoplastic lesions were more common in Group A (odds ratio = 2.60, 95% confidence interval: 1.07–6.28, p = .03 and odds ratio = 2.01, 95% confidence interval: 1.02–3.97, p = .04, respectively).

Conclusions. In octogenarians, small bowel capsule endoscopy may be troublesome for capsule failure in reaching the duodenum. However, the diagnostic yield of small bowel capsule endoscopy and the rate of clinically significant lesions are high.

Key Words: Aging—Capsule endoscopy—Obscure gastrointestinal bleeding—Small bowel.

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Capsule endoscopy (CE) is considered the most accurate diagnostic tool for noninvasive investigation of the small bowel (SB) (1). For its proper clinical use, guidelines have been outlined, and obscure gastrointestinal bleeding (OGB) is the leading clinical indication (2). CE is comfortable for both patient and physician, has a low complications rate (3), and, if a significant lesion in the SB is identified, it is useful in choosing the route of insertion (ante or retrograde) of device-assisted enteroscopy for further investigation, tattooing, or endoscopic treatment (4,5). Clearly, a complete SB evaluation is crucial for CE performance, and success rate (ie, visualization of the cecum) is close to 80% in the largest unselected published series (6).

On the other hand, CE is expensive and its use in clinical practice has to be optimized. In particular, for a good yield of the procedure, two issues are critical: the appropriateness of clinical indication and the exclusion of those patients carrying a high risk of failure. Although only few studies addressed the risk factors for incomplete small bowel capsule endoscopy (SBCE), hospitalization, slow gastric emptying, previous abdominal surgery, and diabetes mellitus seem to be related to a poor performance and a lower rate of completeness (6–10). Not surprisingly, in a small study of patients with established chronic intestinal dysmotility, the completion rate of SBCE was only 61% (11). Age, as a variable of SBCE performance, has been evaluated in two studies, with different criteria and results. In the first, Fireman and co-workers (12), in a retrospective analysis of a large multicenter database, showed that people more than 40 years old have a longer SB transit time; in the second, Papadopulos and co-workers (13) failed to demonstrate any significant difference of SB transit time among three age-related groups (<40, 40–65, and ≥65) of a prospective cohort of 120 patients.

Western countries inhabitants are increasingly aging, and in Italy, people older than 80 years old are up to 5% of the entire population (http://www.istat.it/popolazione/). In this age group, SB morbidity and CE performance are poorly defined and may be difficult to establish the appropriateness...
of SBCE. However, anemia from OGB is a common and often overlooked cause of morbidity and impaired quality of life in elderly people (14). Furthermore, in old series published before the “endoscopic revolution” determined by the advent of SBCE and device-assisted enteroscopy (15), arterovenous malformations (AVMs) outnumbered SB tumors among the most common etiologies of OGB in the old age (16), questioning the need of SB investigation in these patients.

Therefore, to better characterize CE feasibility and diagnostic yield in elderly patients, we undertook a retrospective case-control study on participants older than 80 years old, examined by CE in two northern Italian centers.

**METHODS**

Two secondary referral Centers of Gastroenterology and Digestive Endoscopy of Northern Italy, with large volume Gastrointestinal Endoscopic Units performing more than 12,000 endoscopic procedures yearly and SBCE from October 2001, participated in the study. Each center collected the outstanding data (demographics, clinical indication, complete examination, findings, and adverse events) of all patients examined by SBCE in two different databases. Adjunctive data, such as comorbidity, drug use, and clinical outcome, were available for most patients.

From October 2001 to April 2009, 827 consecutive SBCE on as many inpatients (415 and 412 from Busto Arsizio and Aviano, respectively) were performed using Pillcam SB and Rapid software and their subsequent upgrading (Given Imaging, Yoqneam, Israel). All patients were hospitalized, mainly because the Italian National Health Service does not reimburse the procedure for outpatients. SBCE was carried out after an overnight fast and bowel cleansing by 2 L of polyethylene glycol solution (Selg-S; Promepharm, Milan, Italy), taken the previous afternoon. Prokinetics (metoclopramide, 10 mg i.v. 20–30 minutes before capsule swallowing) were given in 16% of patients. After 4 hours from capsule ingestion, patients were allowed a light snack. The device was removed and digital information downloaded to the workstation after 8 hours. Any symptom, sign, and the time elapsed from ingestion to capsule excretion were recorded for each patient. Written informed consent was obtained from all patients before the procedure.

