Push enteroscopy for gastrointestinal bleeding
Diagnostic yield and long-term follow-up

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SUMMARY
Aim — Little is known about the long-term course of patients explored by push enteroscopy for gastrointestinal bleeding of obscure origin. This study aimed to determine the diagnostic yield and the therapeutic impact of enteroscopy, the rate of rebleeding and predictive factors of rebleeding in these patients.

Patients and methods — One hundred nineteen patients underwent push enteroscopy for overt bleeding (N = 66) or anemia (N = 53).

Results — Enteroscopy was positive in 42% of patients (colon 17%, stomach 13%, small bowel 12%) and diagnosed arteriovenous malformations in two-thirds of patients. Twenty-five additional diagnoses were established during the 2-month follow-up. Treatment was definitive in 13% of patients, without recurrent bleeding. Rebleeding occurred in 45% of patients, and was more frequent when a lesion was visualized (73% vs 28% after 5 years, P = 0.02).

In multivariate analysis, a lesion visualized by enteroscopy was the only independent predictive factor.

Conclusion — Enteroscopy is not a high-performance diagnostic tool for obscure gastrointestinal bleeding and enables definitive treatment in less than 15% of patients.

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RÉSUMÉ
Entéroscopie poussée par double voie pour saignement digestif. Résultats immédiats et suivi à moyen terme
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Objectif — Le suivi des malades explorés par entéroscopie pour saignement digestif a été peu évalué. Les buts de l’étude étaient d’évaluer les résultats, l’impact thérapeutique, le taux de récidive et de rechercher des facteurs prédictifs de récidive chez ces malades.

Malades et méthodes — 119 patients ont eu une entéroscopie poussée pour hémorragie (N = 66) ou anémie (N = 53).

Résultats — Une lésion a été diagnostiquée (2/3 de malformations artério-veineuses) dans 42% des cas (estomac 13%, côlon 17%, grêle 12%). Le suivi sur 29 mois a permis 25 diagnostics supplémentaires. Le traitement de la lésion a été définitif chez 13% des malades. Une récidive est survenue chez 45% des malades. Elle était moins fréquente en l’absence de lésion (28% vs 73% à 5 ans, P = 0.02). Aucun autre facteur prédictif indépendant de récidive n’a été identifié.

Conclusions — L’entéroscopie pour saignement digestif a un rendement diagnostique modeste, et moins de 15 % des lésions sont traitées de façon définitive.

Introduction

The diagnostic and therapeutic potential of enteroscopy has been suggested since the seventies, particularly when searching for a cause of unexplained digestive bleeding by gastroscopy and complete colonoscopy [1-8]. There are however only a small number of studies in the literature designed to assess the real impact of enteroscopy results, and their findings have been rather contradictory [3, 7, 9-12]. In 1998, Landi et al. found that push enteroscopy is useful for gastrointestinal bleeding but contributes little to the search for a cause of iron deficiency [3]. Inversely, in 2000, Sharma et al. demonstrated that enteroscopy is useful when searching for occult bleeding [7].

Five studies have analyzed the outcome of patients after enteroscopic exploration for overt or occult gastrointestinal bleeding [9, 11, 13-15]. Some studies found that the risk of rebleeding is lower after enteroscopy [15], that the need for transfusion is lower if a lesion was identified and treated [11, 15], that later hospital stays are shorter [11], and that prolonged anemia correction can be achieved in certain patients after endoscopic treatment of vascular malformations [9, 14]. Unfortunately, all of these studies involved a small number of patients and lead to discordant conclusions.

We wanted to ascertain what information is provided by this diagnostic method and its usefulness in patients undergoing enteroscopic exploration for gastrointestinal bleeding at the Nantes University Hospital gastroenterology unit between February 1996 and March 2002. The purpose of this study was to determine a) the diagnostic yield of push enteroscopy, b) its impact on patient management, c) the rate of mid-term recurrence, and d) what factors could be predictive of rebleeding.