Data regarding CE failures, rate of completeness, diagnostic yield, findings and complications, and comorbidity of all patients ≥80 years old were retrieved from the database for analysis (Group A). For a comparison, control participants (Group B), aged 20–79 years old, were extracted from the same database, by Lehmer algorithm random numbers generator (17) in a > 2:1 ratio versus Group A. For comorbidity comparison, we used the age-unadjusted Charlson’s comorbidity index (18). Oro-duodenal transit time was defined as the time in minutes elapsed from capsule ingestion to the first duodenal frame, and small bowel transit time was defined as the time in minutes elapsed from the first duodenal frame to the first cecal frame. SBCE was defined complete if cecum was clearly visualized. SBCE findings were grouped in four categories, namely, (a) vascular (ie, AVMs), (b) neoplastic (polyps, mucosal, and submucosal masses), (c) inflammatory (aphthae, erosions, ulcers, congestion, and erythema), and (d) miscellaneous (small bowel diverticula, worms, and atrophy). From 2006, all SBCE findings were labeled using the Capsule Endoscopy Structured Terminology classification (19). Only the authors were responsible for image interpretation, data collection, and retrieval. Institutional Review Board of both centers reviewed and approved the study.

Continuous variables are presented as means and 95% confidence intervals (CIs) or standard deviation, whereas numbers are followed by the sign ±. Two-tailed Student’s t test or, when appropriate, Mann–Whitney test for unpaired data were used for their comparison. In order to assume a normal distribution for oro-duodenal transit time comparison, logarithmic transformation, and Welch correction for unequal variances were required. Frequencies were compared by chi-square and Fisher’s exact tests if appropriate, with calculation of odds ratio (OR) and 95% CI. GraphPad Prism software, version 5 (San Diego, CA) was used for calculations. p Values less than .05 were considered statistically significant.

**RESULTS**

**Patients**

Group A (cases) consisted of 79 patients 84 ± 6 years old, representing the 9.5% of all patients examined in the two centers. Thirty-five (44%) were males, 75 (95%) underwent SBCE for OGB (12 of the overt type), and the remainder for chronic unexplained diarrhea. Additional clinical details were available for all patients. Diabetes and previous abdominal surgery were present in 10 (12.6%) and 12 (15%) patients, respectively; Charlson’s comorbidity index was 0.60 ± 1.14, and prokinetics were administered in 10 (12.6%) patients. Group B (controls) consisted of 188 patients, 44 ± 11 years old. Ninety-eight of them were males (52%), 169 (90%) underwent SBCE for OGB (25 of the overt type) and the remainder for chronic unexplained diarrhea. Additional clinical details were available for 132 of 188 (70.2%) controls. Diabetes and previous abdominal surgery were found in 15 (11.3%) and 12 (9%) patients, respectively; Charlson’s comorbidity index was 0.74 ± 1.21, and prokinetics were administered in 28 (14.8%) patients. As shown in Table 1, the two groups were well matched for the considered variables.

Completeness of SB Evaluation and Adverse Events

The entire SB was visualized only in 59 (74.6%) patients of Group A versus 169 patients (89%) of Group B.
(OR = 0.33, 95% CI: 0.16–0.66, p = .0025), mainly for capsule failure to reach the duodenum. This event occurred in 10 (12.6%) patients of Group A and in 3 (1.5%) of Group B (OR = 9, 95% CI: 2.4–33.4, p = .0004) (Table 2). As all patients underwent a prior unremarkable esophagogastroduodenoscopy, we inferred that most failures (8 of 10 in Group A and 3 of 3 in Group B) were due to unexpected abnormalities of esophageal and gastric motility. Oro-duodenal transit time was available for all but one patient (98.7%) of Group A (two patients who failed to swallow the capsule were withdrawn from the count) and for 169 (90%) of Group B. Oro-duodenal transit time was significantly higher in group A (mean 84.1 minutes, 95% CI: 51.7–116.6) than in group B (mean 32.6 minutes 95% CI: 24.3–41.1, t = 2.51, p = 0.013). Withdrawing from both groups the patients in whom the capsule failed to reach the duodenum, there were no differences in the completion rate of SBCE (Group A, 85%; Group B 91%; OR = 0.55, 95% CI: 0.24–1.29), and small bowel transit time did not differ between the two groups (Group A: 271.7 minutes, 95% CI: 250.5–292.9; Group B: 256.8 minutes, 95% CI: 242.4–271.3, t = 1.09, p = 0.27).

Two complications (one aspiration and one retention) were observed in Group A (2.5%) and one retention (0.5%) in Group B (OR = 4.8, 95% CI: 0.43–54.35, p = .19). The patient who inadvertently aspirated the capsule did not report any symptom either before and after capsule ingestion; the capsule dwelled into trachea until its expulsion 18 hours later by cough. Both capsule retentions (defined as failure to excrete naturally the capsule within 15 days after ingestion) were managed surgically, in election. The patient of Group A was an 81-year-old lady submitted to CE for chronic diarrhea and weight loss; CE disclosed a mid-ileal ulcerated stricture which was surgically resected; the pathological specimen was consistent with lymphoma. The patient of Group B was a 68-year-old lady with OGB of the occult type; CE showed a stenosing mass of the distal ileum, and ileal adenocarcinoma was found in the resected specimen. Capsule failures and complications are summarized in Table 3.

### Diagnostic Yield and Findings

There was no difference in the diagnostic yield of the two groups (72% in Group A vs 70.2% in Group B). In Group A, the following SB lesions were found: 24 patients (30.3%) had AVMs, 11 (13.9%) ulcers or erosions, 7 (8.8%) polyps, 5 (6.3%) submucosal masses, and 5 had lesions missed at previous panendoscopy (2 duodenal ulcer, 2 gastric bleeding from AVMs, and 1 right colon cancer).

### Table 1. Patients’ Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A (N = 79)</th>
<th>Group B (N = 188)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (M ± SD)</td>
<td>84 ± 6</td>
<td>44 ± 11</td>
<td>—</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Males (%)</td>
<td>35 (44)</td>
<td>98 (52)</td>
<td>0.73 (0.43–1.23)</td>
<td>.24</td>
</tr>
<tr>
<td>OGB (%)</td>
<td>75 (95)</td>
<td>169 (90)</td>
<td>2.1 (0.69–6.40)</td>
<td>.18</td>
</tr>
<tr>
<td>Unexplained diarrhea (%)</td>
<td>4 (5)</td>
<td>19 (10)</td>
<td>0.47 (0.15–1.44)</td>
<td>.18</td>
</tr>
<tr>
<td>Prokinetics (%)</td>
<td>10 (12.6)</td>
<td>28 (14.8)</td>
<td>0.82 (0.38–1.79)</td>
<td>.63</td>
</tr>
<tr>
<td>CCI* (M ± SD)</td>
<td>0.60 (1.14)</td>
<td>0.74 (1.21)</td>
<td>—</td>
<td>.27</td>
</tr>
<tr>
<td>Diabetes mellitus* (%)</td>
<td>10 (12.6)</td>
<td>15 (11.3)</td>
<td>1.13 (0.48–2.65)</td>
<td>.77</td>
</tr>
<tr>
<td>Previous abdominal surgery* (%)</td>
<td>12 (15)</td>
<td>12 (9)</td>
<td>1.79 (0.76–4.20)</td>
<td>.18</td>
</tr>
</tbody>
</table>

Notes: Group A, cases; Group B, controls. CCI = Charlson’s comorbidity index; CI = confidence interval; OGB = obscure gastrointestinal bleeding; OR = odds ratio.

*Data available only for 132 patients of Group B.

### Table 2. Small Bowel Capsule Endoscopy Performance and Findings in Cases (Group A) and Controls (Group B)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A, N = 79 (%)</th>
<th>Group B, N = 188 (%)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete SB evaluation</td>
<td>59 (74.6)</td>
<td>169 (89)</td>
<td>0.33 (0.16–0.66)</td>
<td>.0025</td>
</tr>
<tr>
<td>CE failure to reach duodenum</td>
<td>10 (12.6)</td>
<td>3 (1.5)</td>
<td>9 (2.4–33.4)</td>
<td>.0004</td>
</tr>
<tr>
<td>Adverse events</td>
<td>2 (2.5)</td>
<td>10 (0.5)</td>
<td>4.8 (0.43–54.35)</td>
<td>.19</td>
</tr>
<tr>
<td>Diagnostic yield</td>
<td>57 (72)</td>
<td>132 (70.2)</td>
<td>1.09 (0.61–1.96)</td>
<td>.75</td>
</tr>
<tr>
<td>Neoplastic lesions*</td>
<td>18 (22.7)</td>
<td>24 (12.7)</td>
<td>2.01 (1.02–3.97)</td>
<td>.04</td>
</tr>
<tr>
<td>Inflammatory lesions</td>
<td>11 (13.9)</td>
<td>11 (5.8)</td>
<td>2.60 (1.07–6.28)</td>
<td>.03</td>
</tr>
<tr>
<td>AVMs</td>
<td>24 (30.3)</td>
<td>77 (40.9)</td>
<td>0.62 (0.35–1.10)</td>
<td>.10</td>
</tr>
<tr>
<td>Missed lesions*</td>
<td>2 (2.5)</td>
<td>6 (3.1)</td>
<td>0.78 (0.15–3.99)</td>
<td>.77</td>
</tr>
<tr>
<td>Missed lesions²</td>
<td>5 (6.3)</td>
<td>14 (7.4)</td>
<td>0.83 (0.29–2.41)</td>
<td>.74</td>
</tr>
</tbody>
</table>