Patients and methods

Patients

Between February 1996 and March 2002, 119 patients (71 men and 48 women, mean age 58 years, age range 15-88 years) were referred to our unit for enteroscopic exploration of gastrointestinal bleeding. Indications were overt bleeding (N = 66, melena 55, proctorrhagia 11) or anemia (hemoglobin < 12 g/L) in 53 patients. The current episode was the first for 62%. Mean time between discovery of anemia and enteroscopy was 16 months (range 2 days-16 years).
Methods

ENTEROSCOPY

The procedures were performed in the fasting state. Patients were asked not to smoke before the procedure. No preparation was used for upper enteroscopic procedures. For lower or potentially upper and lower procedures, a polyethylene glycol (PEG) solution was used according to the usual modalities for colonoscopy. The procedure was performed under general anesthesia in an operating room equipped with a radioscope. The patient was intubated and was generally placed in the lateral recumbent position (the dorsal position was preferred by some operators). Push enteroscopy was performed with a 2180 mm long 10.9 mm diameter Olympus SIF 100 (Hamburg, Germany). The esophageal and gastric mucosa was examined when descending the enteroscope in order to avoid misinterpreting any injury caused by inserting the overtube which was generally positioned, under radioscopic guidance, in the second duodenum. The small bowel mucosa was examined during progression and during withdrawal of the overtube. An overtube was not used for lower enteroscopy. Rotation-derotation movements were employed to facilitate progression, pushing the enteroscope as far as possible into the small bowel. The exploration was generally performed by a single operator, an assistant maintaining, as needed, loops identified on the radioscope. Drugs usually used for colonoscopy were employed. Drugs affecting bowel transit were not used, before or during the exploration. When upper and lower enteroscopy were performed, the lower procedure was performed immediately after the upper procedure during the same anesthesia. Explorations were redone, at least during the early learning phase, to enable secondary examinations at a slower speed if necessary.

Expression and analysis of results

For upper enteroscopy, the length of bowel explored was determined empirically by radioscopy, by measuring directly on the monitor or by using the number of loops explored. The length of the duodenum (considered as an integral part of the small bowel) was considered to be 40 cm to the Treitz angle. Each bowel loop explored was considered to measure 30 cm. The length of ileum visualized was estimated either radioscopically or, more often endoscopically by measuring the withdrawal distance to the Bauhin valve.

Variables analyzed were: duration of the endoscopic procedure, length of bowel explored, results, tolerance, and immediate complications. The influence of enteroscopy results on later management was determined by considering the medical files, nurses charts, and hospital discharge, endoscopy and anesthesia reports.

Patients were classed into three groups according to the enteroscopy results: no lesion (group A), arteriovenous malformation (group B), other lesion (group C). A patient was considered to have no lesion (group A) if no lesion was visualized or if a visualized lesion could not explain gastrointestinal bleeding (including less than 5 arteriovenous malformations or malformations measuring ≤ 3 mm). Patients were considered to have arteriovenous malformations (group B) if 5 or more lesions were visualized or if the lesions were found at several levels and/or if presence of the endoscope triggered bleeding. Treatments given during the enteroscopy procedure or immediately after the procedure were considered "medically treatment" when iron supplementation or estrogen-progestogens treatment was given and "specific treatment" when endoscopic or surgical treatment was given. Argon plasma treatments (0.5 L min⁻¹) were initiated in 1999.

Table I. – Main features of the 119 patients explored by enteroscopy for overt bleeding or anemia.