Notes: Some patients had more than one lesion. AVMs = arterovenous malformations; CE = capsule endoscopy; CI = confidence interval; OR = odds ratio; SB = small bowel.

*Includes one right colon cancer missed at prior colonoscopy (counted also under missed lesions).

²Includes: small bowel diverticula, worms, and celiac disease.

²Lesion located in the reach of conventional upper and lower endoscopy, missed at previous evaluation.
Including the right colon cancer missed at previous colonoscopy, 18 of 57 lesions disclosed by CE in Group A were neoplastic (31.5% of all lesions, 24% of patients) versus 24 of 132 lesions in Group B (18% of all lesions, 12.7% of patients; OR = 2.01, 95% CI: 1.02–3.97, p = .04). Finally, we found a prevalence of inflammatory lesions in Group A (OR = 2.6, 95% CI: 1.07–6.28, p = .03). No difference for missed and miscellaneous lesions was found between the two groups (Table 2).

### DISCUSSION

In Western countries, the mean age is steadily increasing, resulting in a higher burden for the Health Service. Clinical pictures, such as unexplained anemia and OGB, conditions that deserve endoscopic evaluation (20) and are best investigated by SBCE, are common in elderly patients. (14,21,22).

Our results show, for the first time, that more than a few octogenarians (12.6% of our series) have SBCE failures, mainly for unexpected abnormalities of the foregut motility. In fact, SBCE failure occurred more frequently in octogenarians than in younger controls and in patients reported in previous published series. Rondonotti and co-workers (6) found a capsule failure to enter in duodenum in only 2.34% of their unselected 735 patients. Interestingly, the main difference with controls in reaching the duodenum was due to prolonged esophageal transit time of the capsule. This fact is in accordance with the report of Wong and co-workers (23) who found this problem in 5 of 95 SBCE, and old age was the only statistically significant risk factor among those they sought.

Swallowing difficulties are present in up to 15% of elderly people and are generally asymptomatic (24). Presbyesophagus—a poorly understood abnormality of esophageal motor function due to less effective secondary peristalsis of elderly people (25)—and slow gastric emptying (26) may be responsible for SBCE failure observed in most of our patients. Capsule aspiration, a previously described complication of CE (6,27–29), may cause life-threatening acute respiratory distress if the capsule dwells into a principal bronchus (30). Fortunately, the patient who experienced this complication was asymptomatic, probably because the capsule jigged for several hours above the tracheal carina until its expulsion by cough.

Our results are in contrast with those of Papadopulos and co-workers (13), who failed to prove any age-related failure of SBCE in their prospective study, possibly for three reasons. First, the oldest group they investigated was composed of 52 patients more than 65 years old (range 65–92), but the true number of octogenarians is unavailable from their paper; second, the younger patients of their study underwent SBCE mainly for chronic unexplained diarrhea and suspect Crohn’s disease—a condition associated with a lower chance of SBCE completeness due to capsule retention (31)—in comparison with the oldest group who was mostly investigated for OGB; last, patients having conditions which interfere with gastrointestinal motility, such as diabetes mellitus, previous abdominal surgery, chronic renal failure, use of antispasmodics, antidepressants, and narcotics, were excluded from their study.

In accordance with other reports, we found that the main reason for incomplete SB examination is the prolonged capsule staying in a tract proximal to the pylorus (7–13). Hospitalization, type 2 diabetes mellitus, and previous abdominal surgery are known conditions associated with incomplete SB examination. Prokinetics (32) and chewing gum (33) prior to the procedure have been advocated to overcome these drawbacks, but there are no double-blind randomized trials to prove their effectiveness, and a recent single-blind prospective trial of metoclopramide was disappointing (34). Concerning the other risk factors, our control group of younger patients was well matched not only for gender and clinical indication to SBCE but also for diabetes mellitus, previous abdominal surgery, and comorbidity, suggesting that aging may be a genuine risk factor for SBCE failure.

Although adverse events were more common in cases than controls (2.5% vs 0.5%), they were too infrequent to find any statistical significance within this sample size, and their cumulative occurrence was consistent with that reported in larger series (3).

With regard to the diagnostic yield and findings, we did not find any difference between octogenarians and controls. However, octogenarians presented a higher rate of neoplastic

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**Table 3. Details of Capsule Failures and Adverse Events Occurred in Both Cases and Controls**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Symptoms</th>
<th>Capsule Excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failures</td>
<td>9</td>
<td>3</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Inability to swallow</td>
<td>1</td>
<td>0</td>
<td>No</td>
<td>Natural</td>
</tr>
<tr>
<td>Prolonged esophageal staying</td>
<td>4</td>
<td>0</td>
<td>No</td>
<td>Natural</td>
</tr>
<tr>
<td>Prolonged gastric staying</td>
<td>4</td>
<td>3</td>
<td>No</td>
<td>Natural</td>
</tr>
<tr>
<td>Adverse events</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspiration</td>
<td>1</td>
<td>0</td>
<td>No</td>
<td>By cough, 18 h later</td>
</tr>
<tr>
<td>Small bowel retention</td>
<td>1</td>
<td>1</td>
<td>No</td>
<td>Elective surgical removal</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: NA = not applicable.*
and inflammatory SB lesions, the last probably reflecting ischemic changes and/or drug-induced damage. Aspirin and nonsteroidal anti-inflammatory drugs are associated to a variety of enteric injuries (35,36), and their consumption is widespread in older people (37). Unfortunately, we had insufficient historical data about drug use in both cases and controls to perform further analysis. Near one fourth of our cases had neoplasia, and including the patient with right colon adenocarcinoma missed at a previous colonoscopy, this figure was higher than younger controls. However, the rate of neoplasia we found is higher than that reported by others (38–41), probably for the following reasons. First, we included under the term “neoplasia” findings of submucosal mass with erythematous or erosive changes (ie, not fulfilling the proposed diagnostic criteria for bulge (42)), and polyps with benign appearance and, in contrast to the quoted series, only a few were histologically proven. Second, North Italy is the geographic area with the highest incidence of cancer in our country (43), and finally, the Aviano’s Department is a structure afferent to an oncologic referral center. These issues suggest an overestimation of SB neoplasms in the present series due to selection bias.

Furthermore, we failed to find a higher proportion of AVMs in elderly patients, as reported before the advent of SBCE (16), implying that the new endoscopic techniques (both SBCE and device-assisted enteroscopy), available from the beginning of the new century, might really change the epidemiology of SB diseases and the clinical approach to their most common presentation, that is, OGB and unexplained anemia.

There are some limitations to our study. It is retrospective, and as previously stated, all patients were hospitalized, and there may have been a selection bias due to the participation of an oncologic referral center. Again, incomplete collection of data of control group comorbidity, and transit times (available in 70.2% and 90%, respectively) may have biased the results reducing the goodness of case–control matching. Last, histological confirmation of neoplastic lesions found by CE was not available in the present study, lessening the strength of our conclusions. On the other hand, some hints can be drawn from our results. The frequency of swallowing and forget motility impairment in elderly patients, it may be advisable to perform SBCE after a careful clinical assessment to identify patients with dysphagia and swallowing difficulty. In these patients, endoscopic capsule delivery by the recently Food and Drug Administration-approved device AdvanCE (44) may be considered.

In conclusion, our study showed that SBCE may be troublesome in octogenarians for capsule failure to reach the duodenum. However, the diagnostic yield of SBCE and the rate of clinically significant lesions and neoplasia are high.

ROLES OF AUTHORS
G.C.M.: study concept and design; data collection, data analysis, and drafting of manuscript.
M.S.: data collection, critical revision of manuscript.
P.P.: data collection, critical revision of manuscript.
C.R.: study concept and design, critical revision of manuscript, and study supervision.

CONFLICT OF INTEREST
No conflict of interest declared by the authors.

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