<table>
<thead>
<tr>
<th></th>
<th>Anemia (N = 53)</th>
<th>Bleeding (N = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male</td>
<td>25/28</td>
<td>23/43</td>
</tr>
<tr>
<td>Age (range), years</td>
<td>55 (17-84)</td>
<td>60 (15-88)</td>
</tr>
<tr>
<td>Hemoglobin (N*SD), g/dL</td>
<td>8.0 ± 2.4</td>
<td>7.5 ± 2.4</td>
</tr>
<tr>
<td>Packed red cell units (N, range)</td>
<td>8 (2-65)</td>
<td>10 (2-48)</td>
</tr>
<tr>
<td>Patients (N) given:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>— NSAID</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>— aspirin or antiaggregates</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>— anticoagulants</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Explorations before enteroscopy: N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>— gastroscopy a</td>
<td>53 (100)</td>
<td>65 (98)</td>
</tr>
<tr>
<td>— colonoscopy b</td>
<td>48 (90)</td>
<td>61 (92)</td>
</tr>
<tr>
<td>— abdominal ultrasound</td>
<td>18 (34)</td>
<td>19 (29)</td>
</tr>
<tr>
<td>— abdominal computed tomography</td>
<td>7 (13)</td>
<td>16 (24)</td>
</tr>
<tr>
<td>— small bowel transit study</td>
<td>32 (60)</td>
<td>27 (41)</td>
</tr>
<tr>
<td>— gastrointestinal arteriography</td>
<td>0 (0)</td>
<td>8 (12)</td>
</tr>
<tr>
<td>— barium enema</td>
<td>4 (7)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>— gynecological examination</td>
<td>11 (20)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>— myelogram</td>
<td>4 (7)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

a gastroscopy repeated 2 to 4 times in 4 patients in the anemia group and in 24 patients in the bleeding group
b colonoscopy was repeated 2 to 3 times in 2 patients in the anemia group and in 14 patients in the bleeding group
**Mid-term follow-up**

In order to determine the impact of the enteroscopy results on outcome, a questionnaire was sent to each patient by mail (with a phone reminder if necessary). This 9-item questionnaire was designed to analyze the definitive diagnosis established at enteroscopy or later, surgical interventions, bowel morphology explorations, treatments given after enteroscopy, the number of later hospital stays, rebleeding or anemia and time to occurrence after enteroscopy, the number of packed red cell units administered, and serum hemoglobin. Recurrent anemia was defined as serum hemoglobin < 12 g/dL at a control test irrespective of whether iron supplementation had been given or not.

**Statistical analysis**

Actuarial curves of recurrent bleeding or anemia were established with the Kaplan-Meier method and compared with the Mantel-Cox log-rank test. Univariate and multivariate analyses were used to search for factors predictive of recurrent bleeding. Variables tested were age, sex, hemoglobin level, number of episodes of anemia or bleeding before enteroscopy, duration of symptoms at the time of enteroscopy, number of packed cell units administered, NSAID treatment, anti-aggregate or anti-coagulation treatment, and type of initial bleeding (occult disclosed by anemia or overt). Statistical significance of univariate analysis was tested with the chi-square method for qualitative variables and Student's t test for quantitative variables. Logistic regression was used for multivariate analysis (Statview). P < 0.05 was considered significant.

**Results**

**Enteroscopy results**

None of the procedures enabled exploration of the entire length of the small bowel. Mean length explored (± SD) with upper enteroscopy was 130 ± 45 cm during a procedure which lasted, on average, 40 ± 17 minutes. When the valve was crossed, the mean length of ileum explored was 50 ± 30 cm, for a mean procedure duration of 40 ± 17 minutes. Tolerance was good. Undesirable effects were noted for 21 patients (18%) and were always minor. No complications were recorded. All upper enteroscopic procedures were successful. Seventeen lower enteroscopies (14%) were considered unsuccessful: Bauhin valve not crossed (N = 15), enteroscope dysfunction (N = 1), stenosing cancer of the transverse colon (N = 1).

Enteroscopy identified a lesion potentially responsible for the anemia/bleeding in 42% of patients. The identified lesion was accessible to a standard endoscope in 30% (colonoscope for 17% and gastroscopy for 13%) and was inaccessible other than by enteroscopy in 12%. These results were not different by type of indication for enteroscopy (P = NS). Arteriovenous malformations were recognized in 33 of the 50 identified lesions (66%) (table II).

**Mid-term outcome**

Reliable follow-up data were available for 117 patients (2 patients without enteroscopic lesion lost to follow-up). Median follow-up was 29 months (range 2-77).

Fifty-three of the 117 patients (45%) experienced rebleeding, 36 (30%) with the same signs as initially. Rebleeding was noted in 17 of the 32 patients (53%) given specific treatment (endoscopic 25, surgical 7), and in 36 of the 85 patients (42%) given medical treatment (iron supplementation). The risk of rebleeding was not significantly different between medical and specific treatment, irrespective of the initial symptom (P = 0.89). Enteroscopy provided a direct benefit for 15 patients by enabling definitive treatment (figure 1).

In group A (N = 67 patients with no identified lesion), rebleeding was noted in 23 (34%). An etiological diagnosis was established during follow-up for 25 patients. In group B (N = 33 patients with arteriovenous malformations), rebleed-

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Table II. – Lesions diagnosed by enteroscopy in 119 patients (number and percentage).

<table>
<thead>
<tr>
<th>Gastric or colonic lesions a</th>
<th>Small bowel lesions b</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 (30)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>— AVM a</td>
<td>24</td>
</tr>
<tr>
<td>— AVM d</td>
<td></td>
</tr>
<tr>
<td>— erosive gastritis</td>
<td>2</td>
</tr>
<tr>
<td>— portal hypertensive gastropathy</td>
<td>2</td>
</tr>
<tr>
<td>— fundus ulcer</td>
<td>2</td>
</tr>
<tr>
<td>— duodenal ulcer</td>
<td>2</td>
</tr>
<tr>
<td>— colon cancer</td>
<td>1</td>
</tr>
<tr>
<td>— colonic diverticulosis</td>
<td>1</td>
</tr>
<tr>
<td>— ischemic colitis</td>
<td>1</td>
</tr>
<tr>
<td>— hemorrhoids</td>
<td>1</td>
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<tr>
<td>— ileal varice</td>
<td>1</td>
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</tbody>
</table>

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*positive: detection of a possible cause of anemia or digestive bleeding

a lesion situated above the 2nd duodenum or in the ileum less than 10 cm from the Bauhin valve and theoretically inaccessible to gastroscopy or colonoscopy.

b lesion situated beyond the 2nd duodenum or in the ileum more than 10 cm from the Bauhin valve and theoretically inaccessible to gastroscopy or colonoscopy.

c arteriovenous malformations situated above the 2nd duodenum and accessible to gastroscopy or situated in the colon or close to the Bauhin valve in the ileum and accessible to colonoscopy.

d arteriovenous malformations situated beyond the 2nd duodenum or too far from the Bauhin valve to be accessible to gastroscopy or colonoscopy.
ing was noted in 20 (60%). In group C (N = 17 patients with another lesion), rebleeding was noted in 9 (53%). The overall rate of rebleeding was 34% when the enteroscopic exploration was considered normal and 58% when a lesion was identified. The type of lesion identified had no effect on the number of packed red cell units administered (P = 0.50) nor on the number of hospital stays during subsequent follow-up (P = 0.69), irrespective of treatment modality (medical or specific).

Univariate analysis showed that the following variables were correlated with recurrent bleeding: age > 65 years at the time of enteroscopy (P = 0.03), more than 3 packed red cell units administered before upper enteroscopy (P = 0.03), and identification of a lesion at enteroscopy (P = 0.0003). The results of the univariate analysis are presented in table III.

Recurrence by final diagnosis

Definitive diagnoses established during the follow-up were used to determine the actuarial death and rebleeding rates. Based on these diagnoses, the number of patients in groups A, B, and C were 42, 39, and 36 respectively. The 6-month actuarial rebleeding rate was 26%, 23%, and 14% in the three groups respectively. The corresponding 1- and 5-year rebleeding rates were 28%, 54%, 59% and 28%, 72%, 67% respectively. Recurrence was significantly more frequent when a lesion was identified at enteroscopy (P = 0.02) (figure 2). In multivariate analysis, identification of a lesion was the only factor predictive of recurrence.

The results of the initial enteroscopy had no influence on death rate (figure 3). After 4 years follow-up, death rate tended
to be higher in the group of patients with arteriovenous malformations, but the difference did not reach statistical significance (P = 0.78). This trend might be related to age since mean age in patients with an arteriovenous malformation (62 years) was higher than in the two other groups (56 years, P = 0.57).

**Discussion**

In our patients, pushed enteroscopy provided a positive diagnosis in 42% of patients. This is within the range reported in the literature (30-75%) [1-8]. In the two largest series published (105 and 78 patients), diagnostic yield of push enteroscopy for gastrointestinal bleeding was 44% and 50% [12, 13]. The yield in our slightly larger series of 119 consecutive patients probably reflects the general yield that can be expected in a routine clinical setting. Two-thirds of the diagnosed lesions were arteriovenous malformations, irrespective of the initial symptom (anemia or bleeding). About one-third of the lesions were accessible to colonoscopy (17%) or gastroscopy (13%), so the diagnostic yield of enteroscopy per se falls to 12%. In the two earlier studies [12, 13] the real diagnostic yield of enteroscopy was 15 and 32%. The rate of unrecognized lesions during primary standard endoscopy varies widely, from 20 -75% depending on the series [8, 9, 12]. All of our patients had undergone at least gastroscopy before the enteroscopic procedure and 90% of them had also had a colonoscopy. These data demonstrate the importance of repeating standard endoscopic procedures before opting for push enteroscopy. Future development of high-resolution

| Table III. – Predictive factors for recurrent bleeding according to univariate analysis.  
Facteurs prédictifs de récidive hémorragique en analyse univariée. |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Absence of rebleeding</strong></td>
</tr>
<tr>
<td>Sex M/F</td>
</tr>
<tr>
<td>Age, years (* SD)</td>
</tr>
<tr>
<td>Hemoglobin, g/dL (* SD)</td>
</tr>
<tr>
<td>Number of bleeding episodes, N (* SD)</td>
</tr>
<tr>
<td>Disease duration, months (* SD)</td>
</tr>
<tr>
<td>Packed red cell units*, N (* SD)</td>
</tr>
<tr>
<td>NSAID, anti-aggregant, anticoagulation, yes/no</td>
</tr>
<tr>
<td>Initial anemia/bleeding</td>
</tr>
<tr>
<td>Lesion/No lesion</td>
</tr>
</tbody>
</table>

* before enteroscopy.  
NSAID = nonsteroidal anti-inflammatory drug

in our slightly larger series of 119 consecutive patients probably reflects the general yield that can be expected in a routine clinical setting. Two-thirds of the diagnosed lesions were arteriovenous malformations, irrespective of the initial symptom (anemia or bleeding). About one-third of the lesions were accessible to colonoscopy (17%) or gastroscopy (13%), so the diagnostic yield of enteroscopy per se falls to 12%. In the two earlier studies [12, 13] the real diagnostic yield of enteroscopy was 15 and 32%. The rate of unrecognized lesions during primary standard endoscopy varies widely, from 20 -75% depending on the series [8, 9, 12]. All of our patients had undergone at least gastroscopy before the enteroscopic procedure and 90% of them had also had a colonoscopy. These data demonstrate the importance of repeating standard endoscopic procedures before opting for push enteroscopy. Future development of high-resolution

Fig. 2 – Actuarial rate of rebleeding according to the follow-up findings.  
Group A: no lesion (n = 42) (---).  
Group B: arteriovenous malformation (n = 39) (—).  
Group C: other lesion (n = 33) (AAAAA).  
Taux actuariels de survie sans récidive en fonction des données du suivi.  
Groupe A : absence de lésion (n = 42) (---).  
Groupe B : malformation artério-veineuse (n = 39) (—).  
Groupe C : autre lésion (n = 33) (AAAAA).

Patient survival

Fig. 3 – Actuarial rate of survival according to the follow-up findings.  
Group A: no lesion (n = 42) (---).  
Group B: arteriovenous malformation (n = 39) (—).  
Group C: other lesion (n = 33) (AAAAA).  
Taux actuariels de survie en fonction des données du suivi.  
Groupe A : absence de lésion (n = 42) (---).  
Groupe B : malformation artério-veineuse (n = 39) (—).  
Groupe C : autre lésion (n = 36) (AAAAA).
endoscopes should further accentuate this point. High-resolution colonoscopy with systematic ileoscopy will probably replace lower enteroscopy for most indications.

The real diagnostic yield of push enteroscopy is thus modest at best. This is a long procedure (nearly an hour and a half if both upper and lower procedures are performed) and requires prolonged general anesthesia. Moreover, enteroscopy results have only a modest impact on post-procedure patient management. Only 13% of our patients, who were given specific and definitive treatment of an identified lesion and who did not experience rebleeding, acquired direct benefit from enteroscopy. Push enteroscopy remains however a low-risk procedure, which, in our hands, has never caused any complications.

The overall rate of rebleeding was 45% at 29 months. Most of these episodes were observed early, on average within 7 months. Enteroscopy results appeared to be relatively predictive of rebleeding. When enteroscopy failed to identify any lesion, recurrence was 2-fold less frequent than when arteriovenous malformations were found. At three years, the risk of rebleeding was 54% for patients with an identified arteriovenous malformation and 28% for those without. At five years the rates were 72% and 28%, and were statistically different (P = 0.02). These concordant results reinforce the non-statistically significant difference reported by Landi et al. (25% vs 56% at 2 years) [13].

In our experience, endoscopic treatment of arteriovenous malformations does not appear to affect the rate of rebleeding. Although the majority of our patients were given iron supplementation, specific treatment of individual lesions did not reduce the need for transfusion nor affect the number of hospitalizations needed during follow-up. The therapeutic efficacy of endoscopic or hormonal treatment of visualized arteriovenous malformations remains controversial [16, 17]. Certain authors have found that transfusion needs decline after endoscopic treatment of visualized lesions [10-15] and Adrain et al. [10] also concluded that it can significantly limit the number of hospital stays needed later for gastrointestinal bleeding. Our findings are not in agreement with this conclusion. Multicentric prospective studies applying a standardized treatment for arteriovenous malformations would be needed to come to a definitive conclusion.

Gastrointestinal arteriography or intra-operative enteroscopy has been proposed for patients presenting abundant life-threatening gastrointestinal bleeding. The development of the endoscopic capsule is currently changing the role of enteroscopy in the management of unexplained gastrointestinal bleeding [18]. In the future, enteroscopy will undoubtedly be reserved for patients who have a lesion accessible only to enteroscopic treatment identified by the endoscopic capsule. Unlike Landi et al. [13] we were unable to establish a specific profile of patients at risk of rebleeding. These authors demonstrated that a large number of hemorrhagic episodes before enteroscopy and need for a significant number of packed red cell units were two independent factors predictive of recurrent bleeding. In our series, need for more than 3 packed red cell units and age over 65 years appeared to predict recurrence at multivariate analysis was the presence of an enteroscopically identified lesion.

Our retrospective results could be usefully detailed with a prospective study designed to better analyze the impact of enteroscopy results on patient management for gastrointestinal bleeding. Such a study should use standard treatments and follow-up in a larger number of consecutive patients, and ideally be conducted in a multicentric setting.

In conclusion, the diagnostic yield of enteroscopy is modest for patients with unexplained gastrointestinal bleeding. Thirty percent of the lesions identified in our series were accessible to a standard endoscope, emphasizing the importance of repeating these procedures. Treatment of identified lesions should be re-evaluated. In our experience, endoscopic or surgical treatment of an identified lesion does not provide better results than symptomatic iron supplementation and does not allow any improvement in transfusion needs nor in the number of future hospitalizations. In our overall population, enteroscopy had a direct positive impact for less than 15% of patients who were given adapted treatment and did not experience future recurrence. We were unable to identify any particular type of patient particularly at risk of rebleeding. The role of enteroscopic procedures should be re-examined in light of data provided with the development of the endoscopic capsule.

REFERENCES